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ScienceDirect
Biological Psychology 74 (2007) 116–143
BIOLOGICAL PSYCHOLOGY
www.elsevier.com/locate/biopsycho

The polyvagal perspective☆

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Accepted 26 June 2006
Available online 16 October 2006

Abstract

The polyvagal theory introduced a new perspective relating autonomic function to behavior, that included an appreciation of the autonomic nervous system as a ''system,'' the identification of neural circuits involved in the regulation of autonomic state, and an interpretation of autonomic reactivity as adaptive within the context of the phylogeny of the vertebrate autonomic nervous system. The paper has two objectives: first, to provide an explicit statement of the theory; and second, to introduce the features of a polyvagal perspective. The polyvagal perspective emphasizes how an understanding of neurophysiological mechanisms and phylogenetic shifts in neural regulation leads to different questions, paradigms, explanations, and conclusions regarding autonomic function in biobehavioral processes than peripheral models. Foremost, the polyvagal perspective emphasizes the importance of phylogenetic changes in the neural structures regulating the autonomic nervous system and how these phylogenetic shifts provide insights into the adaptive function and the neural regulation of the two vagal systems.

Keywords: Autonomic nervous system; Heart rate variability; Respiratory sinus arrhythmia; Vagus; Polyvagal theory; Parasympathetic; Respiration; Vagal tone; Evolution; Phylogeny

1. Overview

The polyvagal theory (Porges, 1995) introduced a new perspective relating autonomic function to behavior. This perspective includes an appreciation of the autonomic nervous system as a ''system,'' the identification of neural circuits involved in the regulation of autonomic state, and an interpretation of autonomic reactivity as adaptive within the context of the phylogeny of the vertebrate autonomic nervous system. The polyvagal theory encourages a level of inquiry that challenges scientists to incorporate an integrative understanding of the role neural mechanisms play in regulating biobehavioral processes. The polyvagal theory requires an expansive conceptualization of the autonomic nervous system to include target organ afferent and efferent pathways, and a quest to understand the reciprocal influences and bidirectional communication between the heart and the central nervous system. The polyvagal theory provides a ''perspective'' to frame research questions and is not a static theory. Thus, as knowledge of neurophysiology increases, testable hypotheses will shape and expand the theory.

The paper has two primary objectives: first, to provide an explicit statement of the theory; and second, to introduce the features of a polyvagal perspective. The theory and perspective are discussed within the context of the history of psychophysiology. The polyvagal theory provides an important bridge from a correlative approach, that historically characterized psychophysiology, to a more integrative model, incorporating contemporary knowledge from neurophysiology and vertebrate phylogeny. The polyvagal perspective emphasizes how an understanding of neurophysiological mechanisms and phylogenetic shifts in neural regulation leads to different questions, paradigms, explanations, and conclusions regarding autonomic function in biobehavioral processes than peripheral models.

2. The polyvagal theory

2.1. Introduction

The ability to monitor, conceptualize, and interpret heart rate variability (HRV) is dependent on technologies for observing the beating of the heart, methodologies for quantifying heart rate parameters, knowledge of underlying neural mechanisms mediating beat-to-beat changes, and neurophysiological models linking autonomic regulation to psychological, physiological,

☆ The preparation of this manuscript was supported, in part, by grants MH 067446 and MH 60625 from the National Institutes of Health.
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doi:10.1016/j.biopsycho.2006.06.009

and behavioral processes. Technologies and methodologies metaphorically provide windows of observation into the assumed neural mechanisms that can result in either clear or blurred representations. However, models and theories, which organize knowledge and generate plausible explanations, drive research and create the need for specific methods. Without plausible models to synthesize information from various disciplines, it would be difficult to test hypotheses that would link peripheral autonomic function to neurophysiological theory or clinical status.

Psychophysiology is at the crossroads of several disciplines, each with preferred models, paradigms, and measures. Unlike physiology, with its focus on mechanism and structure, or cardiology, with its focus on clinical status, psychophysiology historically was driven by paradigms derived from psychology, often treating physiological parameters as if they were observable behaviors. The early psychophysiologists, defined by their use of the polygraph, applied the polygraph to ''transform'' unobservable psychological or mental processes into measurable physiological variables (e.g., Razran, 1961).

The early issues of Psychophysiology *echo* this strategy with articles describing an aphysiological treatment of physiological variables and a disinterest in neural mechanisms mediating the variables measured. Although the measures of physiological activity were operationally defined and diligently quantified, the parameters of the physiological processes measured were selected independent of either knowledge of or interest in a neurophysiological model encompassing the dynamic feedback nature of the autonomic nervous system. Even today, few psychophysiologists are trained in neuroanatomy or neurophysiology. In the early days of psychophysiology, physiological variables, transformed into an observable tracing on the polygraph, were treated similarly to overt behaviors or subjective reports. Consistent with an emphasis of treating physiology, as if it were a behavior, most psychophysiological studies applied S–R paradigms in which the stimulus was a sensory variable or psychological task, and the response was a physiological variable (see Stern, 1964). In fact, an attempt was made to use these paradigm constraints to define psychophysiology and to distinguish psychophysiology from physiological psychology, the latter being a discipline focused on manipulating physiology and monitoring behavior. This strict definition of psychophysiology no longer characterizes current research, as psychophysiologists have embraced several paradigms and incorporated an interest in the nervous system. However, an aphysiological ''operational'' model still dominates the literature and greatly influences how HRV is quantified and interpreted in the literature. For example, various strategies to quantify RSA have focused on phenomenological features (e.g., relation to respiration) and not on neurophysiological (e.g., medullary interneurons, neuropeptides, neurotransmitters) or neuroanatomical features (e.g., source nuclei of vagal efferent pathways).

2.2. History of HRV

Most studies investigating HRV have occurred during the past 40 years. Clinical interpretations and applications have an even shorter history. Integrative theories that link central nervous system structures to autonomic function, such as the polyvagal theory (Porges, 1995, 2003), have only emerged during the past few years (Berntson et al., 1994; Benarroch, 1993; Craig, 2005; Critchley, 2005; Taylor et al., 1999; Thayer and Lane, 2000). The study of HRV requires methods with a sufficient precision to accurately time beat-to-beat changes. Since this methodology was inaccessible to many researchers, the study of HRV had a slow trajectory within psychophysiology. When HRV was initially presented as a variable at the Society for Psychophysiological Research, several prominent psychophysiologists (even former presidents of the society) adamantly argued that HRV was an artifact due to poor experimental control. From their perspective, the heart had a stable rhythm and either decelerated or accelerated in response to specific stimulus conditions. To demonstrate that HRV was both an individual difference and a response variable, methods needed to be developed to accurately measure beat-to-beat changes. Techniques were developed to detect and to time accurately the onset of sequential heart beats. Engineers developed electrical circuits to identify the peak of R-waves and to time the intervals between successive heart beats with millisecond accuracy. With the advent of laboratory computers and the availability of analog to digital converters, timing became more precise and accurate and computer algorithms were able to detect R-waves and other components of the ECG. Prior to the accurate timing with laboratory computers, R–R intervals were quantified by measuring the distance between R-waves with a ruler or using a ruler to measure the output of the cardiotachograph. The cardiotachograph, invented by Boas (see Boas and Goldschmidt, 1932), was a welcomed addition to the Grass and Offner (Beckman) polygraphs that populated and defined the psychophysiologist's laboratory in the 1960s. The cardiotachograph not only provided instant visual feedback of heart rate changes, but also reduced the expense of polygraph paper by enabling the paper speed to run slower without influencing the accuracy of measurement.

Since measurement and quantitative procedures were far from standardized, in early research there is little distinction between a global concept of sinus arrhythmia and the more specific rhythmicity of respiratory sinus arrhythmia (RSA). Research on HRV initially progressed in two directions. First, there was a dominant trend towards understanding the physiological mechanisms mediating RSA. Second, clinical medicine identified specific relationships between global measures of HRV and clinical status. These two directions co-existed prior to the emergence of psychophysiology. However, in the late 1960s, with the availability of polygraphs in academic laboratories, a third trend appeared as psychophysiologists began to systematically investigate the relationship between psychological processes and HRV (e.g., Porges and Raskin, 1969).

2.3. Early studies related HRV to physiological mechanisms

Although not exhaustive, several historical studies highlight the emergence of HRV as a physiologically meaningful

measure. References to RSA were made in the early 1900s. Wundt (1902) stated that "... respiratory movements are therefore regularly accompanied by fluctuations of the pulse, whose rapidity increases in inspiration and decreases in expiration." The functional relation between the amplitude of RSA and the concept of vagal tone was clearly stated by Hering (1910). Hering reported that breathing provided a functional test of vagal control of the heart. Hering stated that "it is known with breathing that a demonstrable lowering of heart rate ... is indicative of the function of the vagi." Bainbridge (1920) attempted to explain RSA in terms of alterations in baroreceptor and volume receptor responses to changes in blood flow caused by changes in thoracic pressure associated with respiration. Anrep et al. (1936) investigated the influence of several physiological parameters on RSA, including: the influence of respiratory rate and amplitude, blood gas concentrations, and efferent cardioregulatory neural pathways.

2.4. Early studies using HRV as a clinical indicator

Eppinger and Hess (1915) stated that "... clinical facts, such as respiratory arrhythmia, habitual bradycardia, ... have furnished the means of drawing our attention to the variations in the tonus of the vagal system in man." Although Eppinger and Hess were interested in clinical medicine, their case studies described a relation between clinical problems in the regulation of autonomic function that did not have, with the available technology, a morphological correlate. Their observations are relevant to contemporary psychophysiological investigation of HRV for several reasons, including: (1) they alerted us to the importance of the vagus in mediating atypical physiological responses; (2) they related individual differences in vagal influences to individual differences in psychiatric pathology (i.e., neuroses); (3) they recognized the pharmacological sensitivity of the vagus to cholinergic agents, thereby potentially identifying pharmacological treatments; (4) they brought to the attention of the medical community the commonality of the vagal innervations of various peripheral organs and thus a possible common explanation for several clinical disorders.

2.5. HRV as a psychophysiological variable

Although it might be argued that HRV cannot be studied without an understanding of the neural regulation of the heart and the construct of a feedback system, interest in the neural regulation of the heart was not a major concern during the founding years of psychophysiology as a discipline. During these early years two apparently conflicting models drove research in cardiovascular psychophysiology: one, proposed by Lacey (1967), hypothesized that baroreceptors were involved in mediating the relation between sensory thresholds and short latency directional heart rate changes; and the other, proposed by Obrist (1981), linked heart rate levels to metabolic demands. Both models emphasized heart rate level and the direction of beat-to-beat heart rate changes. Variability of heart rate did not fit within either model. In fact, since early psychophysiology evolved out of S–R paradigms, heart rate changes were viewed as dependent variables similar to psychological processes (e.g., stimulus detection or attention) consistent with the Lacey model, or observable behaviors (e.g., reaction time or movement) consistent with the Obrist model. Within these prevalent models, HRV could be viewed as error variance due to poor experimental control. These theoretical positions, if taken to an extreme, would assume that alterations in heart rate would be entirely under the control of experimental or environmental demands. This, of course, is in direct contradiction to our current knowledge of the dynamic relationship between the heart and the central nervous system and the influence of this interaction on the production of HRV.

Consistent with the descriptive treatment of autonomic responses in psychophysiology, HRV was introduced as an operationally defined descriptive variable, similar to an observable behavior, without neurophysiological attributions. Early studies quantified HRV as the variability of beat-to-beat or second-to-second patterns. Three experimental approaches were applied: (1) an individual difference model treating HRV as a trait-like variable similar to "temperament" or a "clinical diagnosis" variable that predisposes an individual to respond behaviorally and autonomically with a predictable pattern; (2) the measurement of changes in HRV as a measure of mental effort or attention; (3) operant conditioning experiments that demonstrated that HRV could be placed under stimulus control.

Difficulties in conceptualizing HRV as a robust psychophysiological variable, were, in part, due to its use as both an individual difference related to behavioral impulsivity or physiological reactivity and as a dependent variable sensitive to sustained attention. Lacey and Lacey (1958) reported that individuals with greater HRV (i.e., a measure of autonomic lability) were more behaviorally impulsive. This was preceded by Eppinger and Hess (1915), who had described a vagotonic syndrome with clinical features that included an exaggerated RSA. Consistent with this interest in HRV as an individual difference variable, Porges (1972, 1973) reported that individuals with greater baseline HRV had faster reaction times and expressed larger changes in HRV during an attention task. Kalsbeek and Ettema (1963) demonstrated a reduction in HRV during increases in mental load. Lacey (1967) noted, but did not quantify, that heart rate appeared to stabilize during attention. Porges and Raskin (1969) quantified HRV and demonstrated that HRV was significantly depressed during attention demands. These paradigms were extended to human neonates and studies confirmed that during sustained stimulus presentation, HRV was reduced and individual differences in baseline HRV were correlated with heart rate reactivity (Porges, 1973). Additionally, studies from the Lang laboratory investigated the effects of feedback in the regulation of HRV (Hnatiow and Lang, 1965; Lang et al., 1967). Sayers (1973) introduced spectral analyses as a method for quantifying HRV during ergonomic tasks. This was followed by the introduction of cross-spectral analysis (Porges, 1976) as a strategy to describe the coupling between respiration and heart rate and the application of spectral analysis to define a construct of cardiac vagal tone (Porges et al., 1981).

As interest in HRV increased, it was used both as an individual difference variable in obstetrics, pediatrics, developmental psychology, psychiatry, and health psychology, and as a response variable in ergonomics, human factors engineering, and cognitive sciences. The introduction of HRV required a shift in theoretical orientation in cardiovascular psychophysiology, from a paradigm-bound S–R approach that treated heart rate patterns as ''behaviors,'' to an appreciation of both the neural mechanisms mediating the rhythmic changes in heart rate and the methodologies needed for quantification.

To understand HRV from a neurophysiological perspective, it is necessary to conceptualize beat-to-beat variability as the superimposed sum of several rhythmic heart rate oscillations and slow trends most likely covarying with metabolic demands. Each prevalent periodic process is assumed to represent a potentially identifiable and quantifiable neural feedback circuit mediated by various mechanisms. The two most reliably described heart rate periodicities occur at a ''fast'' frequency associated with spontaneous breathing (i.e., RSA) and a slower or ''low'' frequency (LF) assumed to be related to the endogenous rhythm of blood pressure regulation via the baroreceptors and spontaneous vasomotor activity. Each periodicity is a product of a feedback loop, with the period representing the time constant and the amplitude representing a functional neural input modulating the cardiac pacemaker. Thus, methodologies from time series statistics needed to be imported to partition and decompose the beat-to-beat heart rate signal into constituent periodic components representing plausible neurophysiological feedback loops on the cardiac pacemaker.

This change in orientation required a new conceptualization of the autonomic nervous system that shifted emphasis from target organs in the periphery to central-peripheral neural feedback ''circuits.'' With new models came contradictions of earlier views of autonomic function. Psychophysiology had focused on the ''motor'' component of the autonomic nervous system, consistent with Langley's (1921) emphasis on the motor output of the autonomic nervous system solely as a motor system. Thus, heart rate, similar to any other observable behavior, was treated as a ''response.'' In contrast, a ''system'' model incorporates an elaboration of feedback mechanisms from the periphery and central modulators of the output gain of the efferent pathways. Thus, a systems approach would not only describe the components of the feedback loop, but would also attempt to understand the features of central mechanisms mediating the gain of the output system. In the case of RSA, this would result in a focus on the features that mediate frequency and amplitude. In general, the literature demonstrates that the frequency of RSA is generated by the same brainstem mechanisms involved in generating the frequency of respiration, while the amplitude of RSA represents the functional impact of vagal efferent pathways originating in the nucleus ambiguus on the cardiac pacemaker (Haselton et al., 1992; Richter and Spyer, 1990; Spyer and Jordan, 1987).

A naïve treatment of HRV and RSA as output responses without the consequential influence of afferent feedback is consistent with Langley's (1921) definition of a limited autonomic nervous system consisting solely of visceral efferent fibers and excluding the sensory fibers that accompany most visceral motor fibers. Although the definition is often expanded to include both visceral afferents and central structures (e.g., hypothalamus), contemporary textbooks focus on the motor components, minimizing in their description the important role of afferent and central contributions to the regulation of the peripheral autonomic organs. This bias, by ignoring the importance of the afferent pathways, neglects the feedback and central regulatory features of a functional system. Moreover, it limits the study of the dynamic regulatory function of the autonomic nervous system, since the regulation of visceral state and the maintenance of homeostasis implicitly assume a feedback system with the necessary constituent components of motor, sensory, and regulatory components. Thus, from a systems perspective, the autonomic nervous system includes afferent pathways conveying information regarding the visceral organs and the brain areas (e.g., medulla, hypothalamus) that interpret the afferent feedback and exert control over the motor output back to the visceral organs.

3. The polyvagal theory: a phylogenetic theory of adaptive reactions to challenge

Within this historical context, the polyvagal theory was presented (Porges, 1995) as an emerging model of neural regulation of the autonomic nervous system. In the original presentation (Porges, 1995), the following seven points were listed to summarize the theory:

(1) The vagal system does not represent a unitary dimension.
(2) There are two vagal motor systems.
(3) In mammals, the concept that vagal tone represents a single or summed system may have limited physiological or heuristic value.
(4) The functional output on the heart by the vagal efferent pathways originating in nucleus ambiguus may be monitored by RSA.
(5) The magnitude of neurogenetic bradycardia is mediated by the dorsal motor nucleus.
(6) There is a common cardiopulmonary oscillator.
(7) Primary emotions are related to autonomic function.

Additional points, as listed below, embedded in the theory have been discussed and expanded in several manuscripts (Porges, 1995, 1997, 1998, 2001a, 2003):

(1) The phylogenetic development of the neural regulation of the heart.
(2) The functional and structural distinction between the vagal efferent pathways originating in the nucleus ambiguus and the dorsal motor nucleus of the vagus.
(3) The identification and adaptive function of three phylogenetically ordered neural circuits regulating the heart.
(4) The application of the Jacksonian principle of ''dissolution'' to explain the sequencing of the response hierarchy.
(5) A proposed neural process, neuroception, that evaluates risk and modulates vagal output via higher brain structures.

(6) The neuroanatomical and neurophysiological link between the vagal regulation of the heart and the neural regulation of the striated muscles of the face and head.
(7) The important role that physiological state, via afferent feedback to brain structures, has on reactivity to environmental stimuli.
(8) The name polyvagal is used to emphasize the diverse features of the vagus, that include efferents originating primarily from two source nuclei in the brainstem and the prevalence of afferents.

The polyvagal theory provides several insights into the adaptive nature of physiological state. First, the polyvagal theory emphasizes that physiological states support different classes of behavior. For example, a physiological state characterized by a vagal withdrawal would support the mobilization behaviors of fight and flight. In contrast, a physiological state characterized by increased vagal influence (via pathways originating in the nucleus ambiguus) on the heart would support spontaneous social engagement behaviors. Second, the theory emphasizes the functional and structural links between neural control of the striated muscles of the face and the smooth muscles of the viscera. Third, the polyvagal theory (Porges, 2003) proposes a mechanism, neuroception, to trigger or to inhibit defense strategies. Neuroception, as a process, determines whether specific features in the environment elicit specific physiological states that would support either fight–flight or social engagement behaviors. Neuroception may involve areas of the temporal cortex that decode biological movement and detect the intentionality of social interactions.

The polyvagal theory emphasizes the neurophysiological and neuroanatomical distinction between two branches of the vagus and proposes that each branch supports different adaptive behavioral strategies. The theory (Porges, 1995, 1997, 1998, 2001a, 2003) articulates three phylogenetic stages of the development of the vertebrate autonomic nervous system (see Fig. 1). Each stage is associated with a distinct autonomic subsystem or circuit that is retained and expressed in mammals. These autonomic subsystems are phylogenetically ordered and behaviorally linked to social communication (e.g., facial expression, vocalization, listening), mobilization (e.g., fight–flight behaviors), and immobilization (e.g., feigning death, vaso-vagal syncope, and behavioral shutdown). The social communication system (i.e., social engagement system, see below) is dependent upon the functions of the myelinated vagus, which serves to foster calm behavioral states by inhibiting the sympathetic influences to the heart and dampening the HPA axis (e.g., Bueno et al., 1989). 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 three circuits can be conceptualized as dynamic, providing adaptive responses to safe, dangerous, or life-threatening events and contexts.

The three circuits are organized and respond to challenges in a phylogenetically determined hierarchy consistent with the Jacksonian principle of dissolution. Jackson proposed that in the brain, higher (i.e., phylogenetically newer) neural circuits inhibited lower (i.e., phylogenetically older) neural circuits and "when the higher are suddenly rendered functionless, the lower rise in activity" (Jackson, 1958). Although Jackson proposed dissolution to explain changes in nervous system function due to damage and illness, the polyvagal theory proposes a similar phylogenetically ordered hierarchical model to describe the sequence of autonomic response strategies to challenges.

Functionally, when the environment is perceived as safe, two important features are expressed. First, the bodily state is regulated in an efficient manner to promote growth and restoration (e.g., visceral homeostasis). This is done through an increase in the influence of myelinated vagal motor pathways on the cardiac pacemaker that slows the heart, inhibits the fight/flight mechanisms of the sympathetic nervous system, dampens the stress response system of the HPA-axis (e.g., cortisol), and reduces inflammation by modulating immune reactions (e.g., cytokines). Second, through the process of evolution, the brainstem nuclei that regulate the myelinated vagus became integrated with the nuclei that regulate the muscles of the face and head. This link results in the bi-directional coupling between spontaneous social engagement behaviors and bodily states. Specifically, the visceral states that promote growth and

	ANS Component	Behavioral Function	Lower motor neurons
III	Myelinated vagus *(ventral vagal complex)*	Social communication, self-soothing and calming, inhibit "arousal"	Nucleus ambiguus
II	Sympathetic-adrenal system	Mobilization (active avoidance)	Spinal cord
I	Unmeyelinated vagus *(dorsal vagal complex)*	Immobilization (death feigning, passive avoidance)	Dorsal motor nucleus of the vagus

Fig. 1. Phylogenetic stages of the polyvagal theory.

restoration are linked neuroanatomically and neurophysiologically with the muscles that regulate eye gaze, facial expression, listening, and prosody (see Porges, 2001a for review).

The human nervous system, similar to other mammals, did not evolve solely to survive in safe environments, but also to promote survival in dangerous and life-threatening contexts. To accomplish this adaptive flexibility, the human nervous system retained two more primitive neural circuits to regulate defensive strategies (i.e., fight/flight and freeze behaviors). It is important to note that social behavior, social communication, and visceral homeostasis are incompatible with the neurophysiological states and behaviors promoted by the two neural circuits that support defense strategies. Thus, via evolution, the human nervous system retains three neural circuits, which are in a phylogenetically organized hierarchy. In this hierarchy of adaptive responses, the newest circuit is used first, and if that circuit fails to provide safety, the older circuits are recruited sequentially.

By investigating the phylogeny of the regulation of the vertebrate heart (Morris and Nilsson, 1994; Porges, 1995, 1997; Taylor et al., 1999), four principles can be extracted that provide a basis for speculations regarding the neural mechanisms underlying social engagement, as well as fight–flight and freeze behaviors:

(1) There is a phylogenetic shift in the regulation of the heart from endocrine communication, to unmyelinated nerves, and finally to myelinated nerves.
(2) There is a development of opposing neural mechanisms of excitation and inhibition to provide rapid regulation of graded metabolic output.
(3) A face–heart connection evolved as source nuclei of vagal pathways shifted ventrally from the older dorsal motor nucleus to the nucleus ambiguus. This resulted in an anatomical and neurophysiological linkage between the neural regulation of the heart via the myelinated vagus and the special visceral efferent pathways that regulate the striated muscles of the face and head.
(4) 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 neural pathways embedded within cranial nerves V, VII, IX, X, XI), controlling visceromotor structures (i.e., heart, bronchi, thymus) and somatomotor structures (muscles of the face and head).

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 several social, emotional, and communication behaviors and disorders.

3.1. The vagal brake

Unique to mammals, the primary vagal regulation of the heart shifted from the unmyelinated pathways originating in the dorsal motor nucleus of the vagus to include myelinated pathways originating in the nucleus ambiguus. The myelinated vagus functions as an active vagal brake (see Porges et al., 1996), in which rapid inhibition and disinhibition of vagal tone to the heart can rapidly mobilize or calm an individual. The myelinated vagus actively inhibits the sympathetic nervous system's influences on the heart and dampens hypothalamic-pituitary adrenal (HPA) axis activity (see Porges, 2001a). Functionally, the vagal brake, by modulating visceral state, enables the individual to rapidly engage and disengage with objects and other individuals and to promote self-soothing behaviors and calm states. Developmentally, the number of myelinated vagal fibers increases linearly from 24 to 28 weeks gestation until full-term birth, when the number of fibers is comparable to those observed in adolescence (Sachis et al., 1982). In full-term infants, the myelination process is active during the first year of life, particularly during the first 3 months (Pereyra et al., 1992). Thus, deficits in the regulation of the vagal brake may be causal in deficits in social communication observed early in development. Basically, the expression of social engagement behaviors is dependent upon the regulation of visceral state by the vagal brake. If visceral homeostasis is challenged and the vagal brake is unable to regulate visceral state, then social engagement behaviors will be minimized. Thus, it is possible that psychiatric disorders, (e.g., autism, schizophrenia, reactive attachment disorder) in which compromised social behaviors are diagnostic features, are associated with neurobiological state regulation strategies that foster defensive and not social behaviors.

The mammalian heart is characterized by a relatively strong vagal influence, via the myelinated pathways, on the heart's pacemaker (i.e., sino-atrial node). Due to the tonic vagal influences on the sino-atrial node, resting heart rate is substantially lower than the intrinsic rate of the pacemaker. Even within mammals, there are large species differences in RSA, and these differences may be related to species-typical behavioral repertoire and affiliative social behavior (Grippo et al., in press). When the vagal tone to the pacemaker is high, the vagus acts as a restraint or brake, limiting 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 brake metaphor is a useful 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 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 is removed or reduced to support the metabolic requirements for mobilization and maintained or increased to support social engagement behaviors. Although there are several mechanisms to modulate heart rate, only the myelinated vagal efferent pathways, via nicotinic preganglionic receptors on the sino-atrial node, are capable of the rapid instantaneous changes that characterize RSA (see Cheng and Powley, 2000).

Although the vagus influences the heart in other vertebrates (for review, see Taylor et al., 1999), RSA and the vagal brake are constructs that are used in this paper to refer only to the unique characteristics of the myelinated vagus in the mammalian autonomic nervous system. Specifically, RSA is proposed as a portal, allowing accurate measurement of the dynamic influence of myelinated vagal efferent pathways on the sino-atrial node. Consistent with the polyvagal theory, measurement of the dynamic function of the vagal brake, via accurate quantification of RSA, provides a continuous measure of functional influence of the myelinated vagus on the heart.

Neurophysiologically, the vagal brake is removed or reduced to support the metabolic requirements for mobilization (e.g., associated with fight/flight behaviors) and maintained or increased to support social engagement behaviors. Measurement of the amplitude of RSA provides an assessment of the state of the vagal brake. Thus, the polyvagal theory frames a research agenda, by proposing that the vagal brake is related to behavioral and psychological processes along a continuum, from prosocial–affiliative interactions to adaptive fight/flight behaviors.

RSA is a naturally occurring rhythm in the heart rate pattern at approximately the frequency of spontaneous breathing. The amplitude of RSA can be quantified to provide a sensitive index of the impact of the myelinated vagus on the heart (Porges, 1995). By assessing RSA during various challenges, it is possible to measure the dynamic regulation of the vagal brake. The amplitude of RSA is not constant and varies as a function of experimental conditions in which behavioral and psychological demands are manipulated. The sensitivity of RSA to context and task demands creates a statistical problem, since RSA data tend not to be statistically stationary, although the traditional statistical methodologies used to quantify RSA (e.g., spectral analysis, peak–trough) assume stationarity. To deal with this specific statistical challenge, our laboratory developed an innovative methodology to remove the non-stationary trends and slow periodic processes via a moving polynomial procedure (see Bohrer and Porges, 1982; Porges, 1985; Porges and Bohrer, 1990; Porges and Byrne, 1992).

3.2. RSA and behavioral regulation

The literature consistently supports the model relating autonomic state to social engagement behaviors and emotion regulation proposed in the polyvagal theory. First, the literature supports the hypothesis that a high level and, to a greater extent, reliable suppression of RSA are ‘‘positive’’ indices of social and emotional regulation. In contrast, low levels and unreliable RSA modulation appear to be ‘‘risk’’ indices for difficulties in social and emotional regulation and, in some studies, associated with psychiatric disorders. Second, current research being conducted in our laboratory links individual differences in facial expressivity (i.e., facial EMG) to individual differences in RSA, with low amplitude RSA covarying with low muscle tone to the upper face.

Several laboratories report that children with behavioral regulation problems have lower baseline RSA and dampened RSA responses during testing sessions (see Calkins, 1997; Porges et al., 1996; Blair and Peters, 2003). Calkins and Keane (2004) reported that children with stable RSA suppression across the preschool period were less emotionally negative and had fewer behavior problems and better social skills than other children. RSA suppression in children has been reported to moderate social stress within the family and with peers. Only in children who did not suppress RSA was hostile-withdrawn parenting associated with higher levels of peer conflict (Leary and Katz, 2004). The specificity of the vagal branch of the autonomic nervous system in mediating affect was observed in 24-month olds who suppressed RSA, independent of cardiac pre-ejection period, a measure of sympathetic tone (see Berntson et al., 1994), with increasing distress across negative emotion tasks (Buss et al., 2005).

In preschool aged children, higher baseline RSA is correlated with greater emotional expressivity (see Cole et al., 1996). Adolescent brothers of adjudicated delinquents with higher RSA were at reduced risk for delinquency and externalizing psychopathology (see Pine et al., 1998). Katz and Gottman (1995) report that high RSA buffers the child from the effects of marital hostility. In adults, higher RSA predicts greater self-reported regulatory control and decreased negative emotional arousal in response to stressors (Fabes and Eisenberg, 1997). Kennedy et al. (2004) reported that young children with higher RSA moderated maternal restrictive-parenting practices, while mothers of children with lower RSA were more likely to report restrictive parenting practices.

In adults, poorer modulation of RSA was associated with greater social anxiety, and lower RSA was associated with greater defensiveness (Movius and Allen, 2005). Clinically anxious subjects exhibit lower and less suppression of RSA (Lyonsfield et al., 1995; Friedman and Thayer, 1998). RSA level appears to parallel the positive effects of treatment, with increases in RSA being reported only in patients with depression who exhibited a clinically significant response to treatment (Chambers and Allen, 2002). Greater RSA suppression to sad video clips has been reported to predict recovery from depression (Rottenberg et al., 2005). A recent study with borderline personality disorder (Austin et al., in press) illustrates how measures of the dynamic regulation of the vagal brake can provide insight into the behavioral and affective features of the disorder. Although initial levels of RSA in the borderline group were similar to controls, during the experiment (i.e., film clips varying in emotional content), the borderline and control groups had different trajectories. RSA progressively decreased in the borderline group, while RSA progressively increased in the control group. By the end of the

experiment, the groups differed significantly on both RSA and heart rate. The correlation between the changes in RSA and heart rate was significant only for the control group. These findings suggest that vagal mechanisms mediated the heart rate slowing in the control group, but did not mediate the heart rate speeding in the borderline group. Perhaps these findings implicated a sympathetic mechanism, as proposed in the polyvagal theory, that is potentiated only during states when the influence of the vagal brake is reduced. Consistent with this interpretation of a vulnerable state characterized by reduced influence of the vagal brake, others have reported that health factors, including cardiovascular risk (Hayano et al., 1990) and diabetes and obesity (Quilliot et al., 2001), are related to low RSA.

3.3. The social engagement system: phylogenic integration of behavioral and autonomic components

The phylogenic origin of the behaviors associated with the social engagement system is intertwined with the phylogeny of the autonomic nervous system. As the muscles of the face and head emerged as social engagement structures, a new component of the autonomic nervous system (i.e., a myelinated vagus) evolved that was regulated by the nucleus ambiguus, a medullary nucleus ventral to the dorsal motor nucleus of the vagus. This convergence of neural mechanisms produced an integrated social engagement system with synergistic behavioral (i.e., somatomotor) and visceral components, as well as interactions among ingestion, state regulation, and social engagement processes.

The neural pathways originating in several cranial nerves that regulate the striated muscles of the face and head (i.e., special visceral efferent) and the myelinated vagal fibers form the neural substrate of the social engagement system (see Porges, 1998, 2001a, 2003). As illustrated in Fig. 2, the somatomotor component includes the neural structures

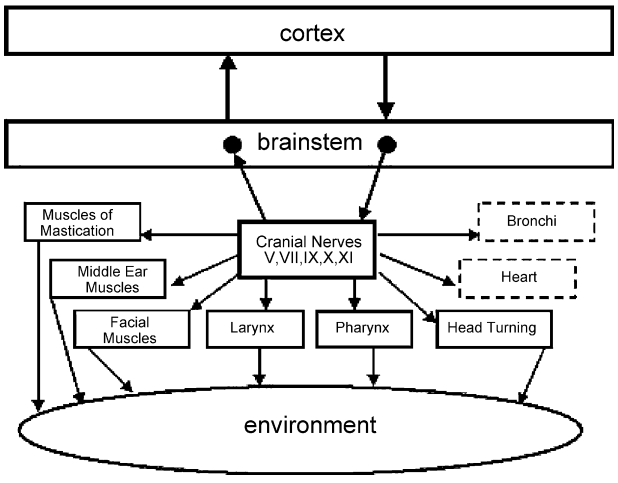

Fig. 2. The social engagement system. Social communication is determined by the cortical regulation of medullary nuclei via corticobulbar pathways. The social engagement system consists of a somatomotor component (i.e., special visceral efferent pathways that regulate the striated muscles of the face and head) and a visceromotor component (i.e., the myelinated vagus that regulates the heart and bronchi). Solid blocks indicate the somatomotor component. Dashed blocks indicate the visceromotor component.

involved in social and emotional behaviors. Special visceral efferent nerves innervate striated muscles, which regulate the structures derived during embryology from the ancient gill arches (Truex and Carpenter, 1969). The social engagement system has a control component in the cortex (i.e., upper motor neurons) that regulates brainstem nuclei (i.e., lower motor neurons) to control eyelid opening (e.g., looking), facial muscles (e.g., emotional expression), middle ear muscles (e.g., extracting human voice from background noise), muscles of mastication (e.g., ingestion), laryngeal and pharyngeal muscles (e.g., prosody and intonation), and head turning muscles (e.g., social gesture and orientation). Collectively, these muscles function both as determinants of engagement with the social environment and as filters that limit social stimuli. The neural pathways that raise the eyelids also tense the stapedius muscle in the middle ear, which facilitates hearing human voice. Thus, the neural mechanisms for making eye contact are shared with those needed to listen to human voice. As a cluster, difficulties in gaze, extraction of human voice, facial expression, head gesture and prosody are common features of individuals with autism and other psychiatric disorders.

There are interneuronal connections between the source nuclei (i.e., lower motor neurons) of special visceral efferent pathways and the source nucleus of the myelinated vagus. These neurophysiological circuits provide an inhibitory pathway to slow heart rate and lower blood pressure, which, by actively reducing autonomic arousal, promotes the calm states necessary to express social engagement behaviors and to support health, growth, and restoration. The brainstem source nuclei of this system are influenced by higher brain structures and by visceral afferents. Direct corticobulbar pathways reflect the influence of frontal areas of the cortex (i.e., upper motor neurons) on the medullary source nuclei of this system. Moreover, feedback through the afferent vagus (e.g., tractus solitarius) to medullary areas (e.g., nucleus of the solitary tract) influences both the source nuclei of this system and the forebrain areas that are assumed to be involved in several psychiatric disorders (e.g., Craig, 2005; Thayer and Lane, 2000). In addition, the anatomical structures involved in the social engagement system have neurophysiological interactions with the HPA axis, the social neuropeptides (e.g., oxytocin and vasopressin), and the immune system (for overview, see Carter, 1998; Porges, 2001b).

Afferents from the target organs of the social engagement system, including the muscles of the face and head, provide potent afferent input to the source nuclei regulating both the visceral and somatic components of the social engagement system. Thus, activation of the somatomotor component (e.g., listening, ingestion, lifting eyelids) could trigger visceral changes that would support social engagement, while modulation of visceral state, depending on whether there is an increase or decrease in the influence of the myelinated vagal efferents on the sino-atrial node (i.e., increasing or decreasing the influence of the vagal brake), would either promote or impede social engagement behaviors. For example, stimulation of visceral states that would promote mobilization (i.e., fight or flight behaviors) would impede the ability to express social engagement behaviors.

The polyvagal theory provides an explicit neurobiological model linking difficulties in spontaneous social behavior to both facial expressivity and the regulation of visceral state. Alternatively, the theory describes mechanisms through which social behaviors may serve as regulators of physiological activity and vice versa. The theory also proposes plausible mechanisms through which visceral states might form a core domain of several psychiatric profiles. Relevant to this focus on psychiatric disorders are the specific deficits, associated with several diagnoses, in both the somatomotor (e.g., poor gaze, low facial affect, lack of prosody, difficulties in mastication) and visceromotor (difficulties in autonomic regulation resulting in cardiopulmonary and digestive problems) components of the social engagement system. For example, clinicians and researchers have documented these deficits in individuals with autism spectrum disorders. Deficits in the social engagement system would compromise spontaneous social behavior, social awareness, affect expressivity, prosody, and language development. In contrast, interventions that improve the neural regulation of the social engagement system, hypothetically would enhance spontaneous social behavior, state and affect regulation, reduce stereotypical behaviors, and improve vocal communication (i.e., including enhancing both prosody in expressive speech and the ability extract human voice from background sounds).

Sound in our environment impinges on the eardrum and causes it to vibrate. These vibrations are transduced from the eardrum to the inner ear via the small bones in the middle ear known as ossicles. The stapedius muscle (innervated via a branch of the facial nerve) and the tensor tympani (innervated via a branch of the trigeminal nerve), when innervated, stiffen the ossicular chain and dampen the amplitude of the low frequency sounds reaching the inner ear. The functional impact of these muscles on the perceived acoustic environment is to markedly attenuate low frequency sounds and to facilitate the extraction of high frequency sounds associated with human voice. For example, our acoustic environment is often dominated by loud low frequency sounds that have the functional effect of masking the soft high frequency sounds associated with human voice. In humans, the ossicular chain is regulated primarily by the stapedius muscle, and tensing the stapedius prevents this masking effect (see Borg and Counter, 1989). In fact, individuals who can voluntarily contract middle ear muscles exhibit an attenuation of approximately 30 dB at frequencies below 500 Hz, while there is no or minimal attenuation at frequencies above 1000 Hz (see Kryter, 1985).

The structures at the end of the mandible (i.e., jaw bone) that define components in the middle ear became detached during the phylogenetic transition from reptiles to mammals (Luo et al., 2001; Rowe, 1996; Wang et al., 2001). It has been proposed that this detachment overcame a structural restriction that allowed the cranium to expand in mammals. With the evolution of a neural system that regulated the ossicles, low amplitude, relatively high frequency, airborne sounds (i.e., sounds in the frequency band of human voice) could be heard, even when the acoustic environment was dominated by low frequency sounds.

Studies have demonstrated that the neural regulation of middle ear muscles is defective in individuals with language delays, learning disabilities and autism spectrum disorders (Smith et al., 1988; Thomas et al., 1985). Middle ear infection (i.e., otitis media) may result in a total inability to elicit the ''reflexive'' contraction of the stapedius muscles (Yagi and Nakatani, 1987). Disorders that influence the neural function of the facial nerve (i.e., Bell's Palsy), not only influence the stapedius reflex (Ardic et al., 1997), but also affect the patient's ability to discriminate speech (Wormald et al., 1995). Thus, the observed difficulties that individuals with language difficulties (e.g., language delay, autism, etc.) have in extracting human voice from background sounds may be dependent on the same neural system that regulates facial expression (i.e., the social engagement system).

3.4. Disorders of the social engagement system: maladaptive or adaptive behavioral strategies?

Several psychiatric and behavioral disorders are characterized as having difficulties in establishing and maintaining social relations. Diagnostic features often include difficulties both in expressing social behavior and in reading social cues (i.e., social awareness). These features are observed in a variety of psychiatric diagnoses, including autism, social anxiety, posttraumatic stress disorder, and reactive attachment disorder.

Although a compromised social engagement system results in ''maladaptive'' social behavior, do these asocial behavioral strategies have ''adaptive'' features? The phylogeny of the vertebrate autonomic nervous system serves as a guide to understand these adaptive features. Phylogenetically, the vertebrate autonomic nervous system follows three general stages of development. In the mammalian autonomic nervous system, the structures and circuits representing each of the stages remain, but have been co-opted for various adaptive functions. The neural circuit associated with each stage supports a different category of behavior, with the phylogenetically most recent innovation (i.e., the myelinated vagus) capable of supporting high levels of social engagement behavior. Since the neural regulation of the myelinated vagus is integrated into the social engagement system, when the social engagement system is compromised, the effects are both behavioral and autonomic. The resultant changes in autonomic state support a range of adaptive defensive behaviors. Specifically, the compromised social engagement system (see Fig. 2) is associated, neurophysiologically, with a change in autonomic regulation characterized by a reduction in the influence of the myelinated vagus on the heart. The removal of the regulatory influence of the myelinated vagus on the heart potentiates the expression of the two phylogenetically older neural systems (i.e., sympathetic nervous system, unmyelinated vagus). These two older neural systems foster mobilization behaviors of fight and flight, via the sympathetic nervous system, or immobilization behaviors of death feigning, freezing, and behavioral shut down via the unmyelinated vagus.

3.5. Neuroception

To effectively switch from defensive to social engagement strategies, the mammalian nervous system needs to perform two important processes: (1) to assess risk, and (2) if the environment is perceived as safe, to inhibit the more primitive limbic structures that control fight, flight, or freeze behaviors. The nervous system, through the processing of sensory information from the environment (and viscera), continuously evaluates risk. Since the neural evaluation of risk does not require conscious awareness and may involve subcortical limbic structures (e.g., Morris et al., 1999), the term neuroception was introduced to emphasize a neural process, distinct from perception, that is capable of distinguishing environmental (and visceral) features that are safe, dangerous, or life threatening. In safe environments, autonomic state is adaptively regulated to dampen sympathetic activation and to protect the oxygen dependent central nervous system, and especially the cortex, from the metabolically conservative reactions of the dorsal vagal complex. However, how does the nervous system know when the environment is safe, dangerous, or life threatening, and what neural mechanisms evaluate this risk?

Neuroception might involve feature detectors in the temporal cortex (see below), since these structures respond to familiar voices and faces and hand movements and influence limbic reactivity. In most individuals (i.e., without a psychiatric disorder or neuropathology), the nervous system evaluates risk (i.e., neuroception) and matches neurophysiological state with the actual risk of the environment. When the environment is appraised as being safe, the defensive limbic structures are inhibited, enabling social engagement and calm visceral states. In contrast, some individuals experience a mismatch, and the nervous system appraises the environment as being dangerous, when it is safe. This mismatch results in physiological states that support fight, flight, or freeze behaviors, but not social engagement behaviors. According to the theory, social communication can be expressed efficiently through the social engagement system, only when these defensive circuits are inhibited. Neuroception represents a neural process that enables mammals to engage in social behaviors by distinguishing safe from dangerous contexts. Neuroception is proposed as a plausible mechanism mediating both the expression and the disruption of positive social behavior, emotion regulation, and visceral homeostasis.

New technologies, such as fMRI, have identified specific neural structures that are involved in detecting risk. The temporal lobe is of particular interest in expanding the construct of neuroception and in identifying neural mechanisms that, by detecting and evaluating risk, modulate the expression of adaptive defensive behaviors and autonomic states. Functional imaging techniques document that areas of the temporal cortex, fusiform gyrus, and superior temporal sulcus are involved in evaluating biological movement and intention, including the detection of features such as movements, vocalizations, and faces, which contribute to an individual being perceived as safe or trustworthy (Adolphs, 2002; Winston et al., 2002). Slight changes in these stimuli can pose threat or signal endearment. Connectivity between these areas of the temporal cortex and the amygdala suggests a top–down control in the processing of facial features that could inhibit activity of the structures involved in the expression of defensive strategies (Pessoa et al., 2002).

Neuroanatomical and neurophysiological research with animals provides additional information regarding the modulation and inhibition of defensive behaviors via well-defined connections among the amygdala, the periaqueductal gray (PAG), and the autonomic nervous system. The PAG is a heterogeneous midbrain structure that consists of gray matter surrounding the cerebral aqueduct that connects the third and fourth ventricles. Studies have identified areas of the PAG that are organized to regulate flight, fight, or freeze behaviors and the autonomic states that support these behaviors (Keay and Bandler, 2001). Stimulating rostrally within the lateral and dorsolateral PAG produces confrontational defensive behaviors (i.e., fight), while stimulating caudally within the lateral PAG and dorsolateral PAG produces escape behaviors (i.e., flight). Autonomic shifts such as increases in heart rate and blood pressure parallel these behaviors. In contrast, stimulation in the region of the PAG ventrolateral to the aqueduct (vlPAG) evokes a passive reaction of immobility, a drop in blood pressure, and a slowing of heart rate. Interestingly, excitation of the vlPAG evokes an opioid-mediated analgesia that might adaptively raise pain thresholds. In addition, there is evidence of a functional connection between the central nucleus of the amygdala and the vlPAG that modulates both antinociception and immobilization (Leite-Panissi et al., 2003). Consistent with the polyvagal theory, the vlPAG communicates with the dorsal vagal complex, while the lPAG and dlPAG communicate with the sympathetic nervous system.

The detection of safety subdues the adaptive defensive systems dependent on limbic structures. This may provide a plausible model through which a neural detection of risk (i.e., neuroception) would modulate behavioral and physiological states to support adaptive behaviors in response to safe, dangerous, or life-threatening environments. In the absence of threat, inhibitory projections from the fusiform gyrus and the superior temporal sulcus to the amygdala would be available to actively inhibit the limbic defense systems. This inhibition would provide an opportunity for social behavior to emerge. Thus, the appearance of a friend or mate would subdue the limbic activation with the biobehavioral consequences of allowing proximity, physical contact, and other social engagement behaviors. In contrast, during situations in which the appraisal of risk is high, the amygdala and various areas of the PAG are activated. The amygdala and PAG only share connections through the central nucleus of the amygdala (Rizvi et al., 1991).

Based on the relative risk of the environment, both social engagement and defense behaviors may be interpreted as either adaptive or maladaptive. For example, the inhibition of defense systems by the social engagement system would be adaptive and appropriate only in a safe environment. From a clinical perspective, it would be the inability to inhibit defense systems in safe environments (e.g., anxiety disorders, reactive attachment

disorder) or the inability to activate defense systems in risk environments (e.g., Williams syndrome) that might contribute to the defining features of psychopathology. Thus, an invalid neuroception of safety or danger might contribute to maladaptive physiological reactivity and the expression of the defensive behaviors associated with specific psychiatric disorders, that include in their diagnostic criteria a social deficit (e.g., autism, social anxiety, Williams syndrome) or fear (e.g., various phobias, obsessive-compulsive disorder) (Leckman et al., 1997). However, in most individuals, neuroception accurately reflects risk and there is a consistency between the cognitive awareness of risk and the visceral response to risk.

3.6. Co-opting the immobilization defense system for reproductive behaviors, nursing, and the formation of social bonds

Immobilization, as a defense system, is phylogenetically old and is associated with reduced metabolic demands and increased pain threshold. In reptiles, with a larger tolerance for reductions in oxygen, immobilization is a very effective defense strategy. In contrast, since mammals have a great need for oxygen, the inhibition of movement coupled with a shift in autonomic state to support the immobilization behavior (i.e., apnea and bradycardia) can be lethal (Hofer, 1970; Richter, 1957). However, several aspects of mammalian social behavior require immobilization, but immobilization without fear. Immobilization without fear is accomplished by co-opting the structures that regulate immobilization to serve a broad range of social needs, including reproduction, nursing, and pair-bonding. By focusing on the area of the PAG that coordinates freezing behavior, the primitive immobilization defense system has been modified in mammals to serve the intimate social needs of mammals. In addition, it has been reported that the vlPAG is rich in receptors for oxytocin, a neuropeptide associated with partuition, nursing, and the establishment of pair bonds (Carter, 1998; Insel and Young, 2001).

Overlapping with the area of the PAG that organizes immobility (i.e., vlPAG) are areas that, when stimulated, produce lordosis and kyphosis. The lordosis reflex is a hormone-dependent behavior displayed by female rodents and other mammalian species during mating. In most mammals, lordosis involves the female immobilizing in a crouching posture with her hind end available to the male for copulation. Neural tracing studies have demonstrated that the vlPAG is part of the neural circuit involved in regulating lordosis (Daniels et al., 1999). Kyphosis is an upright arched back posture that is accompanied by inhibition of limb movements. Kyphosis is stimulated by nipple attachment and provides an opportunity for the dam to feed simultaneously a large litter. When dams initiate a nursing bout, behavioral state shifts immediately from high activity to immobility (Stern, 1997). When the caudal portion of the vlPAG is lesioned there are important consequences: (1) kyphotic nursing decreases, (2) litter weight gains decrease, and (3) the lesioned rats are more aggressive and more frequently attack strange males (Lonstein and Stern, 1998).

3.7. Polyvagal theory: limitations and expanding explanations

The polyvagal theory provides neurophysiological organizing principles to interpret and to test hypotheses relating peripheral cardiovascular state to the psychological processes that have intrigued psychophysiologists (e.g., emotion, social engagement, fight–flight, face-to-face communication). The theory emphasizes that physiological state limits the range of social behavior and the ability to regulate emotion. Thus, creating states of calmness and exercising the neural regulation of the striated muscles of the face and head may potentiate positive social behavior by stimulating the neural regulation of the social engagement system.

The polyvagal theory does not propose that the vagus is the ultimate cause of individual differences in social engagement behaviors or emotional regulation. The efferent vagal pathway originating in the nucleus ambiguus (i.e., manifested in RSA) is one of several output systems related to emotion and social engagement behaviors. In the polyvagal theory, the source nuclei of the myelinated vagus are regulated by complex neural circuits, involving both visceral afferents and higher brain structures that influence the brainstem source nuclei controlling both the myelinated vagus and the striated muscles of the face and head (i.e., the social engagement system).

Specific central pathways from cortical and subcortical areas (involving the temporal cortex, central nucleus of the amygdala, and periaqueductal gray) are involved in the regulation of both the vagal component and somatomotor component of the social engagement system. Consistent with the polyvagal theory, others have proposed direct neural pathways that integrate emotional activity with central structures that influence autonomic function (see Phillips et al., 2003a,b; Thayer and Lane, 2000; Craig, 2005). The asymmetry of higher brain structures may also play a role in linking specific affective experiences with autonomic states. Consistent with the views that the right hemisphere appears to play a greater role in affect, especially the adaptive expression of negative affect (e.g., Canli et al., 1998; Fox, 1991; Noesselt et al., 2005; Simon-Thomas et al., 2005), the right hemisphere also appears to have a greater role in regulation of cardiac function, presumably via shifts in vagal regulation (Ahern et al., 2001; Porges et al., 1994). Although not the focus of the current paper, these central structures and their asymmetrical influence on autonomic function would be likely candidates to be involved in the hypothetical process of neuroception described above.

Most research evaluating autonomic nervous system activity and psychopathology has used designs contrasting depressed or anxious groups with control groups. Whether autonomic dysfunction or atypical autonomic regulation is causal is not established. However, in a prospective study, depressed individuals, who subsequently recovered from depression, reacted with a greater vagal (RSA) withdrawal to a sad video clip that those that did not recover (i.e., Rottenberg et al., 2005). Moreover, as Chambers and Allen (2002) have reported, RSA appears to parallel the positive

effects of treatment, with increases in RSA being reported only in patients who exhibited a clinically significant response to treatment (Chambers and Allen, 2002). Reduced RSA associated with depression has been hypothesized to produce clinically significant cardiac events related to cardiovascular disease (Sloan and Bigger, 1991). This influence might occur through a top–down modulation of the brainstem centers regulating the baroreceptors, and result in increased blood pressure lability. Animal research supports the importance of projections from the medial prefrontal cortex to the nucleus of the solitary tract (i.e., the source nucleus of the afferent vagus) in modulating autonomic state by cortico-solitary projections regulating the baroreflex (Owens et al., 1999).

The polyvagal theory leads to theory-driven research that will provide a plausible neurobiological foundation for the explanation and assessment of variants of social-emotional behavior and disorders, including the compromised social behavior observed during physical illness and psychiatric disorders. The polyvagal theory supports research that breaks the tradition of single variable psychophysiological research, by identifying theoretically relevant variables involved in the regulation of social engagement behaviors. In addition, the theory provides a neurophysiological basis for understanding several relevant issues in health psychology, including the benefits of social support and face-to-face communication on visceral regulation and health. Perhaps most relevant to psychophysiology as a science, the theory leads to testable hypotheses that will, in turn, result in modifications to the theory.

4. The polyvagal perspective

4.1. Levels of inquiry

Imbedded in the polyvagal theory is a generalizable and expansive perspective of inquiry. What are the features of this perspective? How does this perspective influence the conceptualization of research questions and paradigms in psychophysiology? The polyvagal perspective reflects a level of inquiry that emphasizes neurophysiological mechanisms and neurobiological organizing principles to determine how heart rate measures, as non-invasive features of adaptive neural circuits, are related to psychological, behavioral, and health processes. The approach seeks to understand the ''why'' and ''how'' of the observed relations between heart rate variables and psychological, behavioral, and clinical processes. From this perspective, the polyvagal theory is pragmatically fluid as knowledge regarding the ''why'' and ''how'' of neurophysiological regulation of the autonomic nervous system expands.

Cardiovascular psychophysiology is influenced by theories, assumptions, and methodological biases. Often clusters of ideas and traditions within a discipline form assumed, but untested, ''discipline myths'' that drive or limit a research agenda. ''Discipline myths'' often include information that, while accurate on a descriptive level, is naïve on other levels of inquiry. Levels of inquiry drive different questions. These questions lead to different paradigms. Embedded within each paradigm are implicit assumptions regarding the mechanisms mediating heart rate parameters and how these parameters are related to cognitive, affective, or health variables.

Within the discipline of psychophysiology, heart rate and HRV traditionally have been treated as ''operationally'' defined dependent variables, similar to behavior. Within the discipline of physiology, heart rate and HRV have been treated descriptively, and, through the use of stimulation and blockade paradigms, these variables have been used to infer the influence of heart rate on global neural regulation systems (i.e., vagal or sympathetic). However, the polyvagal perspective shifts the metaphor of inquiry by emphasizing neurophysiological mechanisms and adaptive functions. For example, the polyvagal perspective emphasizes the involvement of peripheral physiological activity in a ''system,'' how this ''system'' maintains bidirectional communication between central (e.g., brain) and peripheral (e.g., autonomic, behavioral) components, and how the adaptive functions of this system relate to various phylogenetic stages (e.g., Jackson, 1958). The polyvagal perspective attempts to dispel ''discipline'' myths by questioning assumptions that do not transcend levels of inquiry.

Four global levels of inquiry have been used in the psychophysiology literature. First, heart rate parameters have been used as either dependent or individual difference variables, without acknowledging the role of specific peripheral physiological mechanisms involved in the regulation of beat-to-beat heart rate. By excluding knowledge of peripheral physiology, explanations focus on statistical issues (e.g., reliability) and sensitivity to the experimental manipulation. Second, heart rate parameters have been used as a peripheral physiological response, without acknowledging the role of specific central structures and neural pathways and feedback circuits. By excluding this knowledge, constructs such as cardiac vagal tone emerge without an attribution to the vagal efferent pathways, the source nuclei, the influence of afferent feedback, and the profound effects that central circuits have on the selective modulation of specific vagal pathways to the heart. Third, heart rate parameters have been studied from a neurophysiological perspective. Fourth, heart rate response parameters have, as in the polyvagal theory, been studied from a neurobiological perspective that includes an understanding of phylogenetic and embryological contributions. Incorporation of phylogenetic information allows an understanding of the adaptive nature of the heart rate response.

The polyvagal theory provides a perspective that encourages an appreciation of both underlying neurophysiological processes and neuroanatomical structures that express both developmental and adaptive phylogenetic transitions. The polyvagal perspective builds on the underlying neural structures, mechanisms, and processes related to adaptive autonomic reactions. This perspective guides research toward testing specific hypotheses, searching for specific neural mechanisms and mediators, asking fundamental questions regarding adaptive features of specific responses, and formulating specifications for methods and techniques. For example, the polyvagal perspective could address several contemporary issues including: (1) how RSA is quantified; (2)

how HRV is decomposed and the components interpreted; and (3) how the mechanisms mediating HRV are related to the expression of emotion and the facilitation of social engagement (e.g., social engagement system).

4.2. Heart rate and HRV: a psychological perspective

As psychophysiology grew as a discipline, it influenced several areas of psychology (e.g., developmental, clinical, social, health). Researchers in these subdisciplines embraced the use of physiological variables as an index or window into the psychological processes they studied (e.g., stress, attention, mental effort). Physiological variables were assumed to be objective measures of psychological processes, especially when the processes were difficult to infer from observable behaviors. For example, in the late 1960s, heart rate deceleration was demonstrated to parallel the changes in stimulus parameters theoretically assumed to elicit an orienting response (Graham and Clifton, 1966). Heart rate deceleration, as a quantifiable physiological response, was rapidly transformed into a psychological construct, cardiac orienting (e.g., Jackson et al., 1971). As a construct, cardiac orienting emphasized the covariation between a psychological process (i.e., orienting) and a physiological response (i.e., heart rate deceleration). However, cardiac orienting implied not only that when an individual oriented heart rate decelerated, but also that when heart rate decelerated orienting occurred. This logic illustrates how, without an understanding of the neural regulation of the heart, a false assumption regarding a bidirectional covariation between psychological and physiological processes may be made.

The misunderstanding starts with the application of an experimental design and statistics to test hypotheses related to covariation (i.e., regression). Using this strategy, the literature illustrates a strong covariance between the occurrence of orienting and heart rate deceleration. However, the statistical model employed in the experimental design had an implicit directionality and, while focusing on the link from orienting to heart rate deceleration, did not test adequately whether there was a strong link from heart rate decelerations to orienting. The model neglects the possibility that the heart rate decelerates during conditions that are not related to ‘‘orienting.’’ However, an understanding of neural regulation of the heart would identify several neural mechanisms that produce rapid heart rate decelerations (such as heart rate reactions to movement, intention to move, posture shifts, breaths, and numerous well-documented vagal reflexes) that occur independently from the psychological process of orienting. Thus, a correlation between heart rate deceleration and orienting could approach zero when starting with the data domain of heart rate decelerations, or approach unity when starting with the data domain of orienting behaviors elicited by stimuli in the laboratory.

An extreme example of the successful acceptance of heart rate in psychological paradigms is found in research in which heart rate is treated as an observable behavior similar to the coding of behavior in videos. In this example, coders transcribe heart rate values from digital displays when testing infant responses to various stimuli (e.g., Blass and Watt, 1999). These quantification procedures follow the rules used to code observable behavior. These measures of heart rate, similar to the coding of behavioral data, have high inter-rater reliability. However, this strategy does not question the accuracy of the heart rate displayed on the monitor or the precision of the R-wave detection. Nor does it question the embedded algorithm found in the clinical device that may display a running average and dampen abrupt changes in heart rate. From a dependent variable perspective, the strategy focuses not on mechanism, but solely on reliability of the observer and sensitivity of the operationally defined variable to the experimental manipulation. Research that treated physiology as a behavior dominated the early history of psychophysiology and related areas that have applied physiological variables as ‘‘correlates’’ or indicators of psychological processes or psychiatric conditions. Unfortunately, a lack of knowledge in physiology, neurophysiology, phylogeny, and adaptive function has great impact on the questions, paradigms, methods, and interpretations available in psychophysiology.

In autonomic conditioning paradigms, heart rate measures have been treated similar to observable behaviors. Although these studies are characterized by careful experimental procedures, there have been major failures. Some of these failures may be attributed to a misunderstanding of the neural mechanisms mediating the responses. In some cases, the failure might have been due to the experimental manipulations interacting with the neural regulation of the autonomic nervous system and confounding the ability to quantify the variables being studied.

In the late 1960s, Miller (see Miller, 1978 for review) and others attempted to extend the domain of instrumental learning to the autonomic nervous system. These studies provide an important example of this hypothetical problem. By the early 1960s, there were reliable reports of classical conditioning of heart rate in dogs (Black and Lang, 1964; Smith, 1967). In these studies, to insure that skeletal muscles did not confound or drive the heart rate responses, the dogs were completely paralyzed by curare. Consistent with their colleagues, who studied classical conditioning and were concerned that muscular activity might mediate visceral responses, Miller and others conducted experiments with rats paralyzed by curare and artificially ventilated. The initial studies demonstrated operant conditioning of heart rate and other autonomic variables. Miller (1978) stated that ‘‘these experiments were confirmed by results in three other laboratories, but later the results of apparently similar experiments progressively declined until it became impossible to repeat them in spite of extensive efforts in the author’s laboratory and elsewhere.’’ The ‘‘loss’’ of this phenomenon perplexed the psychophysiological community and the researchers tried to find an explanation (for details, see Roberts, 1978). Experimental procedures were carefully manipulated by controlling for movement and respiration. Were the data from the early studies spurious? Were the studies testing a non-existent phenomenon? Were the protocols inappropriate to study voluntary changes in heart rate and other visceral processes? The observed inability to reliably

demonstrate instrumental heart rate conditioning in a curarized mammal is obvious, if the paradigm is deconstructed from the polyvagal perspective.

From a behavioral perspective, the first concern is to remove the potential influence of skeletal motor activity on autonomic reactivity. Curare is effective in blocking the nicotinic receptors on the post-synaptic membrane of the neuromuscular junction and results in paralysis. Thus, the scientists studying classical and instrumental conditioning were effectively blocking the potential confounding influence of skeletal motor activity on the putative conditioned heart rate responses. This worked fine with the classical conditioning paradigms, but not with the instrumental conditioning paradigms.

From the polyvagal perspective, the first concern is to identify the neural mechanisms of the conditioned heart rate response and to understand the adaptive features of the response. Based on the classical conditioning literature, heart rate deceleration is reliably observed even during states of curare-induced paralysis. This observation enables us to identify the unmyelinated vagus, with its source nucleus in the dorsal motor nucleus of the vagus, as the neural mechanism mediating the classical conditioned heart rate response. This conclusion is based on the selective effects of curare on nicotinic receptors. Not only does curare block nicotinic receptors at the post synaptic membrane of the neuromuscular junction to produce paralysis, but it also blocks nicotinic preganglionic receptors in the sympathetic nervous system and in the sino-atrial node communicating with the myelinated vagus originating in the nucleus ambiguus. Thus, functionally, curare removes the primary modes of rapid neural regulation of heart rate, leaving only neural mechanisms dependent on muscarinic receptors (e.g., the unmyelinated vagus to the heart). This explains the inability to instrumentally condition heart rate in a curare preparation, while preserving the neural mechanism mediating classically conditioned responses that are mediated via muscarinic cholinergic receptors (e.g., heart rate decelerations and sudomotor activity). Roberts (1978) provides additional plausible explanations in a detailed review of the ‘‘fragility’’ of conditioning under curare.

4.3. Heart rate and HRV: a physiological perspective

The study of beat-to-beat heart rate patterns as a peripheral physiological response often involves the application of basic physiological tools (i.e., surgery, stimulation, and pharmacology manipulations) to determine neural function. For example, neural blockades can be used to determine whether vagal or sympathetic pathways regulate the heart rate response to a specific stimulus. Beta-blockers (e.g., propranolol or atenolol) can be used to determine sympathetic influences, and blocking the function of acetylcholine muscarinic receptors with atropine can be used to determine vagal influences.

Hypothetically, pharmacological blockade would be an effective method to evaluate cardiac vagal tone, if two restrictions were met: (1) the variable being measured is determined by vagal efferent action on the heart, and (2) the vagal efferent action on the heart is mediated by a homogeneous neural pathway regulated by a single neurotransmitter via a common receptor. Under these constraints, a blockade would dampen or block vagal influences on the heart without influencing other structures or neural circuits. Unfortunately, such a restricted model seldom occurs in dynamically regulated neurophysiological systems. The vagal influences on the heart via myelinated and unmyelinated vagi constitute two efferent limbs of a complex feedback circuit regulating the heart. Not only are the two vagal pathways originating in different brainstem areas, but the vagal efferent influences on the heart are conveyed through both myelinated fibers with selective influence on nicotinic preganglionic receptors, and unmyelinated fibers with selective influence on muscarinic preganglionic receptors. Since all vagal efferent fibers influence post-ganglionic muscarinic receptors, atropine is an effective blockade of total vagal efferent influence from both vagal pathways.

Standard methods of blockade or surgery, which have been used to identify vagal mechanisms mediating heart rate, cannot distinguish between the specific vagal pathways originating in either the nucleus ambiguus or the dorsal motor nucleus. Since vagal regulation of the heart is part of a complex feedback system, blockade could influence other features of the system regulating the heart. For example, a change in heart rate might, via afferent feedback, influence the heart directly, via neural mechanisms, or indirectly, through changes in vasomotor tone or blood pressure. Similarly, sympathetic blockade could influence vagal pathways indirectly by changing the state of the heart and altering afferent feedback to the central structures regulating cardiac vagal tone. Attempts to create total neural blockade by using more than one drug might, due to complex pharmacokinetics, result in interactions that cannot be explained as an additive model. In addition, partial blockade manipulations with low doses are not reliable manipulations of neural tone, since with low doses there are large individual differences in sensitivity to the traditional blockade drugs. Current research in the neurophysiology of cardiovascular regulation is generating new knowledge regarding the selectivity and specificity of vagal pathways and pre- and post-ganglionic muscarinic and nicotinic receptors (e.g., Wang et al., 1995; Neff et al., 2003). Thus, our understanding of the neural mechanisms mediating heart rate patterns derived via old methods, even the trusted blockade strategy, need to be cautiously evaluated.

4.4. Cardiac vagal tone: the search for a criterion variable

Physiological strategies may result in circular reasoning when defining a criterion variable. For example, to validate RSA, as an index of cardiac vagal tone, the researcher might demonstrate that RSA is depressed by blocking acetylcholine (i.e., the neurotransmitter of the efferent vagal pathways to the heart) transmission with atropine (e.g., Dellinger et al., 1987; Porges et al., 1982). Or, since basal heart rate is primarily under vagal control, the researcher might use the change in heart rate in response to atropine or reversibly cooling the vagus as a criterion measure and correlate this change with RSA (e.g.,

Katona and Jih, 1975). Additional examples exist in which there are attempts to refine the heart rate response as a criterion variable to contrast with RSA. For example, beta-blockers are administered to remove sympathetic influences from the heart rate response (Grossman et al., 1990a). In other studies, minute-to-minute changes in heart rate over a 24 h period, assumed to be related to physical activity, have been used as an index of cardiac vagal tone (Grossman et al., 2004).

What is the criterion variable for cardiac vagal tone? A major problem with concretizing and validating a measure of cardiac vagal tone is the need to identify and to agree on a criterion variable. From a physiological perspective, a variable that is extremely sensitive to manipulations known to attenuate or block vagal efferent activity would qualify. Historically, heart rate in response to atropine has been the most commonly used surrogate variable for cardiac vagal tone. Since all vagal post-ganglionic receptors are muscarinic, high doses of atropine effectively disrupt all vagal influences to the heart. This strategy assumes that the vagus acts as a unitary pathway, the vagal efferent activity can be effectively blocked by atropine, and that the sum of the vagal activity is meaningful and can be accurately assessed by the change in heart rate.

Atropine blockade as a test for vagal influence became part of the physiologist's tool box long before an in depth understanding of the function and structure of the two vagal pathways were acknowledged and studied. In our laboratory, although we acknowledge the limitations of the blockade methodology, we have used atropine blockade to emphasize the sensitivity of RSA to traditional methods for evaluating vagal influences. We have used this blockade approach with several mammalian species to confirm that RSA was mediated via the vagus (see Porges et al., 1982).

Other than correlations, how can the various methods that quantify RSA or other components of HRV be contrasted? Without an accepted criterion variable, how can an index of cardiac vagal tone be established? Consistent with the APA Task Force on Statistical Inference (1999), relative size of effect (i.e., Cohen's *d*) in response to blockade could be used to contrast the sensitivity of RSA and heart rate and to determine which variable is the better surrogate variable for cardiac vagal tone. This procedure provides a metric to contrast the sensitivity of different variables to blockade. The strategy provides a platform to empirically describe the sensitivity of several variables to vagal blockade and to determine which variable (e.g., RSA, global measures of HRV, or heart rate) is most sensitive to atropine or influenced by beta-blockade. Subsequent research can evaluate whether measures that have a validated neurophysiological mechanism are more or less sensitive to specific psychological processes and behaviors. This strategy, by identifying neural mechanisms, provides an opportunity to describe the linkage between a neurophysiological mechanism and the psychophysiological relation being studied.

Several years ago in our laboratory, HRV was monitored in college-aged male subjects during an atropine dose–response experiment (Dellinger et al., 1987). A re-analysis of the available data allows us to contrast the effect size of heart

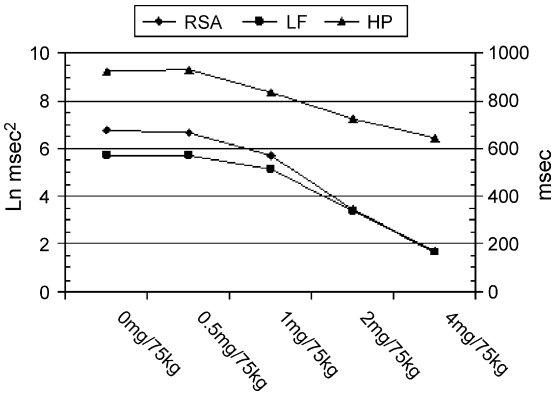

Fig. 3. Atropine sulfate dose–response curve. HP (heart period in ms), RSA (respiratory sinus arrhythmia amplitude in ln ms^2) and LF(low frequency amplitude in ln ms^2). Atropine dose is per 75 kg of body weight. A placebo was used for the 0 mg dose.

period, RSA, and a slower "LF" rhythm (0.06–0.10 Hz). As illustrated in Fig. 3, all variables exhibited strong significant dose-dependent attenuations due to atropine. In response to increasing doses of atropine, heart period became shorter and both measures of HRV substantially decreased and approached measurement error. To contrast the effect size of the variables, Cohen's *d* (Cohen, 1988) was calculated to provide a standardized estimate of effect size for all variables. Cohen's *d* is calculated by dividing the mean of the difference scores (e.g., change from a placebo dose to each dose of atropine) by the standard deviation of the difference scores. Thus, a $d = 1$ would be equivalent of a mean difference of one standard deviation in response to the treatment, independent of the unit of measurement and sample size. As a general guide Cohen proposes interpreting $d = .2$ as a small effect, $d = .5$ as a medium effect, and $d = .8$ as a large effect.

Most interesting is that the two commonly extracted periodic processes from the heart rate spectrum, RSA and LF, were extremely sensitive to atropine with effect sizes of approximately 5.0, which is twice the size of effect for heart period. Note that LF has been assumed in the literature to be sensitive to sympathetic influences and is frequently described as representing sympathovagal balance (for review, see Eckberg, 1997). If the size of effect in response to atropine were used to evaluate cardiac vagal tone, then one could empirically argue that both RSA and LF are more sensitive indices of cardiac vagal tone than heart period. These examples illustrate an application of the physiologist's toolbox in determining plausible surrogate variables for cardiac vagal tone.

In an unpublished study, partial and full neural blockades were administered to older (27–70 years of age) human participants. Consistent with the previous data, the effect size of atropine was greater for the two heart rate rhythms than for heart period. When atropine was given as the first blockade, RSA was totally abolished. The effect size of the immediate administration of atropine was above 2.0 for both RSA and LF and about 1.5 for heart period. In contrast, propranolol (a beta-blocker), although significantly influencing heart period, had no influence on either RSA or LF. However, when propranolol was

administered, while the effects of atropine were still active, there was an increase in RSA and heart period to approximately the mid-point between atropine and baseline. The effect of full blockade on heart rate is predictable and may be explained as the sum of two functional effects, one increasing heart rate (i.e., vagal blockade) and one decreasing heart rate (i.e., sympathetic blockade). However, the effect on RSA is puzzling. How can a sympathetic blockade, which has no influence on RSA when given alone, increase RSA when the participant has been "primed" with atropine? Similarly, the effect of atropine was attenuated to this "midpoint," if atropine was administered while the effects of propranolol were still active. Even more perplexing, LF, which similar to RSA was greatly attenuated with atropine and unaffected by propranolol when given separately, did not express this "midpoint" phenomenon when propranolol was given simultaneously with atropine. We recently completed an autonomic blockade study with prairie voles with similar manipulations (Grippo et al., in press). In the prairie vole, RSA was selectively reduced by atropine and not influenced by atenolol (a beta-blocker). The effect size of atropine on RSA was 2.25 compared to 0.33 for heart period. When atenolol and atropine were simultaneously administered, similar to the dual blockade study with humans described above, both heart period and RSA were at approximately 50% of baseline level. Although beta-blockade appears to diminish the effect of atropine on RSA, it does not imply that there is a sympathetic component to RSA. This effect appears to reflect a complex interaction involving pharmacokinetics and receptors, since beta-blockade by itself had not effect on RSA.

Methods that use change in heart rate in response to blockade as the criterion for quantifying neural regulation are vulnerable to the well-documented neural interactions on heart rate. If we assume that vagal influences from the nucleus ambiguus have an "inhibitory" effect on sympathetic activity, then removal of the vagal influence to the heart would simultaneously disinhibit sympathetic activity, thus, explaining why changes in vagal efferent activity have a larger impact on heart rate when sympathetic activity is high. However, since the sympathetic nervous system appears to have little or no direct influence on RSA and LF, measurement of RSA and/or LF may be more linearly related to vagal efferent activity and insensitive to the interaction due to variations in sympathetic tone observed in heart rate.

Although a powerful tool in determining global neural influences, it could be argued that the physiologist's toolbox is limited because it cannot distinguish the unique contributions of each of the two vagal pathways. A neurophysiological strategy would confirm that although the two vagal pathways are mediated by acetylcholine and can be blocked with atropine, only the vagal fibers originating in the nucleus ambiguus have a respiratory rhythm directly influencing preganglionic nicotinic receptors. Rather than emphasizing this difference between the two vagal pathways, the physiologist's toolbox supports a discipline myth that confuses the relation between RSA and neurophysiological mechanisms by relying on a surrogate criterion variable, such as change in heart rate in response to atropine (e.g., Katona and Jih, 1975), or heart rate changes associated with movement (Grossman et al., 2004), or even heart rate after a partial beta-blockade (Grossman et al., 1990a), that functionally sum across all vagal efferent influences to the heart. These techniques are theoretically and functionally removed from the unique features (e.g., a respiratory rhythm) and functions (e.g., maintaining an appropriate diffusion gradient for oxygen) of the neural pathways originating in the nucleus ambiguus (Hayano et al., 1996; Taylor et al., 1999).

Although there is general acceptance that RSA is mediated through the vagus, there is debate and confusion in the literature about whether the amplitude of RSA is a legitimate index of cardiac vagal tone. Arguments for this relation are based on the findings that RSA is virtually abolished with total vagal blockade and that RSA exhibits a dose response curve to atropine. Moreover, as illustrated in Fig. 4, the effect sizes of atropine dose on RSA are greater than on heart period. Although these findings suggest that RSA is more sensitive to vagal blockade than heart period, it has been argued that RSA must be corrected for breathing parameters to be an accurate index of cardiac vagal tone (e.g., Grossman et al., 1990a).

During the past few years, there has been a better understanding of vagal mechanisms and the neurophysiology of RSA. No longer is RSA defined solely by its covariation with peripheral respiratory activity. Neurophysiologists have established that RSA is the functional output of cardioinhibitory vagal efferent fibers that originate in the nucleus ambiguus (for review, see Porges, 1995; Neff et al., 2003), and that these pathways have a respiratory rhythm, are myelinated B-fibers, respond with short latencies, and function through nicotinic preganglionic receptors (Mendelowitz, 1996; Mendelowitz and Kunze, 1991). These vagal efferent pathways that originate in the nucleus ambiguus are inherently silent and require afferent feedback via the sensory vagus (i.e., tractus solitarius) and inputs from central structures (Neff et al., 1998a,b; Wang et al., 2001) to communicate with the sino-atrial node. Thus, the concept of a constant "central" vagal tone, independent of peripheral feedback and central modulation, is not neurophysiologically valid. Other cardioinhibitory fibers originate in the dorsal motor nucleus of the vagus. These pathways are unmyelinated C-fibers that respond with longer latencies and function through the muscarinic preganglionic receptors (Cheng and Powley, 2000). B-fibers have a faster

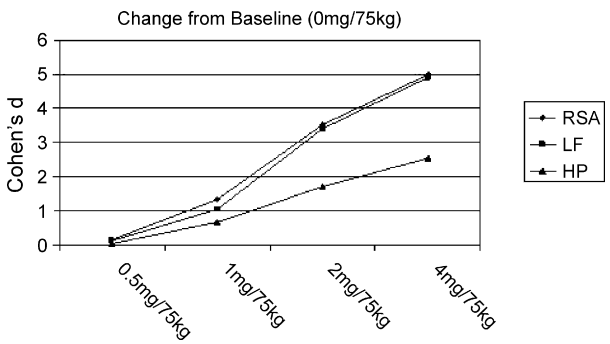

Fig. 4. Atropine sulfate dose–response curve: size of effect. Cohen's *d* is calculated for the effect size for each variable contrasting placebo condition (0 mg) with each of the four doses.

conduction velocity (3–15 m/s) than C-fibers (1–3 m/s). Stimulation of both vagal pathways produces bradycardia, although stimulation of B-fibers produces a shorter latency and larger magnitude heart rate response. Post-ganglionic vagal efferent pathways from both vagal sources function through muscarinic receptors. Thus, atropine is effective in blocking all sources of vagal activity, but does not allow the extraction of an accurate index of the function of either nucleus.

With this knowledge, a plausible model can be structured to relate RSA to cardiac vagal tone. Operationally, cardiac vagal tone (CVT) would be equivalent to the sum of the influences of the cardioinhibitory pathways originating in both the nucleus ambiguus (NA) and the dorsal motor nucleus of the vagus (DMX) or CVT = NA + DMX. Atropine blocks both vagal sources, which results in the monotonic relation between atropine dose and RSA amplitude that is observed (see Fig. 3). However, although RSA appears to be a sensitive index of vagal pathways originating in the nucleus ambiguus, there is no apparent index of the other limb of this additive model (i.e., the influence of vagal pathways originating in DMX on the heart).

4.5. The selection of measurement parameters: an implicit theory

Although less interested in physiological and neurophysiological mechanisms, psychophysiologists have set the standard for methodology by advocating greater precision and accuracy in heart beat detection and expressing a concern for methods to deal with transitory disruptions in the beat-to-beat pattern due to arrhythmia and artifact (see Porges and Byrne, 1992). In contrast, publications in physiology often rely on global measures of HRV (e.g., range, standard deviation), with less precision (e.g., use of slow sampling rates for the ECG or use of pulse waves to detect heart beat changes), and without setting a standard for editing transitory disruptions in the beat-to-beat pattern due to either arrhythmia or recording artifact.

Faulty R-wave detection or the presence of an arrhythmia will influence the timing of sequential R–R intervals with a resultant apparent rapid change in heart rate. The technologies used to describe RSA and other measures of HRV are especially vulnerable to spurious rapid changes in heart rate that will, by default, be attributed to the higher frequencies in the heart rate spectrum. Even when using the time domain algorithms (e.g., overall variance, variance in a frequency band, or breath-to-breath changes) the estimate of RSA can be confounded by faulty R-wave detections (e.g., Byrne and Porges, 1993). Thus, the quantification of RSA, regardless of the method, is extremely sensitive to artifact.

Since arrhythmias are physiological processes, why should they be edited? How would a faulty detection be identified and how should it be edited? If arrhythmias are true physiological processes, why should they be ''edited'' or adjusted in the time series of R–R intervals? Or, more specifically, which types of arrhythmias would confound the quantification of periodic rhythms in heart rate? The polyvagal perspective justifies specific solutions to specific problems of editing artifact and arrhythmias. From a neurophysiological perspective, RSA is linked to the vagal efferent influence on the sino-atrial node. RSA is an atrial rhythm. Thus, ventricular arrhythmias, such as ectopic ventricular complexes followed by a fully compensatory pause, would inflate the quantification of RSA by contributing additional variance due to ventricular activity, independent of the vagal modulation of the sino-atrial node. Therefore, these arrhythmias should be edited by summing the atypical short and compensatory long intervals. The mean of these two intervals will closely approximate the expected atrial rhythm and effectively remove the confounding ''ventricular'' source of variance. Not editing this type of arrhythmia will inflate the estimate of RSA, since the rate of heart rate change between these two beats will, via the statistical decomposition of the time series, attribute additional variance to a frequency band associated with breathing. This will occur regardless of the quantification strategy, including time domain methods (e.g., band-pass), frequency domain methods (e.g., spectral), and global descriptive statistics (e.g., peak-valley, range, variance).

Although movement artifact needs to be edited, the identification of artifact can be difficult. There are several critical issues in developing a strategy to edit artifact. From a ''dependent'' variable model, there is no information to guide the researcher. From a physiological model, we know the range of heart rate in the species. However, from a neurophysiological model, we need to know the range of heart rate change that may occur between two adjacent beats and how this range may vary as a function of neural influences. When a species has low amplitude RSA, rapid heart-to-beat changes are minimal and plotting the data can easily identify abrupt changes. Detections of artifact can be identified with simple algorithms that flag sequential beats that change by a large percent. For example, the beat-to-beat variation in humans usually fluctuates within the range of 75–135%. Missed or ''double'' detections can be corrected with algorithms based on integer arithmetic (i.e., adding or dividing the intervals of two sequential data points). However, difficulties in this decision process occur when the species tested have high amplitude RSA that can be expressed as beat-to-beat changes in the range of 50–200%. For example, adolescent humans, prairie voles, and various species of dogs have very high amplitude RSA. The prairie vole provides an interesting example of this problem. The prairie vole weighs about 50 g and, when physically active, has a heart rate similar to a mouse (see Grippo et al., in press). However, when quiescent with a partner, the heart rate is slower than a 400 g rat. When vole beat-to-beat heart rate is plotted, at times the heart period will rhythmically and rapidly transition between 100 and 200 ms. To confirm that these rapid large changes were not due to faulty R-wave detections, we developed software to superimpose the ECG on the time series of R–R intervals. The software enables the researchers to identify and correct faulty R-wave detections. Without this software, applying general rules across species (e.g., using parameters from humans, rats, or mice) would have attenuated the ''true'' RSA. This attenuation of the true amplitude of RSA would occur even if reliable rules of quantification were applied. Thus, before a strategy for artifact rejection and adjustment can be implemented, an understanding of the beat-to-beat pattern

for the participants needs to be known. The researcher needs to know the expected value of heart rate and an estimate of the distribution of change scores between adjacent beats.

The treatment of heart rate or RSA as a dependent variable similar to behavior requires only an atheoretical empirical perspective. Although this strategy may produce reliable findings, it will not lead to the development and application of methods necessary to investigate the mechanisms mediating the responses. For several years, it was assumed that ±8 ms was sufficient to quantify beat-to-beat heart rate, since many commercial clinical monitors in hospitals had this precision. Similar arguments were made with of pulse measures (e.g., derived via plethysmography, phonography, or ultrasonography) as a surrogate metric for the ECG, such that these measures were sufficient for accurate calculation of heart rate in clinical settings. This, of course, was a truthful statement in estimating average heart rate over a few seconds. However, it imposed a fuzzy lens when researchers attempted to study beat-to-beat patterns and applied statistical methods to decompose HRV into periodic components. Although poor precision in the measurement of heart rate provided stable average values, it impeded the opportunity to study small amplitude periodic components in the HRV.

Although seldom described in manuscripts, the method of beat-detection provides another example of how the precision and accuracy of quantifying R–R intervals may influence the data stream sufficiently to impede the ability to investigate neural mechanisms. Reviewers seldom query authors about the algorithms that they use to detect R-waves. Nor do they distinguish among the major sources of error variance in the quantification of heart rate: timing precision (i.e., sampling rate necessary to quantify R–R intervals), accuracy of the R-wave detection (i.e., how close to the peak of the R-wave is the detection made), treatment of faulty detections, and influence of arrhythmias.

Since cardiovascular psychophysiology is primarily conducted with commercial software and hardware, the researcher is a consumer who is seldom involved in the development and standardization of the parameters of R-wave detection and R–R quantification. Of course, precision is easily understood, and most scientists argue for a higher precision and follow guidelines of quantifying ECG at 500 Hz or 1 KHz. However, the information on R-wave detection is seldom provided. Both the amplitude of R-waves and the baseline ECG pattern influence detection of R-waves, and these parameters are not stable. To facilitate R-wave detection, electrode placement may be manipulated to maximize the R-waves relative to other components, and hardware filters can be used to stabilize the baseline ECG signal. Although filters stabilize the base level of ECG and provide a more easily observable R-wave, filters may distort the shape of the R-wave and may shift the temporal point of the peak by removing some of the higher frequency components that contribute to the R-wave.

In the early days of psychophysiology, voltage level detectors were used to drive tachometers that provided information on heart rate. To maximize the detection of R-waves, the level was often conservatively set to trigger on most beats. Since level was used and the amplitude of the R-wave varied, the part of the R-wave that triggered the level detector varied across beats. This ''error'' variance was reduced with the implementation of slope detectors that, via hardware or software, attempted to identify the inflection point of the R-wave. However, the accuracy of the slope detection is dependent on the algorithm and, in part, on the sampling rate.

The issue of precision and accuracy is imbedded in the polyvagal perspective. The polyvagal perspective motivates the researcher to study both the functional output and the peripheral and central mechanisms mediating the output of the two vagal systems. The polyvagal perspective directs the researcher to apply the best available technologies to measure low amplitude periodic processes in the beat-to-beat pattern. Thus, this perspective enables the researcher to have a vested interest in applying the most accurate and precise methods to measure R–R intervals and to search for underlying mechanisms. These issues become more problematic when organisms with low amplitude RSA are tested, such as anesthetized mammals, preterm infants, and other high-risk clinical populations.

Since the polyvagal perspective is vested in identifying underlying mechanisms, it encourages the researcher to question even the appropriateness of the R–R interval as the metric for the study of vagal influences on heart rate. This question arises through the convergence of several neurophysiological and physiological phenomena. First, cardioinhibitory vagal efferent fibers that originate in the nucleus ambiguus have a respiratory rhythm. Second, the vagal fibers synapse on the sino-atrial node. Third, the sino-atrial node is the heart's pacemaker and initiates the start of a heartbeat. Fourth, the heartbeat is initiated when depolarization spreads from the sino-atrial node through the atria and is manifested in the ECG as a p-wave. Fifth, the ''rhythmic'' cardioinhibitory vagal efferents functionally produce RSA in the heart rate pattern by inhibiting and releasing from inhibition the sino-atrial node.

Although the expected value of R–R intervals is equivalent to the expected value of p–p intervals, the sequential beat-to-beat pattern could vary. Thus, from the polyvagal perspective, the time course of p–p intervals, hypothetically, would be more sensitive than R–R intervals to the cardioinhibitory influence originating the nucleus ambiguus. Unfortunately, due to the low amplitude of the p-wave relative to the R-wave, current technology (i.e., ECG amplifiers, software algorithms) is limited, especially when the signal is being monitored through surface electrodes that have been placed to minimize movement artifact in the ECG signal. Animal models, using mammalian species with high cardiac vagal tone, might provide an opportunity to refine these technologies. However, before resources can be directed towards developing new technologies, the research community must have an in depth understanding of neural influences on the sino-atrial node.

4.6. Statistics may be misleading

Statistical techniques may mislead scientists to overestimate relationships describing the specificity between physiological

responses and psychological processes. Interpretations of strong relations between physiological variables and psychological processes are dependent on observation constraints and an implicit directionality of the relationship. Strong correlations approaching unity can be observed between physiological variables and psychological processes in laboratory paradigms focusing on the psychophysiology of affect and cognition. Although a physiological response with predictable features may always occur during a specific psychological process, this does not provide information regarding the possibility that the same physiological response may occur independent of the psychological process. Scientists often use these strong findings of physiological-behavioral parallels to argue for the identification of a specific physiological, neural, or brain signature for a psychological process. This has occurred with cardiac orienting (see above), in which heart rate deceleration was used inappropriately as an interchangeable construct with orienting and attention. Similar issues are seen with various ERP components that have been assumed only to occur during specific cognitive tasks. Most recently, fMRI imaging procedures have identified areas of the brain that are activated during affective states. These brain areas are often assumed to function solely as a source of affect without an understanding of the interconnectiveness of neural circuits and their potential functions. Other physiological variables that have been embraced by psychology, such as cortisol and oxytocin, have been used in the literature as physiological indices of psychological processes. Increases or high levels of salivary cortisol frequently have been used interchangeably with the construct of stress. This assumed isomorphism neglects the important adaptive functions of cortisol in converting norepinephrine to epinephrine, in breaking down lactate, and in regulating surfactant (e.g., see Porges, 2001b). Similarly, the important findings linking positive social experiences to oxytocin are often discussed independent of the important role that oxytocin has peripherally in regulating autonomic state (i.e., during nursing and partuition) and centrally in modulating the outflow of vagal efferent activity from the dorsal motor nucleus of the vagus (see Porges, 2001a).

A physiological state that covaries with a psychological process will generally be observed in settings independent of the context in which the psychological process occurs. This is, of course, the same problem that may be observed with measures of brain function, since the nervous system is not solely subservient to specific psychological processes, whether or not they require conscious awareness. Thus, physiological ''correlates'' of psychological processes are seldom unique and specific indicators of that process, although psychophysiology has not vested resources in investigating the covariation of psychological processes with physiological processes when ''selecting'' from a time series of physiological activity across contexts, demands, and behavioral states. Unfortunately, the assumption that there are cognitive and affective signatures in the brain and nervous system and that the search for these signatures constitutes valid scientific inquiry, promotes an intellectual drift in our science towards the treatment of physiological or neurophysiological responses as specific (as contrasted with general states that promote a range of behaviors and psychological processes) attributes of the cognitive or affective process.

Extrapolations relating psychological processes to physiological variables are often overstated, because most neurophysiological and physiological systems reflect similar features during other contexts when the psychological process of interest is not occurring. The nervous system is constantly at ''work'' and instances of physiological-behavioral covariation do not necessarily mean that the physiological parameters can be used to index specific psychological processes. The polyvagal perspective, which incorporates an emphasis on both neurophysiological mechanisms and adaptive functions, addresses this problem by proposing the plausibility that specific physiological states support or facilitate general domains of behavior such as social engagement behaviors or the defensive strategies of fight, flight, or freeze. Thus, although the covariation between a physiological variable and a psychological process clearly implicates an important relationship, to better understand the neurobiology underlying specific psychological processes, it is necessary to understand the broader range of functions in which these neural systems are involved.

Statistical techniques may mislead scientists to misinterpret constructs such as cardiac vagal tone. Regression models (i.e., either correlation or analysis of variance) may be problematic when attempts are made to validate the hypothesis that a physiological variable is mediated by a specific neural mechanism (i.e., cardiac vagal tone). Since these validation studies generally apply the physiologist's toolbox (consisting of blockade, surgery, and electrical stimulation), post treatment measures have a restricted range of individual differences relative to pre-treatment measures. Often the studies evaluating neural mechanisms are conducted while the organism is anesthetized. Anesthetics often make it difficult to study neural regulation of the heart, since several anesthetics have direct effects on vagal efferent tone to the heart.

Statistical techniques may mislead scientists to assume that highly correlated methods are interchangeable. Methods of quantifying RSA are not equivalent. Although statistics can be used to demonstrate high inter-variable correlations, these high correlations do not provide evidence of equivalence (e.g., Grossman et al., 1990b). If we return to questions of precision, we can see how this may occur. If we have a dataset of measures of RSA calculated with 1 ms precision and smooth these data to a precision of 5 ms or even 10 ms, the correlation between the two measures will be very strong and approach unity (see Riniolo and Porges, 1997). Alternatively, we can reduce precision by assigning subjects into a high and low RSA groups and correlate group assignment with individual values. With the dataset of 44 normal adults described in Denver et al. (in press), the correlation was .83. Similarly with a dataset of 94 typically developing preschool children, the correlation was .82. When each sample was divided into quartiles, the quartile assignments correlated .94 with the individual measurements of RSA. Since both samples had a similar range of RSA, the correlations were similar. Even with the restricted range of RSA observed in

these samples of healthy normal participants, the global estimate of RSA associated with group assignment (i.e., median split, quartile) was highly correlated with the individual scores. If our correlations included clinical samples with disorders such as hypertension, diabetes and depression, then the range of RSA values would expand and the correlations would potentially increase. Thus, even when the precision and accuracy of the quantification strategy is greatly reduced by smoothing across individual differences, either by reducing sampling rate and decreasing trigger accuracy or by assigning into global groups, the correlations between the highly precise and accurate methodology and the smoothed one will be very high. Thus, methodologies can blur the range of individual differences (see Riniolo and Porges, 1997) and coax investigators into assuming equivalence of methods without testing whether there are differences in sensitivity to experimental manipulations or neural influences. Researchers must, therefore, be extremely cautious of justifications for methods that focus on correlations with other established techniques, because two highly correlated methods might be differentially sensitive to individual differences and to the underlying neurophysiological mechanisms.

4.7. Decomposition of HRV: a polyvagal perspective

The publication of the international guidelines for the quantification of HRV (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996; Berntson et al., 1997) influenced how researchers reported and interpreted HRV. The guidelines proposed an extraction of high and low frequency bands from the heart rate spectrum. The high frequency band (HF) was assumed to represent vagal influences and to be statistically equivalent to the time domain methods frequently used to calculate RSA. The low frequency band (LF) has been considered to be either a marker of sympathetic modulation (e.g., Malliani et al., 1991) or influenced by both sympathetic and vagal influences (Akselrod et al., 1981). Researchers also proposed a ratio measure as a potential index of sympathico-vagal balance (Pagani et al., 1986). Many investigators assume that the frequency bands define variables that accurately assess vagal and sympathetic influences.

There are inherent problems with selecting frequency bands to quantify HRV without an understanding of neurophysiological mechanisms. These problems are exacerbated when the techniques are applied independent of an understanding that respiration parameters are age, species, and context dependent. In several experimental contexts, individual differences in spontaneous breathing rate are distributed across a broad range of frequencies, with individuals with faster breathing frequencies contributing to the HF band and individuals with slower breathing frequencies contributing to the LF band. Also problematic are manipulations that are assumed to control for variations in breathing, such as slow paced breathing (i.e., outside the frequencies defining HF), which would be represented not in the HF band, but in the LF band. In both cases, HF would no longer accurately describe RSA. However, it is possible to use a frequency band in the heart rate spectrum to quantify RSA, when the distribution of breathing frequencies is spontaneous and confirmed to reside within a selected spectral band. As demonstrated in the Denver et al. (this volume) study, the spectral decomposition of HRV provides a reliable method to estimate breathing frequency and to confirm (even if respiration is not monitored) that the selection of the frequency band to represent RSA is inclusive of individual differences in spontaneous breathing frequencies.

A disconnect between operationally defined objective measures and the physiological processes that mediate these measures has resulted in inappropriate analysis strategies. Studies have reported correlations between HF and RSA, as if these were different processes. In addition, researchers have used the frequency parameters for HF and LF developed for adult studies on human neonates (who breathe substantially faster than adults), without a consideration of what the frequency bands reflect in terms of neurophysiological processes.

The quantification of RSA is an important step towards the treatment of HRV as a defined physiological process with a specific identifiable neurophysiological mechanism. Traditional physiological techniques (i.e., cholinergic blockade with atropine) determined that RSA, as a physiological variable, is a vagal phenomenon. In our laboratory, we have focused on developing methods designed to extract accurate measures of RSA. Our methods modified time-series technologies to conform to the dynamic and often non-stationary characteristics of the beat-to-beat heart rate pattern (Porges and Bohrer, 1990; Porges and Byrne, 1992). These methods assume that HRV is a complex process in which components dynamically vary. Our methods provided new opportunities to measure how RSA interacts with behavior, psychological processes, and neurophysiological mechanisms. The methods, however, made no explicit assumption regarding potential influences on RSA from other variables, including pulmonary, movement, and the influence of special visceral efferent pathways such as nerves regulating laryngeal activity that also originate in the nucleus ambiguus. Rather, the availability of these methods provides an opportunity to evaluate and to study the dynamics of possible covariation and interaction between RSA and other physiological variables. From the polyvagal perspective, RSA is a direct measure of the vagal efferent outflow originating in the nucleus ambiguus that influences the nicotinic preganglionic receptors on the sino-atrial node. Thus, the measurement of RSA provides a unique opportunity for psychophysiologists to monitor central regulation via a peripheral measure of a neural circuit involved in the coordination of visceral state and the expression of emotion and social communication.

Consistent with the polyvagal perspective, our interest in RSA focuses on the established findings that the cardioinhibitory vagal fibers that originate in the nucleus ambiguus have a respiratory rhythm. To emphasize that our measure of RSA reflected vagal influences only from the nucleus ambiguus, we labeled the variable, V_{NA} (Porges et al., 1996). The amplitude of RSA, which we, as well as others (e.g., Grossman and Svebak, 1987), had assumed to be an index of cardiac vagal tone, was

redefined to emphasize that RSA represented only the functional output of the vagal efferent pathways originating from the nucleus ambiguus that terminate on the sino-atrial node. In the past, we have not defined or speculated what would index vagal efferent pathways originating in the dorsal motor nucleus of the vagus. However, in this paper, a method will be proposed to separate and quantify the two vagal sources from the beat-to-beat heart rate pattern.

4.8. Respiration and RSA

From a physiological perspective, RSA has been assumed to be related to breathing. For example, studies were conducted to evaluate the effect of breathing frequency and tidal volume on RSA (Hirsch and Bishop, 1981; Eckberg, 2003). These studies were conducted through the ''lens'' of a peripheral physiological model in which RSA was construed to be a dependent variable. Insights from contemporary neurophysiology and neuroanatomy have changed our view of how respiration and RSA are related. First, the medullary region, in which the vagal fibers producing RSA originate, are inherently silent and require input from other neural pathways in the brain to activate and produce the output that is manifested as RSA. Second, common medullary structures are involved in the regulation of both respiration and RSA. Third, afferent feedback, not only from the pulmonary stretch receptors, but also from chemoreceptors, baroreceptors, and other afferents traveling through the afferent vagus, influence the central mechanisms mediating RSA. Fourth, neuropeptides such as oxytocin and vasopressin influence the medullary structures regulating RSA (see Porges, 2003). Finally, higher brain structures modulate the output of the medullary nuclei and dynamically adjust the ''gain'' of the afferent feedback on the medullary structures regulating RSA.

It has been argued that RSA cannot be measured without ''pacing'' breathing or statistically correcting for respiration. What is the basis for these arguments? What does the literature tell us? A survey of the literature (see Denver et al., this issue) argues that during spontaneous breathing baselines, breathing frequency is not related to RSA. Even inspection of the early studies manipulating breathing illustrate that the strongest effect on RSA occurs when breathing is paced substantially slower than the spontaneous rate (Hirsch and Bishop, 1981). However, during conditions requiring an increase in cardiac output, within subject correlations illustrate a coordinated linear relation between breathing frequency and a decrease in RSA (e.g., Hatfield et al., 1998). Although tidal volume is influenced by changes in cardiac activity, the relationship with RSA is not linear (e.g., Hatfield et al., 1998).

If the relation between spontaneous breathing frequency and RSA is weak and may vary from study to study (and perhaps from condition to condition within subject), why is this a major argument? If the relation between RSA and tidal volume is not linear, why would linear regression models be used (e.g., Grossman et al., 2004)? Is this bias due to the method of RSA quantification? The strongest proponents for ventilatory corrections employ peak–trough methods, a technique that has been demonstrated to be vulnerable to breathing frequency (see Byrne and Porges, 1993).

Although methodology might contribute to the debate, it is not the prime issue in understanding the justification for advocating correction procedures for RSA. Rather, the debate focuses on the conflict between fundamentally different levels of inquiry and how these different levels foster the statement of research questions. The physiological perspective asks research questions relating RSA to cardiac vagal tone. The polyvagal perspective asks research questions relating RSA to neural circuits and linking these circuits to cognitive, affective, and health processes. The physiological perspective focuses on physiological models in which cardiac vagal tone is an accepted and meaningful construct when describing autonomic regulation. The polyvagal perspective focuses on the neuroanatomical, neurophysiological, and functional differences between the two vagal pathways. For example, from a physiological level of inquiry, research may be focused on establishing RSA as an index of cardiac vagal tone by applying regression models to improve the covariation of RSA with change in heart rate in response to atropine. This research strategy might include statistical adjustments involving measures of pulmonary function and motor activity. In contrast, from a polyvagal perspective, research is directed at investigations of the specific vagal pathways that originate in the two source nuclei, the nucleus ambiguus and the dorsal motor nucleus. From the polyvagal perspective, statistical adjustments (e.g., regression models adjusting for pulmonary variables) or pacing of breathing confound and distort RSA as a measure of the direct neural outflow from the nucleus ambiguus. This does not preclude the study of a global cardiac vagal tone that would include the sum of the efferent outflow from the source nuclei of both vagal pathways. For example, concepts of autonomic balance might be better described on the physiological level, since the focus is on the state of the peripheral organ.

Arguing that RSA correction procedures are a methodological issue has displaced the important dialogue questioning fundamental levels of inquiry and their related paradigms. Thus, the focus on methods and the proposition that RSA cannot be quantified without correcting or adjusting for respiration silenced the opportunity to question the mechanisms mediating RSA, the criteria for measures of cardiac vagal tone, and the use of measures of cardiac vagal tone in psychophysiological research.

4.9. Is RSA a valid measure of cardiac vagal tone?

This question depends on how cardiac vagal tone is operationally defined. The literature reliably demonstrates that cholinergic blockade depresses RSA, while RSA is insensitive to B-adrenergic blockade. Thus, the argument is not whether RSA is mediated via vagal pathways, but whether RSA can be a surrogate measure of cardiac vagal tone. Following a physiological perspective, changes in heart rate in response to cholinergic blockade has served as a surrogate criterion variable for cardiac vagal tone. This surrogate variable can be correlated with either RSA or change in RSA to the blockade. When these

variables are correlated, the relations are very strong, but not perfect. From a physiological perspective, this points to a weakness in RSA as an index of cardiac vagal tone and leads to strategies to ''correct'' RSA. However, from a neurophysiological perspective, this discrepancy is obvious. First, RSA is vagal, but it reflects only the vagal efferent pathways from the nucleus ambiguus. The vagal influence from the dorsal motor nucleus of the vagus is not included in the calculation of RSA, although it contributes to heart rate.

Why should corrections related to respiration improve the sensitivity of RSA to cardiac vagal tone? Cardiac vagal tone, by definition, represents influences from both vagal nuclei to the sino-atrial node. This can be described by the following heuristic model: CVT = NA + DMX (CVT is cardiac vagal tone, NA is the vagal tone originating from the nucleus ambiguus, DMX is the vagal tone originating from the dorsal motor nucleus of the vagus). In this model, RSA can be substituted for NA (CVT = RSA + DMX). Thus, if atropine blockade affects the post-ganglionic transmission from both vagal pathways, the relation between changes in cardiac vagal tone and changes in RSA should be monotonic, but not unity. This, of course, is seen in Fig. 3 from the atropine dose response study.

Based on data obtained using the physiologist's toolbox, a strong argument could be made that RSA is a fine surrogate for cardiac vagal tone. However, this proposition is based on an assumption that the vagal influences originating in the dorsal motor nucleus of the vagus are constant or minimal. Without measuring this vagal component, the covariation between cardiac vagal tone and RSA would be dependent of the state of the dorsal vagal system. The polyvagal theory has provided a perspective to study states in which the two systems deviate. For example, there are easily identified clinical conditions of severe and potentially lethal bradycardia that are mediated by the vagus in the absence of RSA (see Reed et al., 1999).

Is the output of the dorsal motor nucleus of the vagus influencing heart rate and the surrogate measures of cardiac vagal tone? Applying the polyvagal perspective to this question provides both an explanation of ''why'' paced breathing might improve the covariation with traditional global measures of cardiac vagal tone, and how to devise a method to extract a dynamic index of the changing influence of the DMX on the heart.

In a bold paper, Eckberg (1997) challenged the use of the LF component as an index of sympathico-vagal tone balance. The paper resulted in an interesting dialogue published in conjunction with Eckberg's article in Circulation. *Eckberg* described the paradox in which LF was sensitive to atropine, although argued to be a sensitive indicator of sympathetic activity. Most interesting, this point was not refuted in any of the comments following the paper. We observed the same effect. As illustrated in Fig. 3, LF follows an atropine dose–response curve similar to both RSA and heart period. Note that the effect sizes for LF were equivalent with RSA and about twice the size as heart period, thus, demonstrating the dependence of the LF (i.e., THM) on vagal pathways (see Fig. 4). In other research, we demonstrated that this frequency band was selectively sensitive to vagal blockade and that sympathetic blockade had no effect. Other researchers have argued similar points (Houle and Billman, 1999).

If the LF is not a direct index of sympathetic influences on the heart, could it reflect activity from the DMX? Knowledge regarding the influence of vagal fibers on the heart rate pattern is expanding. In 1995, when the polyvagal theory was published, little was known about the impact on the heart via the C-fibers originating in the DMX. It was assumed that the primary vagal influence on the heart was mediated via the B-fibers originating in the nucleus ambiguus. In addition, since few DMX fibers synapse on the sino-atrial node, it was thought that their impact on the regulation of heart rate would be minimal. Unlike global measures of heart rate or HRV, RSA was solely regulated via vagal fibers originating in the nucleus ambiguus. Thus, it appeared that RSA would be an excellent criterion variable for cardiac vagal tone. However, recent findings in neuroanatomy and neurophysiology force a reconceptualization of cardiac vagal tone and measures of HRV. This new conceptualization provides us with a basis to propose that the spectral decomposition of HRV may provide information regarding the function of both NA and DMX vagal pathways.

There is little disagreement regarding the robust relation between RSA and vagal efferent activity being transmitted from the nucleus ambiguus through the myelinated vagal fibers to the heart. The rapid transmission through nicotinic preganglionic receptors provides an opportunity to track this system, even when respiratory frequencies are very high. Contemporary research on the DMX pathways suggests that, due to unmyelinated fibers and preganglionic muscarinic receptors, cardioinhibitory traffic is slower than that originating in the nucleus ambiguus (Cheng and Powley, 2000). There are several important unanswered questions about the mechanisms and the function of these pathways on the heart. These issues include questions related to the number of preganglionic and post-ganglionic fibers, the ratio of preganglionic to post-ganglionic fibers, and the specific cardiac function of these pathways.

If we assume that CVT = LF + RSA, we can approach this model through a physiological level of inquiry. First, we could block the effect of the nicotinic receptors with hexamethonium and evaluate the effect on HRV. Since hexamethonium selectively blocks nicotinic acetylcholine receptors, it would block the vagal traffic originating only in the nucleus ambiguus. The literature demonstrates selective blockade of these pathways in animal models (e.g., Cheng and Powley, 2000), but has not evaluated its effect on RSA and whether slower oscillations remain in the heart rate spectrum. Research needs to be directed to evaluate changes in the heart rate spectrum in animal models following the administration of hexamethonium. Interestingly, since several inhalant anesthetics block nicotinic receptors, validation of the sensitivity of RSA to the nicotinic pathways could be demonstrated by monitoring RSA during the induction and maintenance of anesthesia. Under these conditions, RSA could potentially be a useful selective marker of depth of anesthesia. In the first

demonstration that the quantification of RSA could be used as an index of depth of inhalant anesthesia, we reported that isoflurane selectively depressed RSA, while not reliably influencing heart period (Donchin et al., 1985). At the time of the study, the mechanism through which isoflurane influenced RSA was not known. Consistent with the polyvagal perspective, a figure in the paper documents that the slower oscillations (LF) in the beat-to-beat pattern were preserved during anesthesia, while RSA was totally depressed. Thus, the depression of RSA might be due to the selective impact of isoflurane on the preganglionic nicotinic receptors that characterize the myelinated vagal pathways originating in the nucleus ambiguus.

Alternatively, paced breathing could be used to shift the frequency of RSA towards the endogenous rhythm associated with LF. Under conditions when participants pace breathing at 0.1 Hz, the LF (0.06–0.1 Hz) would include RSA. During this unique manipulation, if we assume that DMX pathways contribute to LF during spontaneous breathing, then slow paced breathing in the LF band would represent the summed influence of both DMX and NA vagal pathways on the heart. Interestingly, this may be the neurophysiological substrate underlying how manipulation of ventilatory parameters can change the covariation between RSA and surrogate measures of total cardiac vagal tone. However, under these constrained conditions, it would be impossible to extract information regarding the function of the two vagal systems. Also, we need to question whether a global measure of cardiac vagal tone is of use to psychophysiologists. Other strategies, relying on statistical adjustments based on simultaneously monitored ventilatory parameters, often result in derived variables adjusting RSA, not only by breathing frequency, but also by tidal volume (e.g., Grossman et al., 2004). If these derived variables are to be used as a surrogate measure for global cardiac vagal tone, generalizability needs to be investigated to determine whether they reflect parameters of an over specified statistical model.

The polyvagal perspective approaches questions regarding mechanisms, adaptive function, and specific neural pathways. In dealing with investigations relating respiration to RSA, the strategy focuses on central neural regulation and does not focus on peripheral physiology. The polyvagal perspective directs, based on our current interests, research questions towards the involvement of the nucleus ambiguus in regulating heart rate (i.e., producing RSA) and whether this area of the brainstem is causal, interactive, or consequential to respiratory and pulmonary influences. From this perspective, several research questions would be of interest. Since afferents from the trigeminal and facial nerves provide input to the nucleus ambiguus, the polyvagal perspective would focus on the influence of respiratory resistance on RSA (e.g., Sargunaraj et al., 1996).

The concept of a common cardiopulmonary oscillator fits well within a polyvagal perspective. Researchers have documented the importance of a hypothetical ‘‘respiratory gate’’ on the vagal outflow (see Eckberg, 2003). Since the respiratory rhythm is selectively gating only the vagal outflow from the nucleus ambiguus, the polyvagal theory would speculate that inspiration/expiration (*I*/*E*) ratios would influence the amplitude of RSA. Based on this neurophysiological model, vagal outflow to the sino-atrial node increases during expiration, with higher amplitude of RSA being associated with relatively longer exhalation durations. Thus, the amplitude of RSA should be related to the ratio of inspiratory and expiratory durations. There are two ways of approaching this hypothesis: (1) manipulating inspiration and expiration ratios during paced breathing, or (2) evaluating individual differences during spontaneous baseline breathing. The first strategy may confound the phenomenon, since task demands and the deviation from normal breathing patterns might trigger adaptive changes in autonomic state. The second strategy may also confound the phenomenon, since during baseline there is a restricted range of breathing patterns and the *I*/*E* ratio may covary with other variables such as weight, age, and health.

Strauss-Blache et al. (2000) approached this relation by manipulating breathing, and in our laboratory we approached the relation by investigating individual differences during spontaneous baseline breathing. Strauss-Blache et al. demonstrated that, during trials with short inspiration followed by long expiration, the amplitude of RSA was significantly greater than during trials with long inspiration followed by short expiration. These effects could not be accounted for by differences in breathing rate or amplitude. In our laboratory, we conducted a naturally occurring experiment relating individual differences in the *I*/*E* ratio to RSA. We monitored participants during a baseline condition with a Vivometrics LifeShirt. The LifeShirt monitors ECG and several ventilatory parameters including calibrated measures of tidal volume, inspiration and expiration duration, and breathing rate. Consistent with the Strauss-Blache et al. study, we observed that the *I*/*E* ratio was significantly related to the amplitude of RSA ($r(41) = -.50$, $p < .001$). However, the relations between RSA and both respiration frequency ($r = -.08$) and tidal volume ($r = -.11$) were not significant.

4.10. Conclusion

The polyvagal perspective is an attempt to apply constructs derived from the polyvagal theory to understand the discrepancies in the literature related to method of measurement, neurophysiological and neuroanatomical mechanisms, and adaptive functions of vagal efferent pathways. The approach emphasizes that biases or discipline myths occur when investigations are limited to psychological or physiological levels of inquiry. The polyvagal perspective proposes that it is necessary, not only to understand the vagal efferent actions on the heart from a neurophysiological level of inquiry, but also the adaptive function of neural regulation of the heart, interpreted within the context of the phylogeny of the autonomic nervous system. In the sections above, several discipline myths have been deconstructed and interpreted based on level of inquiry. These points are summarized below to provide targeted statements to stimulate further scientific investigations and challenges via well-designed experiments.

4.10.1. Discipline myth 1: cardiac vagal tone is a useful construct in psychophysiological research

Although tonic measures of cardiac vagal tone have an important role in understanding visceral states and in developing constructs related to autonomic balance, it is of limited use in describing and understanding response strategies to environmental and visceral stimuli. Cardiac vagal tone as a global construct provides limited information regarding specificity of the neural mechanisms through which heart rate patterns react to specific psychological stimuli, reflect health risk, and change with interventions or challenges. Measures of more specific vagal regulation, via either the nucleus ambiguus (i.e., RSA) or the dorsal motor nucleus (i.e., LF), may provide more meaningful information.

4.10.2. Discipline myth 2: to be a meaningful index of vagal influences, RSA must be adjusted by either paced breathing or by statistically adjusting for ventilatory parameters

The motivation to adjust RSA is based on empirical reports of a divergence between surrogate measures of cardiac vagal tone and RSA. Adjustments are proposed to improve the relation between RSA and the surrogate measure for total cardiac vagal tone. Although RSA is not the equivalent of total cardiac vagal tone, as an ''index'' of total cardiac vagal tone, it is at least as sensitive to blockade as traditional measures. Moreover, the validity of ''adjusted'' RSA variables as indices of cardiac vagal tone needs to be challenged by conducting dose–response blockade challenges. Even if RSA were not as sensitive as other indices of total cardiac vagal tone, RSA should be studied without adjustment. RSA is an important variable reflecting the functional output of specific vagal pathways originating in the nucleus ambiguus that are neurophysiologically and neuroanatomically linked to several processes of interest to psychophysiologists (e.g., emotion, social engagement, ingestion, health). Thus, there is no advantage in correcting RSA to map into a global surrogate variable for total cardiac vagal tone.

4.10.3. Discipline myth 3: the low frequency (LF) in the heart rate spectrum is related to sympathetic activity or sympathetic-vagal balance

The low frequency in the heart rate spectrum is exquisitely sensitive to muscarinic blockade. LF can be totally blocked when the vagal efferent influences are blocked. In fact, LF is as sensitive to vagal blockade as RSA and more sensitive to vagal blockade than heart rate. Although sympathetic influences might be involved in triggering this neural circuit, the final common pathway is purely vagal. Since features of this periodicity respond differently than RSA to various challenges and appear to be preserved during inhalant anesthesia, the time course of LF may index vagal output from the dorsal motor nucleus.

4.10.4. Discipline myth 4: methods to quantify RSA are equivalent, if they are highly correlated

High correlations, even those above 0.9, can be demonstrated between low and high-resolution measures. Measures that smooth across a broad range of individual and intra-individual differences may be correlated with methods that provide high resolution and greater sensitivity to experimental manipulations or diagnostic features. Measures that have poor precision in timing, poor accuracy in detecting the peak of the R-wave, and may be influenced by other sources of variance including baseline trends, may be highly correlated with more precise and accurate measures of RSA that incorporate statistically well defined algorithms to extract accurately the amplitude of RSA. These high correlations are not arguments for equivalence. More appropriate tests would contrast size of effects in response to known methods of vagal blockade, including manipulations that would selectively block or increase the outflow from the source nuclei of the myelinated vagal efferents located in nucleus ambiguus.

The polyvagal perspective, with an emphasis on nervous system regulation, is a major shift for psychophysiological researchers, who historically have not attributed mechanism to heart rate or HRV. In addition, this perspective leads the researcher to ask new questions, including such rudimentary issues as the establishment of data collection parameters, the methods developed to quantify various components of the heart rate pattern, and even the strategies used to correct artifact. The polyvagal perspective encourages researchers interested in autonomic-behavioral relations to expand their research agenda to include questions related to: (1) features of the source nuclei in the nucleus ambiguus and the dorsal motor nucleus of the vagus, (2) influences of the afferent vagus via the nucleus tractus solitarius on the source nuclei of both vagi, (3) the influence of ascending pathways from the nucleus tractus solitarius on brain areas regulating cognition and affect, (4) the functional differences between the vagal efferent pathways characterized by preganglionic nicotinic and muscarinic acetylcholine receptors, (5) the functional differences in the effect of myelinated and unmyelinated vagal efferent pathways on the sino-atrial node, (6) the interaction between the regulation of the special visceral efferent and myelinated vagal pathways, and (7) the influence of peripheral and central structures and circuits on modulating the output of the vagal efferent pathways.

By investigating the contradiction between methods used to measure RSA, we can see how different research questions and assumptions lead to different methods and paradigms. When research strategies are based on a peripheral physiological level of inquiry, then cardiac vagal tone is assumed to represent a unitary construct. However, when research strategies are based on a neurophysiological level of inquiry, then the quest for a measure of cardiac vagal tone is refined to focus on methods that selectively measure each of the two vagal systems. The latter strategy should be appealing to psychophysiologists, since the two vagal systems evolved to support different classes of behavior. Vagal activity originating in the nucleus ambiguus is neurophysiologically and neuroanatomically linked to the regulation of the striated muscles of the face and head, structures that are involved in social interaction and emotion. Theoretically, RSA should closely parallel individual and intra-individual variations in emotion expression, social communication, and

behavioral state. In contrast, vagal activity originating in the DMX should reflect tonic influences to the visceral organs (i.e., primarily subdiaphragmatic). Rapid and massive increases in the output of the DMX that may produce bradycardia, apnea, or defecation would occur as a defense strategy to reduce metabolic demands. Perhaps, the negative features of stress and health vulnerability being associated with the slower rhythms may have led scientists to assume that these rhythms were influenced by the sympathetic nervous system.

The polyvagal perspective shifts research from atheoretical strategies towards theory driven paradigms dependent upon explicit neural mechanisms. Foremost, the polyvagal perspective emphasizes the importance of phylogenetic changes in the neural structures regulating the autonomic nervous system. The phylogenetic strategy provides insights into the adaptive function and the neural regulation of the two vagal systems (see Porges, 1995, 2001a). Without having constructs from the polyvagal theory to describe adaptive functions and to determine the measurement specifications of the two vagal systems (one associated with calm states and social engagement behaviors and the other a vestigial defense system that is potentially lethal to mammals), it would not be possible to disentangle the mechanisms and functions of the components of cardiac vagal tone.

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