



ELSEVIER

International Journal of Psychophysiology 42 (2001) 123–146

---

---

INTERNATIONAL  
JOURNAL OF  
PSYCHOPHYSIOLOGY

---

---

www.elsevier.com/locate/ijpsycho

# The polyvagal theory: phylogenetic substrates of a social nervous system

Stephen W. Porges

*Department of Psychiatry, University of Illinois at Chicago, 1601 W. Taylor Street, Chicago, IL 60612-7327, USA*

Received 16 October 2000; received in revised form 15 January 2001; accepted 22 January 2001

---

## Abstract

The evolution of the autonomic nervous system provides an organizing principle to interpret the adaptive significance of physiological responses in promoting social behavior. According to the polyvagal theory, the well-documented phylogenetic shift in neural regulation of the autonomic nervous system passes through three global stages, each with an associated behavioral strategy. The first stage is characterized by a primitive unmyelinated visceral vagus that fosters digestion and responds to threat by depressing metabolic activity. Behaviorally, the first stage is associated with immobilization behaviors. The second stage is characterized by the sympathetic nervous system that is capable of increasing metabolic output and inhibiting the visceral vagus to foster mobilization behaviors necessary for ‘fight or flight’. The third stage, unique to mammals, is characterized by a myelinated vagus that can rapidly regulate cardiac output to foster engagement and disengagement with the environment. The mammalian vagus is neuroanatomically linked to the cranial nerves that regulate social engagement via facial expression and vocalization. As the autonomic nervous system changed through the process of evolution, so did the interplay between the autonomic nervous system and the other physiological systems that respond to stress, including the cortex, the hypothalamic–pituitary–adrenal axis, the neuropeptides of oxytocin and vasopressin, and the immune system. From this phylogenetic orientation, the polyvagal theory proposes a biological basis for social behavior and an intervention strategy to enhance positive social behavior. © 2001 Elsevier Science B.V. All rights reserved.

*Keywords:* Vagus; Respiratory sinus arrhythmia; Evolution; Autonomic nervous system; Cortisol; Oxytocin; Vasopressin; Polyvagal theory; Social behavior

---

## 1. Introduction

Embedded in the mammalian nervous system are neuroanatomical structures related to the ex-

pression and experience of social and emotional behavior. Several of these structures are shared with other vertebrates and represent the product of phylogenetic development. Comparative re-

search across vertebrate classes provides evidence that mammalian stress and coping response strategies are hierarchically ordered according to a phylogenetic stage (Porges, 1997, 1998). Although research has demonstrated the relevance of neuroanatomical structures and neurophysiological processes to the expression of emotion and the regulation of social behavior, contemporary theories have not incorporated an ‘evolution’ perspective.

## 2. Evolution as an organizing principle

Evolutionary forces have molded both contemporary physiology and behavior. The mammalian nervous system is a product of evolution. Via evolutionary processes, the mammalian nervous system has emerged with specific 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 potentials. We can intuitively grasp the limitations of behavior when described in terms such as dexterity, speed and strength. However, we have difficulties when the limitations are manifested in the neural regulation of physiological state. The regulation of visceral state is an important substrate of behavior that has been both a product of and contributor to our evolutionary adaptive success. The phylogeny of vertebrates illustrates a progressive increase in the complexity of the neural mechanisms available to regulate neurobehavioral state to deal with the challenges along a continuum, defined by survival on one end, and positive social-emotional experiences on the other.

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 chal-

lenge. This knowledge of how the mammalian nervous system changes neurobehavioral states to adapt to challenge provides us with an opportunity to design living environments, which may foster both the expression of positive social behavior and physical health.

## 3. The social engagement system

Through stages of phylogeny mammals and especially primates have evolved a functional neural organization that regulates visceral state to support social behavior. A social engagement system, which focuses only on the neural regulation of the striated muscles of the face and head and the specific autonomic functions mediated by the myelinated vagus, has been proposed as part of a more global social nervous system. Although other neural systems and behaviors are involved in social behavior, such as signaling with trunk and limbs, the proposed social engagement system is conceptualized to emphasize a system that has a common neural substrate composed of several cranial nerves that develop embryologically together (see Porges, 1998).

The social engagement system has a control component in the cortex (upper motor neurons) that regulates brainstem nuclei (i.e. lower motor neurons controlling special visceral efferent pathways) to control: eyelid opening (e.g. looking); facial muscles (e.g. emotional expression); middle-ear muscles (e.g. extracting human voice from background noise); muscles 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 both regulate social engagement and modulate the sensory features of the environment. The neural control of these muscles contributes to the richness of both social expressions and social experiences. Important to a psychophysiological perspective, the source nuclei of these nerves located in the brainstem communicate directly with the visceromotor portion of the nucleus ambiguus. Functionally, the visceromotor portion of the nucleus ambiguus provides the source nuclei for an inhibitory com-

ponent of the autonomic nervous system, which communicates via the myelinated vagal efferents to target peripheral organs, including the sinoatrial node. This inhibitory system promotes calm states consistent with the metabolic demands of growth and restoration by slowing heart rate, lowering blood pressure, and inhibiting sympathetic activation at the level of the heart.

The social engagement system is intimately related to stress reactivity. In addition, the anatomical structures involved in the social engagement system have neurophysiological interactions with the hypothalamic–pituitary–adrenal (HPA) axis, the neuropeptides of oxytocin and vasopressin, and the immune system. Thus, the social nervous system provides a theoretical model to explain the interactive and stress-related functions of several physiological systems that have central regulatory components, but are expressed in the periphery.

The social nervous system functions from birth and rapidly develops to support communication with the environment. For example, when a healthy infant encounters the caregiver's face, the infant will attempt to engage via facial expression and vocalizations. The infant may use vocalizations (cry) and facial expressions (grimace) to signal negative states to the caregiver. Or, to signal more positive states, a wide-eyed, smiling infant would attempt to elicit positive vocalizations and smiles from the caregiver. Even in the young infant, the social engagement system expects face-to-face interactions, with contingent facial expressions and vocalizations. Studies (e.g. Bazhenova et al., in press) have demonstrated that when the face of the caregiver is not responsive, the infant will initially attempt to socially engage the caregiver with display behaviors (e.g. vocalizations, facial expressions). If the infant is unsuccessful in engaging the caregiver, the infant will become agitated and may, in the case of having a depressed mother, exhibit symptoms of depression.

#### **4. Neurophysiology of stress: limitations of arousal theory**

For over a century, researchers have measured

autonomic variables (e.g. heart rate, palmar sweat-gland activity) as indicators of emotional state related to perceived stress (e.g. fear, mental effort, workload, anxiety). Interest in measuring heart rate and sweat gland activity was theoretically supported by acceptance of the arousal theory. Arousal theory made the assumption that peripheral physiological measures regulated by the sympathetic branch of the autonomic nervous system provided sensitive indicators of brain arousal or activation. This view was based on a rudimentary understanding of the autonomic nervous system, in which changes in easily measured peripheral organs (e.g. sweat glands, heart) were assumed to be accurate indicators of how the brain is processing emotional stimuli. Usually, the emotional states were associated with fight–flight behaviors and the sympathetic-adrenal system (e.g. increases in heart rate, sweat gland activity, and circulating catecholamines) as described by Cannon (1928). The current emphasis on cortisol as a dependent variable in stress research is consistent with historical views of stress-related arousal involving the adrenal gland.

Such measures, due in part to their availability and their neuroanatomical association with the target organs of the sympathetic nervous system (sweat glands, heart rate) and with secretions from the adrenal medulla (epinephrine and norepinephrine) and the adrenal cortex (cortisol), have become the primary variables used to assess physiological reactivity. Not by plan, but by default, an arousal-theory emphasis created a research environment that minimized the importance of neurophysiological processes (e.g. feedback) and neuroanatomical structures (e.g. brain) in the regulation of autonomic function. Thus, there was little interest in several important research questions, including evolution of the neuroregulation of autonomic function and how the autonomic nervous system interacted with the immune system, the HPA axis, and the neuropeptides, oxytocin and vasopressin.

An emphasis on a global construct of 'arousal' still abides within various sub-disciplines of psychology, psychiatry and physiology. This outdated view of 'arousal' may restrict an understanding of how the autonomic nervous system interfaces with

the environment and the contribution of the autonomic nervous system to psychological and behavioral processes. In contrast, more recent neurophysiological data promote a more integrative view of the autonomic nervous system.

The flexibility and variability of autonomic nervous system function is totally dependent upon the structure of the nervous system. By mapping the phylogenetic development of the structures regulating autonomic function, it is possible to observe the dependence of autonomic reactivity on the evolution of the underlying structure of the nervous system, and consequently the dependence of social behavior on autonomic reactivity. The phylogenetic approach highlights a shift in brainstem and cranial nerve morphology, and functions from a digestive and cardiopulmonary system to a system that integrates the regulation of facial muscles, cardiac output and the vocal apparatus for affective communication.

### **5. The evolution of the autonomic nervous system: emergent structures and the expression of emotions**

Although there is an acceptance that the autonomic nervous system and the face play a role in emotional expression and social behavior, there is great uncertainty regarding the autonomic signature of specific or discrete emotions and the function of the autonomic nervous system in regulating social behavior. Most researchers evaluating autonomic responses during affective experiences, assumed, as did Cannon, that the sympathetic nervous system was the determinant of emotion, or at least the primary physiological covariate of emotion and an index of stress. This, of course, neglects the potential role of the parasympathetic nervous system and its neurophysiological affinity to structures of the face and head that regulate facial expression, eye movements, pupil dilation, salivation, swallowing, vocalizing, hearing and breathing. By investigating the evolution of the autonomic nervous system, we may gain insight into the interface between autonomic function and facial expression. In the following sections, the phylogenetic development

of the autonomic nervous system will be used as an organizing principle to categorize affective experiences.

The polyvagal theory is derived from investigations of the evolution of the autonomic nervous system. The theory includes assumptions that impact on psychological, behavioral and physiological processes associated with emotional regulation and social behavior. Thus, consistent with the polyvagal theory, behavioral and autonomic responses associated with emotional regulation and social behavior reflect adaptive strategies emergent from the phylogeny of the mammalian nervous system.

1. Evolution has modified the structures of the autonomic nervous system.
2. The mammalian autonomic nervous system retains vestiges of phylogenetically older autonomic nervous systems.
3. Emotional regulation and social behavior are functional derivatives of structural changes in the autonomic nervous system due to evolutionary processes.
4. In mammals, the autonomic nervous system response strategy to challenge follows a phylogenetic hierarchy, starting with the newest structures and, when all else fails, reverting to the most primitive structural system.
5. The phylogenetic stage of the autonomic nervous system determines affective states and the range of social behavior.

### **6. Polyvagal theory: three phylogenetic systems**

The polyvagal theory (Porges, 1995, 1997, 1998) emphasizes the phylogenetic origins of brain structures that regulate social and adaptive survival-oriented defensive behaviors. 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 the 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 social, emotional and communication behaviors and disorders. The theory also provides an explanation of stress-related responses.

The polyvagal construct was introduced to emphasize and document the neurophysiological and neuroanatomical distinction between two branches of the tenth cranial nerve (vagus) and to propose that each vagal branch was associated with a different adaptive behavioral strategy. The vagus nerve, a primary component of the autonomic nervous system, exits the brainstem and has branches that regulate the striated muscles of the head and face (e.g. facial muscles, eyelids, middle-ear muscles, larynx, pharynx, muscles of mastication) and in several visceral organs (e.g. heart, gut). The theory proposes that the different branches are related to unique, adaptive behavioral strategies and articulates three phylogenetic stages of the development of the mammalian autonomic nervous system (see Table 1). These stages reflect the emergence of three distinct subsystems, which are phylogenetically ordered and behaviorally linked to communication (e.g. facial expression, vocalization, listening), mobilization (e.g. fight–flight behaviors) and immobilization (e.g. feigning death, behavioral ‘shutdown’ and syncope). The mobilization system

is dependent on the functioning of the sympathetic nervous system. The most phylogenetically primitive component, the immobilization system, is dependent on the unmyelinated or ‘vegetative’ vagus, which is shared with most vertebrates. With increased neural complexity due to phylogenetic development, the organism’s behavioral and affective repertoire is enriched. The current paper expands the polyvagal theory to include response systems that interact with the autonomic nervous system (i.e. neuropeptides, HPA axis and the immune system) to mediate physiological state in order to promote or limit social behavior.

Table 2 illustrates the phylogenetic differences in the structures that regulate the heart in vertebrates (Taylor, 1992; Morris and Nilsson, 1994; Santer, 1994). The heart is selected, because regulation of the heart determines the availability of the metabolic resources required for mobilization, as well as for growth and restoration. For example, cardiac output must be regulated to remain calm in safe environments, to mobilize for fight or flight behaviors, or to immobilize for feigning death or avoidance behaviors. To regulate cardiac output, several efferent structures have evolved. These structures represent two global, and often opposing, systems: one, a sympathetic-catecholamine system, including catecholamine-secreting chromaffin tissue and spinal sympathetic nerves; and secondly, a vagal system (a component of the parasympathetic nervous system) with branches originating in medullary source nuclei (i.e. dorsal motor nucleus of the vagus and nucleus ambiguus).

In the jawless fish, neural control of the heart is very primitive. Some jawless fish, such as hag-

Table 1

The three phylogenetic stages of the neural control of the heart proposed by the polyvagal theory

Phylogenetic stage	ANS 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 (feigning death, passive avoidance)	Dorsal motor nucleus of the vagus

Table 2  
Neural regulation of the heart as a function of vertebrate phygeny

Group	CHM	DVC	SNS	AD/m	VVC
Jawless fish	X +	(X +)			
Cartilaginous fish	X +	X -			
Bony fish	X +	X -	X +		
Amphibians	X +	X -	X +		
Reptiles	X +	X -	X +	X +	
Mammals	X +	X -	X +	X +	X -

*Abbreviations:* CHM, chromaffin tissue; DVC, dorsal vagal complex with vagal efferent pathways originating in the dorsal motor nucleus of the vagus and vagal afferents terminating in the nucleus of the solitary tract (NTS); SNS, spinal sympathetic nervous system; AD/m, adrenal medulla; and VVC, ventral vagal complex with efferent pathways originating in the nucleus ambiguus that regulate visceral structures (heart, bronchi, thymus) and striated muscles via special visceral efferents and afferents via the solitary tract, trigeminal and facial nerve. X + indicates a cardioexcitatory influence (e.g. increases in heart rate). X - indicates a cardioinhibitory influence (e.g. decreases in heart rate).

fish, rely on circulating catecholamines from diffuse chromaffin tissue to provide excitatory influences on the heart. Other jawless fish, such as lampreys, have a cardiac vagus. However, in contrast to all other vertebrates, which have a cardio-inhibitory vagus that acts via muscarinic cholinceptors, the lamprey vagus is cardio-excitatory and acts via nicotinic receptors.

The cartilaginous fish, such as the sharks, rays and skates, have an unmyelinated cardio-inhibitory vagus. Similar to the more recent vertebrates, the vagus has cells of origin in the dorsal motor nucleus of the vagus located in the medulla. The vagus in these fish is inhibitory and the cholinceptors (the primary neurotransmitter of the vagus in all vertebrates is acetylcholine) on the heart are muscarinic, as they are in other vertebrates. The cardioinhibitory vagus is functional in the cartilaginous fish. In conditions of hypoxia, the metabolic output is adjusted by lowering heart rate. This modification of neural regulation may provide a mechanism to enable the cartilaginous fish to increase their territorial range, by providing a neural mechanism that adjusts metabolic output to deal with changes in

water temperature and oxygen availability. However, unlike the phylogenetically more recent bony fish and tetrapods, the cartilaginous fish do not have direct sympathetic input to the heart. Instead, cardiac acceleration and increases in contractility are mediated via  $\beta$ -adrenergic receptors stimulated by circulating catecholamines released from chromaffin tissue. Thus, since activation of metabolic output is driven by circulating catecholamines, and not by direct neural innervation, once the excitatory system is triggered, the ability to self-soothe or calm is limited.

The bony fish are phylogenetically the first group of vertebrates in which the heart is regulated by both sympathetic and parasympathetic neural pathways. With opposing neural mechanisms from sympathetic and vagal pathways, rapid transitory changes in metabolic output are possible to support immediate changes in behavior from mobilization to immobilization. In bony fish, this is observed as darting and freezing, with direct neural components from the spinal cord via the sympathetic chain producing increases in heart rate and contractility, and direct neural pathways from the brainstem via the vagus producing cardio-inhibitory actions.

Amphibians, similar to the bony fish, have dual innervation of the heart via systems, with direct neural components from the spinal cord via the sympathetic chain producing increases in heart rate and contractility, and direct neural pathways from the brainstem via the vagus producing cardioinhibitory actions.

A distinct adrenal medulla formed of chromaffin tissue is present in reptiles (Santer, 1994). The medulla is of ectodermal origin, from which the epidermis, nervous tissue and, in vertebrates, sense organs develop. Neural regulation by sympathetic nerves of the adrenal medulla provides a mechanism for rapid and controlled release of epinephrine and norepinephrine to increase cardiac output to match the metabolic demands of mobilization behaviors. In bony fish, chromaffin tissue is primarily found in parts of the cardiovascular system, although there is also chromaffin tissue associated with the kidney. In amphibians, chromaffin tissue is primarily associated with the

kidney, and there are substantial aggregations of chromaffin cells located along the sympathetic chain ganglia.

In mammals, the morphology of the vagus changes. Unlike other vertebrates with a cardioinhibitory vagus, the mammalian vagus contains two branches. One branch originates in the dorsal motor nucleus of the vagus and provides the primary neural regulation of subdiaphragmatic organs, such as the digestive tract. However, at the level of the heart, the dorsal motor nucleus of the vagus does not play a major role in the normal dynamic regulation of cardiac output. Rather, during embryological development in mammals, cells from the dorsal motor nucleus of vagus migrate ventrally and laterally to the nucleus ambiguus (Schwaber, 1986). There they form the cell bodies for visceromotor myelinated axons that provide potent inhibition of the sinoatrial node, the pacemaker for the heart. Three phylogenetic principles can be extracted from Table 2. 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 myelinated motor nerves emerging from the brainstem (e.g. specific visceral neural pathways embedded within cranial nerves V, VII, IX, X and XI).

These phylogenetic principles provide a basis for speculations regarding the behavioral and physiological responses associated with mammalian social and emotional behavior, which is neurophysiologically and behaviorally linked to adaptive stress and coping strategies. 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. This phylogenetic course results in greater central nervous system regulation of behavior, especially behaviors needed to engage and disengage with environmental challenges. Birds are conspicuously missing from Table 2, since Table 2 includes the phylogenetic stage preceding mammals. Although mammals and birds are phylogenetic descendants of reptiles, mammals are not 'direct' phylogenetic descendants of birds.

By transitory down-regulation of the cardioinhibitory vagal tone to the heart (i.e. removing the *vagal brake*), the mammal is capable of rapid increases in cardiac output without activating the sympathetic-adrenal system. By engaging this system, rather than the sympathetic-adrenal system, mammals have the opportunity to rapidly increase metabolic output for immediate mobilization. Under prolonged challenge, the sympathetic system may also be activated. However, by rapidly re-engaging the vagal system, mammals have the capacity to inhibit sympathetic input to the heart (Vanhoutte and Levy, 1979) and rapidly decrease metabolic output to self-soothe and calm.

## 7. The vagal brake

The myelinated mammalian vagus is actively inhibitory of the sympathetic nervous system at the level of the heart. The mammalian vagus may function as an active *vagal brake* (see Porges et al., 1996) in which rapid inhibition and disinhibition of the vagal tone to the heart can rapidly mobilize or calm an individual. In addition, since the mammalian vagus has distinct pathways involved in the *voluntary* regulation of the striated muscles (e.g. corticobulbar pathways, afferents from face and mouth, efferents to larynx and

pharynx), the regulation of heart rate is neuroanatomically and neurophysiologically linked to the function of the special visceral efferents.

Due to the tonic vagal influences to the sinoatrial node (the heart's pacemaker), resting heart rate is substantially lower than the intrinsic rate of the pacemaker. When the vagal tone to the pacemaker is high, the vagus acts as a brake on the rate at which the heart is beating. When vagal tone to the pacemaker is low, there is little or no inhibition of the pacemaker. Thus, the vagal brake may be used as a construct to describe the functional modulation of heart rate by the myelinated vagal efferent pathways. The vagal brake provides a neural mechanism to rapidly change visceral state by slowing or speeding the heart rate. Consistent with the assumptions of the polyvagal theory, the vagal brake contributes to the modulation of cardiac output by decreasing the inhibitory vagal control of the heart to speed heart rate and by increasing the inhibitory vagal control of the heart to slow heart rate. Thus, neurophysiologically, the vagal brake provides a mechanism to support the metabolic requirements for mobilization and communication behaviors. Functionally, the vagal brake, by modulating visceral state, enables the individual to rapidly engage and disengage objects and other individuals and to promote self-soothing behaviors and calm behavioral states.

Difficulties in regulating the vagal brake result in the recruitment of other neural mechanisms (e.g. sympathetic regulation of the heart) and neural chemical mechanisms (e.g. stimulation of the HPA axis) to regulate physiological state. Thus, consistent with the polyvagal theory, if the vagal brake is not functioning or will not serve the survival needs of the organism, the phylogenetically *older* systems (e.g. the sympathetic-adrenal system) will be recruited to regulate metabolic output to deal with environmental challenges. For example, if the vagal brake is not functioning, there is the potential for greater dependence on the sympathetic excitation of the cardiovascular system with the associated health-related (e.g. hypertension) and behavioral (e.g. irritable and reactive) costs.

## 8. Evolution and dissolution: a hierarchical response strategy

The evolution of the autonomic nervous system provides substrates for the emergence of three adaptive stress and coping subsystems, each linked to structures that evolved during identifiable phylogenetic stages. The polyvagal theory proposes that during danger or threat the older, less social systems are recruited. The older systems, although functional in the short term, may result in damage to the mammalian nervous system when expressed for prolonged periods. Thus, the stress and coping neurophysiological strategies that are adaptive for reptiles (e.g. apnea, bradycardia, immobilization) may be lethal for mammals.

Rather than describing the autonomic nervous system as a linear 'arousal' system focused on the sympathetic nervous system, or a balance system focused on the opposing influences of the sympathetic and parasympathetic pathways, the function of the autonomic nervous system is hierarchically organized. As emphasized above, the hierarchical organization is phylogenetically determined and can be summarized as the following three sequential functional subsystems:

1. The ventral vagal complex (VVC): a mammalian signaling system for motion, emotion, and communication.
2. The sympathetic nervous system (SNS): an adaptive mobilization system supporting fight or flight behaviors.
3. The dorsal vagal complex (DVC): a vestigial immobilization system.

Each of these three neural constructs is linked with a specific response strategy observable in humans. Each strategy is manifested via differentiated motor output from the central nervous system to perform specific adaptive functions: to immobilize and conserve metabolic resources (DVC), to mobilize in order to obtain metabolic resources (SNS), or to signal with minimal energy expense (VVC). The constituent responses associated with each subsystem are listed in Table 1.

### 8.1. *The ventral vagal complex (VVC)*

The primary efferent fibers of the VVC originate in the nucleus ambiguus. The primary afferent fibers of the VVC terminate in the source nuclei of the facial and trigeminal nerves. The VVC has the primary control of supradiaphragmatic visceral organs, including the larynx, pharynx, bronchi, esophagus, and heart. Motor pathways from the VVC to visceromotor organs (e.g. heart and bronchi) and somatomotor structures (e.g. larynx, pharynx, esophagus) are myelinated to provide tight control and speed in responding. In mammals, the visceromotor fibers to the heart express high levels of tonic control and are capable of rapid shifts in cardioinhibitory tone to provide dynamic changes in metabolic output to match environmental challenges. This rapid regulation characterizes the qualities of the mammalian vagal brake that enable rapid engagement and disengagement in the environment without mobilizing the sympathetic nervous system.

A major characteristic of the VVC is the fact that the neural fibers regulating somatomotor structures are derived from the branchial or primitive gill arches that evolved to form cranial nerves V, VII, IX, X and XI. Somatomotor fibers originating in these cranial nerves control the branchiomeric muscles, including those of the face, mastication, neck, larynx, pharynx, esophagus, and middle ear. Visceromotor efferent fibers control salivary and lachrymal glands, as well as the heart and bronchi. The primary afferents to the VVC come from facial and oral afferents traveling through the facial and trigeminal nerves and the visceral afferents terminating in the nucleus of the solitary tract (NTS). The VVC is involved in the control and coordination of sucking, swallowing, and vocalizing with breathing.

### 8.2. *The sympathetic nervous system (SNS)*

The sympathetic nervous system is primarily a system of mobilization. It prepares the body for emergency by increasing cardiac output, stimulating sweat glands to protect and lubricate the skin, and by inhibiting the metabolically costly gastrointestinal tract. The evolution of the sympa-

thetic nervous system follows the segmentation of the spinal cord, with cell bodies of the preganglionic sympathetic motor neurons located in the lateral horn of the spinal cord. The sympathetic nervous system has long been associated with emotion and stress. The label sympathetic reflects the historical identity of this system as a nervous system with feelings and contrasts it with the parasympathetic nervous system, a label that reflects a nervous system that guards against feelings.

### 8.3. *The dorsal vagal complex (DVC)*

The dorsal vagal complex (DVC) is primarily associated with digestive, taste, and hypoxic responses in mammals. It includes the nucleus of the solitary tract (NTS) and the interneuronal communication between the NTS and dorsal motor nucleus of the vagus (DMX). The efferents for the DVC originate in the DMX and primary vagal afferents terminate in the NTS. The DVC provides the primary neural control of subdiaphragmatic visceral organs. It provides low tonic influences on the heart and bronchi. This low tonic influence is the vestige from the reptilian vagal control of the heart and lung. In contrast to reptiles, mammals have a great demand for oxygen and are vulnerable to any depletion in oxygen resources.

The DVC provides inhibitory input to the sinoatrial node of the heart via unmyelinated fibers, and thus is less tightly controlled than the myelinated fibers from the VVC. Hypoxia or perceived losses of oxygen resources appear to be the main stimuli that trigger the DVC. This response strategy is observed in the hypoxic human fetus. Although adaptive for the reptile, the hypoxic triggering of this system may be lethal for mammals. In addition, it is important to note that the DVC has beneficial functions in humans. Under most normal conditions, the DVC maintains tone to the gut and promotes digestive processes. However, if up-regulated, the DVC contributes to pathophysiological conditions including the formation of ulcers via excess gastric secretion and colitis. Recent research supports the importance of the unmyelinated vagal fibers in bradycardia

(Cheng and Powley, 2000) and suggests the possibility that massive bradycardia may be determined by the unmyelinated vagal fibers associated with the DVC recruiting myelinated vagal fibers to maximize the final vagal surge on the heart (Jones et al., 1995).

#### 8.4. Dissolution

The polyvagal theory proposes a hierarchical response strategy to environmental challenges, with the most recent modifications employed first and the most primitive last. However, the response strategy is not all-or-none, and may include transitional blends between the boundaries of the three hierarchical stages. These transitional blends may be determined by both visceral feedback and higher brain structures (including the HPA axis and vasopressinergic and oxytocinergic pathways that communicate between the hypothalamus and the DVC). Thus, the neurophysiological substrate of specific behavioral states and coping strategies may incorporate activation of a sequence of response systems representing more than one phylogenetic stage.

This phylogenetically based hierarchical response strategy is consistent with the concept of dissolution proposed by John Hughlings Jackson (1958) to explain disease of the nervous system. Jackson proposed that:

The higher nervous arrangements inhibit (or control) the lower, and thus, when the higher are suddenly rendered functionless, the lower rise in activity.

The polyvagal theory (Porges, 1995, 1997, 1998) proposes dissolution, not in response to disease or brain trauma, but as an adaptive biobehavioral response strategy to differential challenges (i.e. threats to survival). Although reminiscent of the triune brain proposed by MacLean (1990), the polyvagal theory emphasizes that even the phylogenetically more primitive structures have changed in structure and function. This phylogenetic adjustment of the autonomic nervous system represents an exaptation (i.e. a shift in function) of structures to express emotions and to adapt to the complex environment.

Expanding the Jacksonian construct of dissolution from disease and trauma, the polyvagal theory proposes that adaptive response strategies to survival challenges follow a phylogenetically defined hierarchy. The VVC, with its mechanisms of signaling and communication, provides the initial response to the environment. The VVC inhibits, at the level of the heart, the strong mobilization responses of the sympathetic nervous system. Withdrawal of VVC, consistent with Jackson's model, results in a disinhibition of the sympathetic control of the heart. Similarly, withdrawal of sympathetic tone results in a disinhibition of the DVC control of the gastrointestinal tract and vulnerability of the bronchi and heart. There are several clinical consequences to unopposed DVC control including: defecation, due to a relaxation of the sphincter muscles and increased motility of the digestive tract; apnea, due to constriction of the bronchi; and bradycardia, due to stimulation of the sinoatrial node. Thus, when all else fails, the nervous system elects a metabolically conservative course that is adaptive for primitive vertebrates. For mammals, this strategy may be adaptive in the short term, but lethal if maintained. Consistent with the Jacksonian principle of dissolution, specific psychopathologies defined by affective dysfunction may be associated with autonomic correlates consistent with the three phylogenetic levels of autonomic regulation. The three levels do not function in an all-or-none fashion; rather, they exhibit gradations of control determined by both visceral feedback and higher brain structures.

#### 9. The social engagement system: an emergent property of the ventral vagal complex

Phylogenetically, the ventral vagal complex (VVC) is the most recent neurophysiological affect system. The VVC is composed of a somatomotor component, consisting of the special visceral efferent pathways, and a visceromotor component, consisting of the myelinated vagal pathways from the nucleus ambiguus to the sinoatrial node of the heart and the bronchi. As illustrated

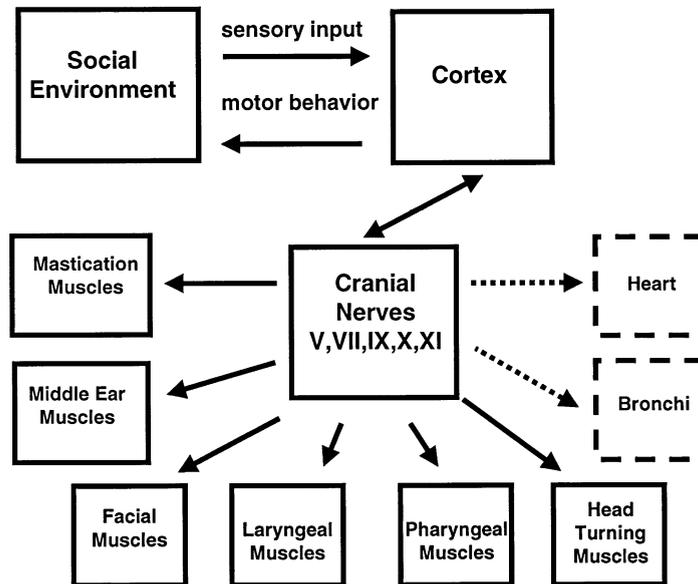


Fig. 1. The social engagement system: social communication is determined by the cortical regulation of medullary nuclei via corticobulbar pathways. The social engagement system consists of a somatomotor component (i.e. special visceral efferent pathways that regulate the muscles of the head and face)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

in Fig. 1, the special visceral efferents and the vagal brake collectively constitute an emergent *social engagement system*. The somatomotor components of the VVC contribute to the regulation of behaviors involved in exploration of the social environment (e.g. looking, listening, ingesting) and behaviors involved in acknowledging social contact (e.g. facial and head gestures, vocalizing). More specifically, the somatomotor components of the VVC are involved in head-turning (via cranial nerve XI), vocalizations (IX, X), facial expression (VII, V), the filtering of low-frequency sounds via the middle-ear muscles to extract human voice from background sounds (VII), and mastication (V). The visceromotor components of the VVC contribute to the rapid modulation of vagal (X) control of the heart and the bronchi (X), which provides metabolic resources to engage and disengage in a social setting.

Three important features define the *social engagement system*. First, the efferent pathways that regulate the social engagement system originate in medullary structures (i.e. nucleus of cranial nerve V, nucleus of cranial nerve VII, nucleus

ambiguus). Second, corticobulbar pathways, which originate in frontal cortex (i.e. upper motor neurons), enable the possibility of efficient cortical regulation of these medullary source nuclei (i.e. lower motor neurons). Third, on the medullary level, the structures that regulate the efferent regulation of social-communication behaviors neuroanatomically communicate with structures that regulate ingestion (e.g. sucking, swallowing, salivation) and cardiac output. Thus, modulation of the vagal brake may either promote calming and self-soothing states (i.e. attenuate the influence of the sympathetic nervous system on the heart) or support mobilization (i.e. potentiate the influence of the sympathetic nervous system on the heart).

Consistent with the polyvagal theory, difficulties in regulating the *vagal brake* may result in the phylogenetically older systems (i.e. neural regulation of the adrenal and the sympathetic nervous system) being recruited to regulate metabolic output to deal with environmental challenges. Thus, the polyvagal theory would predict that during states of mobilization, characterized by classic

‘fight–flight’ behaviors and sympathetic excitation, both the *vagal brake* and the behavioral components of the *social engagement system* would not be easily accessible.

## 10. Measurement

In the psychophysiological literature, there is an assumption that respiratory sinus arrhythmia is an index of vagal influences to the heart. The polyvagal theory distinguishes between the rhythmic beat-to-beat changes in heart rate, mediated via the myelinated vagal pathways that originate in the nucleus ambiguus, and the conservative responses of bradycardia, mediated via the unmyelinated vagal pathways that originate in the dorsal motor nucleus of the vagus.

The nucleus ambiguus is a component of a network of structures that generate a respiratory rhythm to foster coordination among cardiac and respiratory processes (Richter and Spyer, 1990). In support of this model, vagal fibers originating from the nucleus ambiguus and terminating in both the bronchi (Haselton et al., 1992) and the sinoatrial node (Spyer and Jordan, 1987) have a respiratory rhythm. In contrast, vagal fibers originating from the dorsal motor nucleus of the vagus do not have a respiratory rhythm.

Recent work by Jones et al. (1995) provides support for this model. They note that the preganglionic unmyelinated vagal fibers originating in the dorsal motor nucleus of the vagus do not have an obvious input from peripheral or central respiratory or cardiac related inputs, but are activated by stimulation of pulmonary unmyelinated afferent fibers. Convergent support comes from Paton (1998), who reported that stimulation of unmyelinated vagal afferents produces reflex bradycardia and depresses central respiratory activity, consistent with an adaptive shutdown system as proposed by the polyvagal theory. Thus, the vagal responses mediated by the unmyelinated vagus, being part of an ancient conservation system, are reflected in mammals as adaptive responses triggered by life-threatening events, such as hypoxia (see Potter and McCloskey, 1986),

and can be observed as clinical bradycardia in the fetus (Reed et al., 1999).

Neuroanatomical confirmation that the two vagal pathways in mammals have different functional impact on the heart (i.e. beat-to-beat variability and level) has been confirmed (Jones et al., 1995; Cheng and Powley, 2000). However, the functions of the unmyelinated fibers are not totally understood. For example, the myelinated and unmyelinated fibers differentially respond to rates of stimulation, suggesting different functional properties (Fan and Andresen, 1998). Although stimulation of the unmyelinated fibers originating in the dorsal motor nucleus of the vagus can produce heart-rate slowing and an attenuation of contractility (see Cheng et al., 1999), whether the unmyelinated fibers are responsible for clinical bradycardia has been contested (see Jones et al., 1995; Hopkins et al., 1996).

Alternative explanations might be considered. For example, it is possible that the myelinated vagal fibers originating in the nucleus ambiguus might contribute to clinical bradycardia. This explanation would suggest that the myelinated vagal pathways might, under different conditions, respond to two regulatory systems. During conditions when blood gases are within normal range, part of a rhythmic vagal system may produce a coordinated respiratory rhythm in heart rate and bronchial activity to facilitate oxygen diffusion. However, during conditions of compromise when blood gas status threatens survival, both RSA and respiratory drive would be suppressed. In the absence of the rhythmic vagal system, a tonic vagal system may drop heart rate level to reduce metabolic demands. Perhaps during fetal distress, a tonic increase in the influence of the myelinated vagal fibers to the heart (i.e. producing bradycardia) is paralleled by the increase in the tonic influence of the unmyelinated vagal fibers to the gut (i.e. producing meconium). Consistent with this premise, there are reports that selective stimulation of the myelinated vagal fibers induce bronchoconstriction and potentiate the recruitment of non-myelinated fibers (Lama et al., 1988).

Based on the above neurophysiological evidence, the functional impact of the myelinated

vagus on the heart is easily calibrated by quantifying the amplitude of respiratory sinus arrhythmia (i.e. the rhythmic increase and decrease in heart rate observed at the frequency of spontaneous breathing). In addition, the period of the oscillations in heart rate (the period of RSA) would provide a valid index of the output frequency of the *cardiopulmonary oscillator*. In addition, since the brainstem nuclei that regulate the myelinated vagal pathways to the heart are neuroanatomically and neurophysiologically linked to the brainstem source nuclei of the special visceral efferents that regulate facial expression, monitoring dynamic changes in RSA and heart rate (i.e. the *vagal brake*) provides an efficient and non-invasive method of assessing the status of the *social engagement system*.

### 11. Voodoo or vagus death: a test of the polyvagal theory

The polyvagal theory provides a theoretical framework to interpret the phenomenon of Voodoo or fright death described by Cannon (1957) and Richter (1957). Cannon believed that extreme emotional stress, regardless of the specific behavioral manifestation, could be explained in terms of degree of sympathetic-adrenal excitation. Voodoo death was assumed to be directly attributable to emotional stress. Being wed to a sympatho-adrenal model of emotional experience (see above), Cannon assumed that Voodoo death would be the consequence of the state of shock produced by the continuous outpouring of epinephrine via excitation of the sympathetic nervous system. According to the Cannon model, the victim would be expected to breathe very rapidly and have a rapid pulse. The heart would beat fast and gradually lead to a state of constant contraction, and ultimately, to death in systole. Since his speculations were not empirically based, he offered the following challenge to test his model of Voodoo death:

If in the future, however, any observer has opportunity to see an instance of voodoo death, it is to be hoped that he will conduct the simpler tests before the victim's last gasp.

Curt Richter (1957) responded to Cannon's challenge with an animal model. Rats were pre-stressed, placed in a closed, turbulent water tank, and the latency to drowning was recorded. Most domestic laboratory rats lasted for several hours, while, unexpectedly, all of the wild rats died within 15 min. In fact, several wild rats dived to the bottom, and without coming to the surface, died. To test Cannon's hypothesis, that stress-induced sudden death was sympathetic, Richter monitored heart rate and determined whether the heart was in systole or diastole after death. He assumed, based upon Cannon's speculations, that tachycardia would precede death, and that at death, the heart would be in a state of systole, reflecting the potent effects of sympathetic excitation on the pacemaker and the myocardium. However, Richter's data contradicted the Cannon model. Heart rate slowed prior to death, and at death the heart was engorged with blood, reflecting a state of diastole. Richter interpreted the data as demonstrating that the rats died a vagus death, the result of over-stimulation of the parasympathetic system, rather than of the sympathico-adrenal system. However, Richter provided no physiological explanation, except the speculation that the lethal vagal effect was related to a psychological state of hopelessness.

The immediate and reliable death of the wild rats in Richter's experiment may represent a more global immobilization strategy. Sudden prolonged immobility or feigned death is an adaptive response exhibited by many mammalian species. Hofer (1970) demonstrated that several rodent species when threatened exhibited an immobility that was accompanied by very low heart rate. For some of the rodents, heart rate during immobility was less than 50% of the basal rate. During the prolonged immobility, respiration became so shallow that it was difficult to observe, although the rate greatly accelerated. Although physiologically similar, Hofer distinguished between prolonged immobility and feigned death. The onset of feigned death, unlike the behavior of 'hopelessness' described by Richter, occurred suddenly with an apparent motor collapse during active struggling. Similar to Richter, Hofer interpreted this

fear-induced slowing of heart rate as a vagal phenomenon. In support of this interpretation, he noted that of the four species that exhibited prolonged immobility, 71% of the subjects had cardiac arrhythmias of vagal origin; in contrast, in the two species that did not exhibit immobility behaviors, only 17% exhibited cardiac arrhythmias of vagal origin.

The polyvagal theory places Richter's and Hofer's observations in perspective. Following the Jacksonian principle of dissolution, the rodents would exhibit the following sequence of response strategies: (1) removal of VVC tone; (2) increase in sympathetic tone; and (3) a surge in DVC tone. It appears that the more docile domestic rats in Richter's experiment progressed from a removal of VVC tone, to an increase in sympathetic tone, and then died via exhaustion. However, the profile of the wild rats was different. Being totally unaccustomed to enclosures and handling, and also having their vibrissae cut, a mobilization strategy driven by increased sympathetic tone was not functional. Instead, these rats reverted to their most primitive system to conserve metabolic resources via DVC. This strategy promoted an immobilization response characterized by reduced motor activity, apnea, and bradycardia. Unfortunately, this mode of responding, although adaptive for reptiles, is lethal for mammals. Similarly, the onset of feigned death, as described by Hofer, illustrates the sudden and rapid transition from an unsuccessful strategy of struggling, requiring massive sympathetic activation, to the metabolically conservative immobilized state, mimicking death, associated with the DVC.

These data suggest that the vagus contributes to severe emotion states and may be related to emotional states of immobilization, such as extreme terror. Application of the polyvagal approach enables the dissection of vagal processes into three strategic programs: (1) when tone of the VVC is high, there is an ability to communicate via facial expressions, vocalizations, and gestures; (2) when tone of the VVC is low, the sympathetic nervous system is unopposed and easily expressed to support mobilization, such as fight or flight behaviors; and (3) when tone from DVC is high, there is immobilization and poten-

tially life-threatening bradycardia, apnea, and cardiac arrhythmias.

## **12. How does the polyvagal theory provide a theoretical platform to understand the functional interactions of the HPA axis, the neuropeptides of oxytocin, and vasopressin with the autonomic nervous system?**

### *12.1. Structures and functions of the adrenal gland*

The adrenal gland exhibits phylogenetic changes in structure and function. Above, because of its complimentary function to the sympathetic nervous system, the adrenal medulla was discussed. However, since the adrenal cortex is treated as an endocrine organ and part of the HPA axis, it is traditionally studied and discussed independently of the adrenal medulla and the autonomic nervous system. Unlike the medulla, which is of ectodermal origin, the cortex is of mesodermal origin. The adrenal cortex secretes cortisol, which is frequently used to index stress.

All vertebrates produce corticosteroids and catecholamines. However, the structures that produce these secretions follow a phylogenetic trend that results in two anatomical changes. First, the chromaffin tissue and the adrenocortical cells, which are scattered through the viscera in the primitive vertebrates, cluster together to form functional structures. Second, these structures establish a close anatomical relation (the adrenal) with communication between the secretions of the two components of the adrenal, and only in mammals does the adrenal have its own vascular supply and venous drainage.

Only mammals have adrenocortical cells clustered as a cortex of the adrenal. Interestingly, several reptiles (e.g. lizards and some snakes) that have a functioning adrenal medulla have the adrenocortical cells partially encapsulated by the chromaffin cells. In the more primitive fish (jawless and cartilaginous), the chromaffin and adrenocortical cells are entirely separate. In the bony fish, both the adrenocortical cells and chromaffin tissue are scattered as independent groups within the 'head' kidney. In amphibians, the chro-

maffin and adrenocortical tissues are scattered over the ventral surfaces of the kidney. In reptiles, the chromaffin and adrenocortical tissues become consolidated into distinct adrenal glands. Reptiles provide a phylogenetic marker, in which the interrenals have an independent vascular supply and venous drainage and no longer (as in amphibians and bony fish) rely on the kidney and a renal portal system for the distribution of secretory products.

Several investigators have explored the adaptive function of the close proximity of the cortisol-secreting adrenocortical cells (that subsequently form the adrenal cortex) and the catecholamine-secreting chromaffin tissue (that subsequently forms the adrenal medulla) (Norris, 1997). The medulla receives large quantities of corticosteroids through the adrenal vascular system, and these hormones activate the enzyme system for converting norepinephrine into epinephrine. This effect would support sympathetic-adrenal medulla functions associated with mobilization and increased metabolic activity. Epinephrine has a potent effect on the elevation of blood glucose, convergent with the influences of some of the adrenal steroids. Additionally, cortisol may directly enhance mobilization by converting lactate to glucose via gluconeogenesis in the liver. This process would contribute to the metabolic demands of mobilization by increasing the availability of glucose, and also by reducing oxygen debt due to the accumulation of lactate.

Vagal activity has been implicated in the function of the adrenal cortex. Reports suggest that afferents originating in the subdiaphragmatic vagus (i.e. DVC) exhibit an inhibitory influence on the HPA axis and reduce cortisol secretion (e.g. Bueno et al., 1989; Miao et al., 1997). Other research has demonstrated a covariation between increases in cortisol and decreases in cardiac vagal tone measured via RSA (Gunnar et al., 1995), which, consistent with the removal of the vagal brake and the stimulation of the sympathetic nervous system, would promote mobilization. Similarly, psychological stressors, which reduce cardiac vagal tone, increase cortisol plasma level (e.g. Cacioppo et al., 1995). Thus, in several situations there appears to be a coordinated response

that functions to promote metabolic activity and mobilization behaviors by withdrawal of VVC tone and increasing both SNS activity and activation of the HPA axis.

In general, functioning of the adrenal cortex and the secretion of cortisol appear to be integrated into the mobilization function of the autonomic nervous system by increasing sympathetic activation and circulating catecholamines. These effects suggest that, consistent with the phylogenetic approach described in the polyvagal theory, cortisol secretion may be related to maintenance of mobilization (i.e. the conversion of norepinephrine into epinephrine) for fight–flight behaviors, and recovery from the lactate build-up that may contribute to a functional oxygen debt (i.e. gluconeogenesis).

In addition, the reports of dysregulation of the HPA axis, low cortisol or low cortisol reactivity in social and affective disorders, such as schizophrenia (Jansen et al., 2000), posttraumatic stress disorder (Yehuda et al., 1996) and the consequences of neglect and abuse in children (De Bellis et al., 1994), may be explained within the context of the polyvagal theory. According to the theory, when mobilization strategies (fight–flight behaviors) are ineffective in removing the individual from the stressor and modulating stress, then the nervous system may degrade to a phylogenetically earlier level of organization. Thus, low cortisol or a hyporesponsive HPA axis may reflect a neural strategy associated with immobilization (e.g. passive avoidance, death feigning, dissociative states) that would require a reduction in energy resources.

## 12.2. *Oxytocin / vasopressin*

Phylogenetically, although all vertebrates have peptides similar in structure to both oxytocin and vasopressin, only mammals have the specific receptors for both peptides. Oxytocin and vasopressin are synthesized primarily in the paraventricular and supraoptic nuclei of the hypothalamus and released centrally via parvocellular neurons and systemically via magnocellular neurons (Swanson and Sawchenko, 1977). The central and systemic effects of these neuropeptides are different. Central release of oxytocin regulates the

output of the dorsal motor nucleus of the vagus, usually maintaining output within levels optimal to support homeostasis and providing a proposed ‘anti-stress’ function (see Carter, 1998). Peripheral release of oxytocin is related to milk ejection, uterine contractions and ejaculation. Central release of vasopressin appears to modulate afferent feedback from the viscera and to shift set-points, independent of sensitivity, for vagal reflexes, such as the baroreceptor reflex (Micheline, 1994). The raising of the baroreceptor set-point, by increasing cardiac output, potentiates fight–flight behaviors and allows sympathetic excitation of the heart to be unopposed by homeostatic vagal reflexes. Thus, central levels of oxytocin have been assumed to be associated with vagal processes, and central levels of vasopressin have been assumed to be associated with sympathetic processes (Uvnas-Moberg, 1997).

Because the peripheral influences of oxytocin and vasopressin function through feedback, primarily via the sensory component of the DVC, the peripheral effects of these peptides are less clear and may be level-dependent, or differ as a function of acute versus chronic exposure. For example, it is possible that peripheral vasopressin may, by stimulating vagal afferents, trigger massive vagal responses via the dorsal motor nucleus of the vagus. In support of this speculation, it is known that in humans, peripheral vasopressin, and not oxytocin, is related to the nausea experienced during motion sickness (Koch et al., 1990). In addition, systemic vasopressin may induce a baroreceptor-mediated bradycardia and a fall in plasma concentration of norepinephrine (Buwalda et al., 1992; Micheline, 1994).

Oxytocin may be part of a complex response profile related to the perception of the environment as safe (see Fig. 2). Consistent with this view, Uvnas-Moberg (1997) and Carter and Altemus (1997) propose that oxytocin promotes states resistant to stress (i.e. anti-stress). In contrast, vasopressin may be part of a complex response profile related to the perception that the environment is challenging or unsafe (see Fig. 3). In fact, central vasopressin could potentiate mobilization responses via sympathetic excitation, while high levels of systemic vasopressin may potentiate a

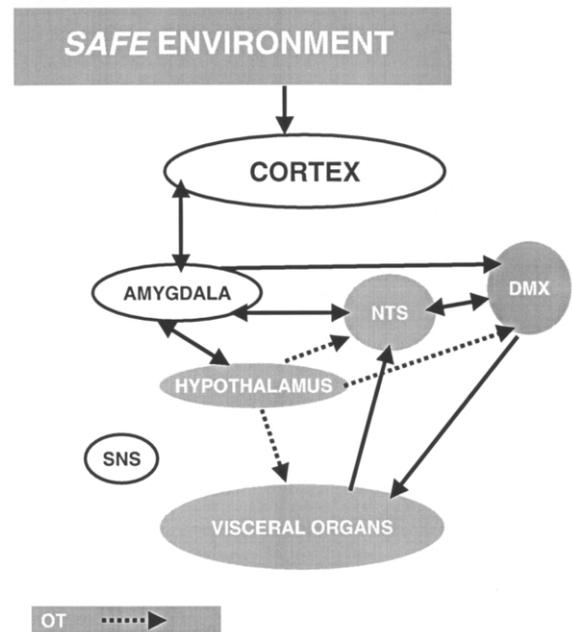


Fig. 2. Neural and neuropeptide regulation of the dorsal vagal complex (DVC) in a safe environment. The DVC includes sensory nuclei in the nucleus of the solitary tract (NTS) and area postrema, and motor nuclei in the dorsal motor nucleus of the vagus (DMX). During states when the individual perceives the environment as safe, oxytocin (OT) is released centrally to the sensory and motor portions of the DVC and systemically to the visceral organs. Functionally, OT fosters a calm immobilization or ‘anti-stress’ state.

physiological shutdown associated with fear (e.g. bradycardia) via feedback to the dorsal motor nucleus and inhibition of sympathetic outflow (Ferguson and Lowes, 1994). In addition, lesions of vagal afferents, which functionally block the visceral input to the sensory component of the DVC (areas sensitive to vasopressin), attenuate or abolish specific, conditioned taste aversions (Andrews and Lawes, 1992).

Paralleling the phylogenetic shift in the cells of origin and the myelination of the vagus, emphasized in the polyvagal theory, is a modification of the hypothalamic regulation of the DVC via both oxytocin and vasopressin. In mammals, the advent of specific receptors for oxytocin and vasopressin increases the range of adaptive functions involving the DVC. In mammals, the dorsal motor nucleus of the vagus, the motor component of the

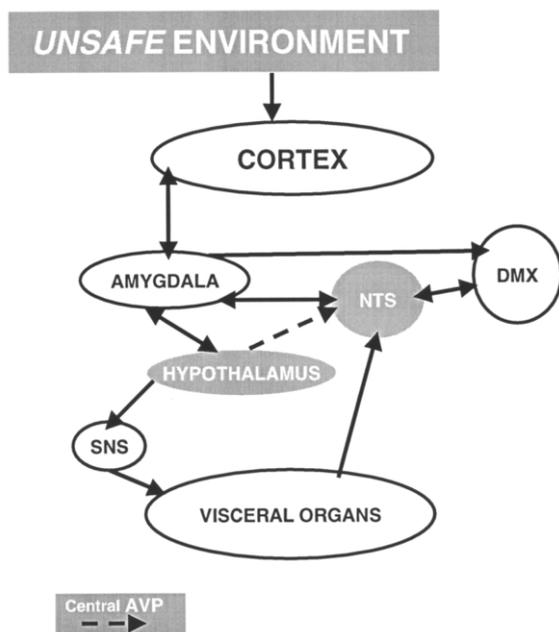


Fig. 3. Neural and neuropeptide regulation of the dorsal vagal complex (DVC) in an unsafe environment. During perceived danger, when mobilization is adaptive, central vasopressinergic pathways (AVP) communicate between the hypothalamus and both NTS and area postrema to change the set-point of vagal reflexes (e.g. baroreceptor reflex) to facilitate sympathetic excitation.

DVC, is sensitive to oxytocin and insensitive to vasopressin. In contrast, the sensory components of the DVC, nucleus of the solitary tract and area postrema, are most sensitive to vasopressin. Area postrema, a medullary structure, interacts with vagal afferents and communicates with the nucleus of the solitary tract. Area postrema is a circumventricular organ, which has a rich capillary plexus and lacks a blood brain barrier. Area postrema plays a major role in vasopressin synthesis and release (Arima et al., 1998). Since area postrema lacks a blood brain barrier, it provides a portal for circulating peptides such as vasopressin to influence brain function. Research has demonstrated that activation of the neurons in area postrema augments the NTS-mediated arterial baroreflex via vasopressin administered, either by direct microinjection into area postrema, or via venous infusion (Qu et al., 1997). Although the nucleus of the solitary tract has receptors for

oxytocin (Landgraf et al., 1990), area postrema may not be directly influenced by oxytocin (Carpenter, 1990). The differential sensitivity of specific components of the DVC to these two neuropeptides (the differential effects of central and systemic release on visceral function and a potential level dependency) results in a wider range of response options, including maximizing mobilization behaviors and co-opting of the primitive vagal system associated with immobilization to support ‘anti-stress’ functions, such as social engagement and growth and restoration (see Porges, 1998). In support of this model, it has been reported that oxytocinergic projections to the DVC restrain exercise-induced tachycardia (Braga et al., 2000).

Although the polyvagal theory has emphasized the potentially lethal shutdown behaviors associated with massive surges from the dorsal motor nucleus of the vagus, the DVC is involved in other functions. The DVC, with motor fibers originating in the dorsal motor nucleus of the vagus and afferent fibers terminating in the nucleus of the solitary tract and area postrema, has been assumed to be involved primarily in homeostatic functions (Leslie, 1985). The DVC promotes anabolic activities related to the restoration and conservation of bodily energy and the resting of vital organs. The DVC regulates digestion by modulating digestive polypeptides and gastric motility (Rogers and Hermann, 1992). In addition, Uvnas-Moberg (1989, 1994) has proposed a parallel between DVC regulation of gastrointestinal hormones and the regulation of visceral states, including stress, hunger and satiety. Without external challenges, the DVC optimizes the function of the internal viscera. In contrast, by increasing metabolic output to deal directly with external challenges, the SNS attempts to optimize the organism’s relationship with the environment. Thus, increases in ambient temperature, noise, pain and pyrogenic agents produce not only increased sympathetic activity, but also an active inhibition of DVC actions on the gut (Uvnas-Moberg, 1987).

The paraventricular nucleus of the hypothalamus is an important regulator of the DVC. Neural communication between the paraventricular

nucleus and the DVC is involved in responses that are not only homeostatic, but also protective and defensive (e.g. nausea and vomiting, conditioned taste aversion, behavioral defense) (Lawes, 1990). Communication between the paraventricular nucleus and the DVC changes with experience, and thus may exhibit a type of learning or memory. Associations may be established rapidly between environmental features or experiences and visceromotor responses. Perhaps, as in conditioned taste aversion, this memory is expressed as a learned association between a specific environmental feature and nausea. Once the association is made, subsequent exposure to the environmental feature may result in immediate nausea and defensive avoidance behaviors. These speculations regarding the changing communication between the paraventricular nucleus and the DVC with experience are consistent with general theories of aversion learning (Garcia et al., 1985).

The paraventricular nucleus regulation of the DVC evolved in phylogenetically older vertebrates, in which escape and avoidance behaviors contributed to the maintenance of visceral homeostasis (Lawes, 1990). Because the early vertebrates lacked an elaborate nervous system to control their viscera, behavior was a primary mechanism for the maintenance of homeostasis (e.g. moving to regulate thermoregulatory and oxygen requirements). As the nervous system evolved, an autonomic nervous system and neuroendocrine mechanisms emerged and displaced the need to use behavior to regulate internal state. The neural and neuroendocrine regulation of internal state allowed behavioral processes to be directed toward environmental challenges. However, the brain structures, specifically the paraventricular nucleus, that govern the homeostatically driven behaviors in the phylogenetically older species evolved into the structures responsible for regulating internal homeostatic functions in the phylogenetically newer species (Leslie et al., 1992).

The role of the paraventricular nucleus in the regulation of the DVC in modern vertebrates retains phylogenetically older functions and continues to respond to life-threatening situations by contributing to visceral and endocrine responses

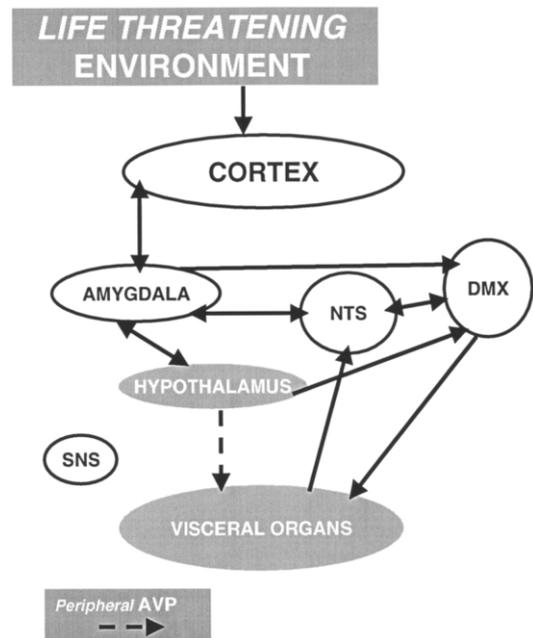


Fig. 4. Neural and neuropeptide regulation of the dorsal vagal complex (DVC) in a life-threatening environment. During life-threatening events when fight–flight behaviors are not an option, immobilized fear responses are elicited. Immobilized fear is fostered by vagal surges from the DMX to visceral organs, which are potentiated by systemic AVP. Systemic AVP triggers increased DMX output by stimulating visceral afferents via NTS and area postrema.

(see Fig. 4). However, this phylogenetic organization results in vulnerabilities, because perceived challenges to survival, whether or not truly life-threatening, may elicit visceral and endocrine reactions that compromise normal physiological function.

The phylogenetic approach of the polyvagal theory emphasizes that defense and avoidance behaviors have a vagal component manifested through the DVC. For example, a physiological shutdown mediated by the DVC would support avoidance behaviors, such as feigning death or freezing (see Fig. 4). However, the evolution of hypothalamic regulation of the DVC provides response alternatives. Specifically, in mammals, the paraventricular nucleus produces two neuropeptides, oxytocin and vasopressin, that differentially communicate with the sensory and motor portions of the DVC. Using the push–pull perfusion

technique, Landgraf et al. (1990) demonstrated that both oxytocin and vasopressin are released in the DVC. Binding sites for vasopressin are prevalent in the sensory component, but are not represented in the motor component (Fuxe et al., 1994). In contrast, oxytocin appears to provide a primary pathway from the paraventricular nucleus to the dorsal motor nucleus of the vagus, with oxytocin injections into the DVC mimicking the vagal responses normally observed immediately following feeding (Rogers and Hermann, 1992). Direct pathways from the nucleus of the solitary tract to the paraventricular nucleus provide a potential source of feedback for hypothalamic influences on visceromotor functions (Sawchenko and Swanson, 1982). Communication between the DVC and the paraventricular nucleus appears to modulate specific visceromotor reflexes involving cardiovascular (Nissen et al., 1993) and gastrointestinal systems (Bray, 1985).

### **13. A phylogenetic approach to the study of emotion, stress, and social behavior**

The phylogenetic orientation focuses our interest on the neural structures and neurobehavioral systems that we share with, or have adapted from, our phylogenetic ancestry. First, the three response systems proposed in the polyvagal theory (i.e. the cranial nerve regulation of the striated muscles of the face coordinated with a myelinated vagus that inhibits sympathetic activity at the level of the heart, a sympathetic-adrenal system to increase metabolic output, and an inhibitory vagal system to decrease metabolic output and promote freezing and immobilization behaviors) are the products of distinct neurophysiological systems. Second, these distinct neurophysiological systems represent a phylogenetically dependent hierarchy, with the use of cranial nerves to regulate facial expression emerging in mammals (well-developed in primates), the sympathetic-adrenal system shared with other vertebrates, including reptiles, and the inhibitory vagal system shared with more primitive vertebrates, including amphibians, and bony and cartilaginous fish (see Porges, 1997, 1998). The three systems, which

have been frequently studied in emotion research, represent different phylogenetic stages of neural development. This phylogenetic development starts with a primitive behavioral inhibition system, progresses to a fight–flight system, and in humans (and other primates), culminates in a complex facial gesture and vocalization system. Thus, from a phylogenetic perspective, the nervous system of vertebrates evolved to support a greater range of behaviors and physiological states, including states that we often associate with stress, as well as positive social behavior.

Even if we focus on stress, the physiological responses of mammals do not fit concisely into a single neurophysiological system. Although cortisol has often been labeled as the ‘stress’ hormone, other neurally mediated systems clearly respond to stress. Moreover, there are situations of severe stress in which cortisol is neither responsive, nor at a high level. By expanding the phylogenetic model proposed in the polyvagal theory to include the HPA axis, the hyporesponsive HPA can be interpreted as reflecting a primitive passive avoidance system. The view that the adrenal cortex is the sole stress system at the periphery limits scientific inquiry into the mechanisms and adaptive functions of several interactive and complex stress response patterns. Other systems, including the neuropeptides oxytocin and vasopressin, influence the regulation of homeostasis, growth and restoration, metabolism and mobilization. These systems form a complex set of mutually interacting neurophysiological pathways that communicate via nerves and neurally active chemicals (e.g. neurotransmitters, neuropeptides, hormones) to cope with survival challenges. This paper has attempted to employ phylogeny as an organizing principle to illustrate the interactive and adaptive nature of several physiological systems that respond to stress and contribute to the expression of positive social behavior.

### **14. Clinical applications of the polyvagal theory**

The polyvagal theory, by describing both the phylogenetically based hierarchy of autonomic

states and the specific triggers that cause a dissolution of this hierarchy, provides a new way of investigating atypical behavior. The theory emphasizes that the mammalian nervous system is not only sensitive to environmental demands and perceived stresses and threats, but that the mammalian nervous system will, in a predictable order, also rapidly reorganize to different neural-mediated states. Unlike models of psychopharmacology that also emphasize the importance of state in regulating behavior, the polyvagal theory emphasizes neural mechanisms that regulate state, and the order in which these neural mechanisms are elicited. The polyvagal theory emphasizes the flexibility of the nervous system in modulating autonomic state. This view contrasts with pharmacological strategies that are effective in changing autonomic state without engaging the nervous system.

A new paradigm based on the polyvagal theory has been tested. This new paradigm assumes that state can be changed in a predictable manner and that specific state changes would be associated with potentiating or limiting the range of specific behaviors. This new paradigm distinguishes between state changes associated with shifts in the neural regulation of the autonomic nervous system and specific responses elicited by quantifiable stimuli. The paradigm enables: (1) the manipulation and evaluation of autonomic state; and (2) the manipulation and evaluation of learning, social behavior, and other mental processes. This paradigm should enable the demonstration that the range of observable behaviors (including physiological reactions) will change in a predictable manner as the context (i.e. perceived safety) driving the neural regulation of the autonomic nervous system is manipulated. By applying this paradigm, we can evaluate the influence of specific contexts on neural regulation of the autonomic state. Some contexts may promote states related to antisocial behavior (i.e. aggression) and health vulnerability, while other contexts may promote states related to positive social behavior, health and development. Thus, unless the design features of the nervous system are understood within the context of the organism's interaction with the environment, an individual may be interacting in

an environment that is not only inefficient in stimulating social behavior and intellectual growth, but may also be harmful to both mental and physical health.

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 also emphasizes that mobilization and immobilization behaviors may be adaptive strategies to a challenged (i.e. frightened) individual. Thus, it may be possible that creating states of calmness and exercising the neural regulation of brainstem structures may potentiate positive social behavior by stimulating and exercising the neural regulation of the social engagement system. This perspective or intervention paradigm, which focuses on biologically based behaviors, might be viewed as a fourth paradigm or approach to modify behavior in contrast to behavioral (i.e. learning theory-based), biochemical (i.e. pharmacological), and psychotherapeutic (i.e. including psychoanalysis and cognitive therapies) 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 (nucleus ambiguus) that regulates the heart (i.e. via the 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, eyelid opening, prosody and listening). 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), emotional states during severe challenge (e.g. grief, rage, anger, loneliness) or medical illness (e.g. senility, AIDS, fever).

Second, the middle-ear muscles play an important role in extracting human voice from our complex acoustic environment. When 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 the human voice. This difficulty in listening to the human voice might even occur in an individual who has normal hearing (i.e. normal function of the cochlea, auditory nerve, and the brain areas processing acoustic information).

Third, neural regulation of the middle-ear muscles is linked to that of the other muscles of the face, which control facial expression and vocal intonation. Thus, stimulation to improve neural regulation of the middle-ear muscles should integrate and stimulate 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 expressiveness, vocal intonation), the lower motor neurons are regulated by the upper motor neurons in the frontal cortex. During periods characterized by fight–flight behaviors and fear-induced shut-down 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 on 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 feigning death). 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 cortical regulation of the social engagement system to promote the voluntary prosocial behaviors that are lacking in autistic children. The model is optimistic, 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. 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 the 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.

Our model emphasizes the importance of extracting the human voice in social settings via cortical neural regulation of the middle-ear muscles. The intervention uses a relatively narrow frequency band that focuses on frequencies of the human voice. The acoustic stimuli are computer-altered by applying digital filters to extract specific frequencies. The filters are part of a complex

algorithm that modulates the acoustic frequency band and energy to exercise and stimulate the neural regulation of the middle-ear muscles and, hypothetically, to integrate the components of the social engagement system. We focus on the human voice because processing of the human voice is neurobiologically different from the processing of other acoustic signals, and according to our model, processing of the human voice is a component of a human social communication system, the social engagement system.

Our initial research protocol applied the intervention to children between the ages of 3 and 5 years who had a diagnosis of autism. Computer-altered acoustic stimulation was presented in a 45-min session, during which attempts were made to maintain the child in a calm behavioral state. The intervention consisted of five sessions presented on sequential days. Across the five sessions, the width of the frequency band and the total acoustic energy being presented to the child varied.

We have tested more than 65 children in a double-blind, randomized control experimental design. Most children experienced noticeable improvements in social behavior and communication skills immediately following the intervention. In addition, there were noticeable changes in parental interaction styles with the children, with the parents being less intrusive following the intervention. The improvements in the children's behavior persisted when assessed during a 3-month follow-up. We believe that although the intervention was initially tested with children diagnosed with autism, it will be useful for other populations with difficulties in listening, communicating and organizing social behavior.

## 15. Conclusions

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. 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 leads not only 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.

## Acknowledgements

This manuscript is based on an invited keynote address delivered at the 10th World Congress of the International Organization of Psychophysiology, which was held in Sydney, Australia, in February 2000. The preparation of this manuscript was supported in part by grants HD 22628 and MH60625 from the National Institutes of Health and Human Development. Several of the ideas and concepts described in this paper were the product of discussions with C. Sue Carter during a residency at the Rockefeller Foundation Conference Center in Bellagio, Italy.

## References

- Andrews, P.L.R., Lawes, I.N.C., 1992. A protective role for vagal afferents: a hypothesis. In: Ritter, S., Ritter, R.C., Barnes, C.D. (Eds.), *Neuroanatomy and Physiology of Abdominal Vagal Afferents*. CRC, Boca Raton, FL, pp. 280–302.
- Arima, H., Kondo, K., Murase, T. et al., 1998. Regulation of vasopressin synthesis and release by area postrema in rats. *Endocrinology* 139, 1481–1486.
- Bazhenova, O.V., Plonskaia, O., Porges, S.W. Vagal reactivity and affective adjustment in infants during interaction challenges. *Child Dev.*, in press.
- Braga, D.C., Mori, E., Higa, K.T., Morris, M., Michelini, L.C., 2000. Central oxytocin modulates exercise-induced tachycardia. *Am. J. Physiol.* 278, R1474–R1482.

- Bray, G.A., 1985. Autonomic and endocrine factors in the regulation of food intake. *Brain Res. Bull.* 9, 279–286.
- Bueno, L., Gue, M., Fargeas, M.J., Alvinerie, M., Junien, J.L., Fioramonti, J., 1989. Vagally mediated inhibition of acoustic stress-induced cortisol release by orally administered kappa-opioid substances in dogs. *Endocrinology* 124, 1788–1793.
- Buwalda, B., Koolhaas, J.M., Bohus, B., 1992. Behavioral and cardiac responses to mild stress in young and aged rats: effects of amphetamine and vasopressin. *Physiol. Behav.* 51, 211–216.
- Cacioppo, J.T., Malarkey, W.B., Kiecolt-Glaser, J.K. et al., 1995. Heterogeneity in neuroendocrine and immune responses to brief psychological stressors as a function of autonomic cardiac activation. *Psychosom. Med.* 57, 154–164.
- Cannon, W.B., 1928. The mechanism of emotional disturbance of bodily functions. *N. Engl. J. Med.* 198, 877–884.
- Cannon, W.B., 1957. 'Voodoo' death. *Psychosom. Med.* 19, 182–190.  
reprinted from *American Anthropologist* 44, 169 (1942).
- Carpenter, D.O., 1990. Neural mechanisms of emesis. *Can. J. Physiol. Pharmacol.* 68, 230–236.
- Carter, C.S., 1998. Neuroendocrine perspectives on social attachment and love. *Psychoneuroendocrinology* 23, 779–818.
- Carter, C.S., Altemus, M., 1997. Integrative functions of lactational hormones in social behavior and stress management. *Ann. NY Acad. Sci.* 807, 164–174.
- Cheng, Z., Powley, T.L., 2000. Nucleus ambiguus projections to cardiac ganglia of rat atria: an anterograde tracing study. *J. Comp. Neurol.* 424 (4), 588–606.
- Cheng, Z., Powley, T.L., Schwaber, J.S., Doye, F.J., 1999. Projections of the dorsal motor nucleus of the vagus to cardiac ganglia of rat atria: an anterograde tracing study. *J. Comp. Neurol.* 410, 320–341.
- De Bellis, M.D., Chrousos, G.P., Dorn, L.D. et al., 1994. Hypothalamic–pituitary–adrenal axis dysregulation in sexually abused girls. *J. Clin. Endocrinol. Metab.* 78, 249–255.
- Fan, W., Andresen, M.C., 1998. Differential frequency-dependent reflex integration of myelinated and non-myelinated rat aortic baroreceptors. *Am. J. Physiol.* 44, H632–H640.
- Ferguson, A.V., Lowes, V.L., 1994. Functional neural connections of the area postrema. In: Barraco, I.R.A. (Ed.), *Nucleus of the Solitary Tract*. CRC, Boca Raton, FL, pp. 147–157.
- Fuxe, K., Agnati, L.F., Covenas, R., Narvaez, J.A., Bunemann, B., Bjelke, B., 1994. Volume transmission in transmitter peptide costoring neurons in the medulla oblongata. In: Barraco, I.R.A. (Ed.), *Nucleus of the Solitary Tract*. CRC Press, Boca Raton, FL, pp. 75–89.
- García, J., Laister, P.S., Bermudez-Rattoni, F., Deems, D.A., 1985. A general theory of aversion learning. In: Braveman, N.S., Bronstein, P. (Eds.), *Experimental Assessments and Clinical Applications of Conditioned Food Aversions*. Annals of the New York Academy of Sciences.
- Gunnar, M.R., Porter, F.L., Wolf, C.M., Rigatuso, J., Larson, M.C., 1995. Neonatal stress reactivity: predictions to later emotional temperament. *Child Dev.* 66, 1–13.
- Hofer, M.A., 1970. Cardiac respiratory function during sudden prolonged immobility in wild rodents. *Psychosom. Med.* 32, 633–647.
- Hopkins, D.A., Bieger, D., de Vente, J., Steinbusch, W.M., 1996. Vagal efferent projections: viscerotopy, neurochemistry, and effects of vagotomy. *Prog. Brain Res.* 107, 79–96.
- Haselton, J.R., Solomon, I.C., Motekaitis, A.M., Kaufman, M.P., 1992. Bronchomotor vagal preganglionic cell bodies in the dog: an anatomic and functional study. *J. Appl. Physiol.* 73, 1122–1129.
- Jackson, J.H., 1958. Evolution and dissolution of the nervous system. In: Taylor, J. (Ed.), *Selected Writings of John Hughlings Jackson*. Stapes Press, London, pp. 45–118.
- Jansen, L.M.C., Gispen-de Wied, C.C., Kahn, R.S., 2000. Selective impairments in the stress response in schizophrenic patients. *Psychopharmacology* 149, 319–325.
- Jones, J.F.K., Wang, X.Y., Jordan, D., 1995. Heart rate responses to selective stimulation of cardiac vagal C fibers in anesthetized cats, rats and rabbits. *J. Physiol.* 489, 203–214.
- Koch, K.L., Summy-Long, J., Bingaman, S., Sperry, N., Stern, R.M., 1990. Vasopressin and oxytocin responses to illusory self-motion and nausea in man. *J. Clin. Endocrinol. Metab.* 71, 1269–1275.
- Lama, A., Delpierre, S., Jammes, Y., 1988. The effects of electrical stimulation of myelinated and non-myelinated vagal motor fibres on airway tone in the rabbit and the cat. *Respir. Physiol.* 74, 265–274.
- Landgraf, R., Mallkinson, T., Horn, T., Veale, W.L., Lederis, K., Pittman, Q.J., 1990. Release of vasopressin and oxytocin by paraventricular stimulation in rats. *Am. J. Physiol.* 258, 155–159.
- Lawes, I.N.C., 1990. The origin of the vomiting response: a neuroanatomical hypothesis. *Can. J. Physiol. Pharmacol.* 68, 254–259.
- Leslie, R.A., 1985. Neuroactive substances in the dorsal vagal complex of the medulla oblongata: nucleus of the tractus solitarius, area postrema, and dorsal motor nucleus of the vagus. *Neurochem. Int.* 7, 191–211.
- Leslie, R.A., Reynolds, D.J.M., Lawes, I.N.C., 1992. Central connections of the nuclei of the vagus nerve. In: Ritter, S., Ritter, R.C., Barnes, C.D. (Eds.), *Neuroanatomy and Physiology of Abdominal Vagal Afferents*. CRC, Boca Raton, FL, pp. 81–98.
- MacLean, P.D., 1990. *The Triune Brain in Evolution*. Plenum Press, New York.
- Miao, F. J-P., Janig, W., Green, P.G., Levine, J.D., 1997. Inhibition of bradykinin-induced plasma extravasation produced by noxious cutaneous and visceral stimuli and its modulation by vagal activity. *J. Neurophysiol.* 78, 1285–1292.
- Micheline, L.C., 1994. Vasopressin in the nucleus tractus solitarius: a modulator of baroreceptor reflex control of heart rate. *Braz. J. Med. Biol. Res.* 27, 1017–1032.
- Morris, J.L., Nilsson, S., 1994. The circulatory system. In: Nilsson, S., Holmgren, S. (Eds.), *Comparative Physiology and Evolution of the Autonomic Nervous System*. Harwood Academic Publishers, Switzerland, pp. 193–246.

- Nissen, R., Cunningham, J.R., Renaud, L.P., 1993. Lateral hypothalamic lesions after baroreceptor-evoked inhibition of rat supraoptic vasopressin neurones. *J. Physiol. (Lond.)* 470, 751–766.
- Norris, D.O., 1997. *Vertebrate Endocrinology*. Academic Press, New York.
- Paton, J.F., 1998. Pattern of cardiorespiratory afferent convergence to solitary tract neurons driven by pulmonary vagal C-fiber stimulation in the mouse. *J. Neurophysiol.* 79 (5), 2365–2373.
- Porges, S.W., 1995. Orienting in a defensive world: mammalian modification of our evolutionary heritage. A polyvagal theory. *Psychophysiology* 32, 301–318.
- Porges, S.W., 1997. Emotion: an evolutionary by-product of the neural regulation of the autonomic nervous system. *Ann. NY Acad. Sci.* 807, 62–77.
- Porges, S.W., 1998. Love: an emergent property of the mammalian autonomic nervous system. *Psychoneuroendocrinology* 23, 837–861.
- Porges, S.W., Doussard-Roosevelt, J.A., Portales, A.L., Greenspan, S.I., 1996. Infant regulation of the vagal 'brake' predicts child behavior problems: a psychobiology model of social behavior. *Dev. Psychobiol.* 29, 697–712.
- Potter, E.K., McCloskey, D.I., 1986. Effects of hypoxia on cardiac vagal efferent activity and on the action of the vagus nerve at the heart in the dog. *J. Autonomic Nerv. Syst.* 17, 325–329.
- Qu, L., Hay, M., Bishop, V.S., 1997. Administration of AVP to the area postrema alters response of NTS neurons to afferent inputs. *Am. J. Physiol.* 272 (2 Pt. 2), R519–R525.
- Reed, S.F., Ohel, G., David, R., Porges, S.W., 1999. A neural explanation of fetal heart rate patterns: a test of the polyvagal theory. *Dev. Psychobiol.* 35, 108–118.
- Richter, C.P., 1957. On the phenomenon of sudden death in animals and man. *Psychosom. Med.* 19, 191–198.
- Richter, D.W., Spyer, K.M., 1990. *Cardiorespiratory control*. In: Loewy, A.D., Spyer, K.M. (Eds.), *Central Regulation of Autonomic Function*. Oxford University Press, New York, pp. 189–207.
- Rogers RC, Hermann, GE (1992) Central regulation of brainstem gastric vago-vagal control circuits. In: Ritter S, Ritter, RC, Barnes CD (Eds), *Neuroanatomy and physiology of abdominal vagal afferents*. CRC, Boca Raton, Florida, pp. 99–134.
- Santer, R.M., 1994. Chromaffin systems. In: Nilsson, S., Holmgren, S. (Eds.), *Comparative Physiology and Evolution of the Autonomic Nervous System*. Harwood Academic Publishers, Switzerland, pp. 97–117.
- Sawchenko, P.E., Swanson, L.W., 1982. The organization of noradrenergic pathways from the brainstem to the paraventricular and supraoptic nuclei in the rat. *Brain Res. Rev.* 4, 275–325.
- Schwaber, J.S., 1986. Neuroanatomical substrates of cardiovascular and emotional-autonomic regulation. In: Magro, A., Osswald, W., Reis, D., Vanhoutte, P. (Eds.), *Central and Peripheral Mechanisms of Cardiovascular Regulation*. Plenum Press, New York, pp. 353–384.
- Spyer, K.M., Jordan, D., 1987. Electrophysiology of the nucleus ambiguus. In: Hainsworth, R., Williams, P.N., Many, D.A.G.G. (Eds.), *Cardiogenic Reflexes: Report of an International Symposium*. Oxford University Press, Oxford, pp. 237–249.
- Swanson, L.W., Sawchenko, P.E., 1977. Hypothalamic integration: organization of the paraventricular and supraoptic nuclei. *Annu. Rev. Neurosci.* 6, 269–324.
- Taylor, E.W., 1992. Nervous control of the heart and cardiorespiratory interactions. In: Hoar, W.S., Randall, D.J., Farrell, A.P. (Eds.), *Fish Physiology: The Cardiovascular System, XII*. Academic Press, New York, pp. 343–387.
- Uvnas-Moberg, K., 1987. Gastrointestinal hormones and pathophysiology of functional gastrointestinal disorders. *Scand. J. Gastroenterol.* 22 (128), 138–146.
- Uvnas-Moberg, K., 1989. Gastrointestinal hormones in mother and infant. *Acta Paediatr. Scand.* 351 (Suppl.), 88–93.
- Uvnas-Moberg, K., 1994. Role of efferent and afferent vagal nerve activity during reproduction: integrating function of oxytocin on metabolism and behaviour. *Psychoneuroendocrinology* 19, 687–695.
- Uvnas-Moberg, K., 1997. Physiological and endocrine effects of social contact. *Ann. NY Acad. Sci.* 807, 146–163.
- Vanhoutte, P.M., Levy, M.N., 1979. Cholinergic inhibition of adrenergic neurotransmission in the cardiovascular system. In: Brooks, C.McC., Koizumi, K., Sato, A. (Eds.), *Integrative Functions of the Autonomic Nervous System*. The University of Tokyo Press, Tokyo, pp. 159–176.
- Yehuda, R., Teicher, M.H., Trestman, R.K., Levengood, R.A., Siever, L.J., 1996. Cortisol regulation in posttraumatic stress disorder and major depression: a chronobiological analysis. *Biol. Psychiatry* 40, 79–88.