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Psychosomatics and psychopathology: looking up and down from the brain

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Summary The autonomic nervous system (ANS) plays a role in a wide range of somatic and mental diseases. Using a model of neurovisceral integration, this article describes how autonomic imbalance and decreased parasympathetic tone in particular may be the final common pathway linking negative affective states and conditions to ill health. The central nervous system (CNS) network that regulates autonomic balance (central autonomic network, CAN) is closely related and partially overlaps with networks serving executive, social, affective, attentional, and motivated behavior (anterior executive region, AER; and Damasio's [Damasio, A.R., 1998. Emotion in the perspective of an integrated nervous system. Brain Res. Rev. 26, 83–86.] 'emotion circuit'). A common reciprocal inhibitory cortico-subcortical neural circuit serves to regulate defensive behavior, including autonomic, emotional and cognitive features. This inhibitory cortico-subcortical circuit may structurally, as well as functionally, link psychological processes with health-related physiology. When the prefrontal cortex is taken 'offline' for whatever reason, parasympathetic inhibitory action is withdrawn and a relative sympathetic dominance associated with disinhibited defensive circuits is released, which can be pathogenic when sustained for long periods. This state is indicated by low heart rate variability (HRV), which is a marker for low parasympathetic activation and prefrontal hypoactivity. Consistent with this, HRV is associated with a range of psychological and somatic pathological conditions, including immune dysfunction. Finally, we discuss supportive evidence from recent studies of the reflexive startle blink, attention and working memory, which shows that low HRV predicts hypervigilance and inefficient allocation of attentional and cognitive resources.

There is growing evidence for the role of the autonomic nervous system (ANS) in a wide range of somatic and mental diseases. The ANS is generally conceived to have two major branches—the sympathetic system, associated with energy mobilization, and the parasympathetic system, associated with vegetative and restorative functions. Normally, the activity of these branches is in

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dynamic balance. When this changes into a static imbalance, for example, under environmental pressures, the organism becomes vulnerable to pathology. Modern conceptions of organism function based on complexity theory hold that organism stability, adaptability, and health are maintained through variability in the dynamic relationship among system elements (Thayer and Friedman, 1997; Friedman and Thayer, 1998a,b; Thayer and Lane, 2000). Thus, patterns of organized variability, rather than static levels, are preserved in the face of constantly changing environmental demands. One can compare this with genetic variation, which is vital in the adaptation of species. These demands can be conceived in terms of energy regulation, such that the points of relative stability represent local energy minima required by the situation. Because the system operates 'far-from-equilibrium', the system is always searching for local energy minima to minimize the energy requirements of the organism. Consequentially, optimal system functioning is achieved via lability and variability in its component processes, to allow the flexible regulation of local energy expenditure. In contrast, rigid regularity is associated with mortality, morbidity, and ill health (Lipsitz and Goldberger, 1992; Peng et al., 1994).

A corollary of this view is that autonomic imbalance, in which one branch of the ANS dominates over the other, is associated with a lack of dynamic flexibility and health. Empirically, there is a large body of evidence to suggest that autonomic imbalance, in which typically the sympathetic system is hyperactive and the parasympathetic system is hypoactive, is associated with various pathological conditions (Brook and Julius, 2000; Thayer and Friedman, 2004). In particular, when the sympathetic branch dominates for long periods of time, the energy demands on the system become excessive and ultimately cannot be met, eventuating in death. The prolonged state of alarm associated with negative emotions likewise places an excessive energy demand on the system. On the way to death, however, premature aging and disease characterize a system dominated by negative affect and autonomic imbalance.

Like many organs in the body, the heart is dually innervated. Although a wide range of physiologic factors determines heart rate (HR), the ANS is the most prominent. Importantly, when both cardiac vagal (the primary parasympathetic nerve) and sympathetic inputs are blocked pharmacologically (for example, with atropine plus propranolol, the so-called double blockade), intrinsic HR is higher than the normal resting HR (Jose and Collison, 1970). This fact supports the idea that the heart is under tonic inhibitory control by parasympathetic influences. Thus, resting cardiac autonomic balance favors energy conservation by way of parasympathetic dominance over sympathetic influences. In addition, the HR time series is characterized by beat-to-beat variability over a wide range, which also implicates vagal dominance, as the sympathetic influence on the heart is too slow to produce beat-to-beat changes. Low heart rate variability (HRV) is associated with increased risk of all-cause mortality, and low HRV has been proposed as a marker for disease (Task Force of the European Society of Cardiology and the North American Society of Pacing Electrophysiology, 1996).

1. The importance of inhibition

Importantly, like the heart, sympathoexcitatory subcortical threat circuits are under tonic inhibitory control by the prefrontal cortex (Amat et al., 2005; Thayer, in press). For example, the amygdala, which has outputs to autonomic, endocrine, and other physiological regulation systems, and becomes active during threat and uncertainty, is under tonic inhibitory control via GABAergic-mediated projections from the prefrontal cortex (Davidson, 2000; Thayer, in press). Thus the default response to uncertainty, novelty, and threat is the sympathoexcitatory preparation for action commonly known as the fight or flight response. From an evolutionary perspective, this represents a system that errs on the side of caution—when in doubt prepare for the worst—thus maximizing survival and adaptive responses (LeDoux, 1996). However, in normal modern life this response has to be tonically inhibited and this inhibition is achieved via top-down modulation from the prefrontal cortex. Thus, under conditions of uncertainty and threat, the prefrontal cortex becomes hypoactive. This hypoactive state is associated with disinhibition of sympathoexcitatory circuits that are essential for energy mobilization. However, when this state is prolonged, it produces the excess wear and tear on the system components that has been characterized by McEwen (1998) as allostatic load. It is also important to note that psychopathological states such as anxiety, depression, post-traumatic stress disorder, and schizophrenia are associated with prefrontal hypoactivity and a lack of inhibitory neural processes as reflected in poor habituation to novel neutral stimuli, a pre-attentive bias for threat information, deficits in working memory and

executive function, and poor affective information processing and regulation (Thayer and Friedman, 2004). Proper functioning of inhibitory processes is vital to the preservation of the integrity of the system and therefore is vital to health. Importantly for our discussion, these inhibitory processes can be indexed by measures of vagal function such as HRV as we will illustrate below.

2. Vagal function, autonomic balance and disease

There are multiple measures that can be used to index activity of the vagus nerve. Resting HR, by virtue of its tonic inhibitory control via the vagus, is a simple, inexpensive, and non-invasive measure of vagal function and autonomic balance. The HR change following cessation of exercise is another measure that has been used to characterize vagal function. The decrease in HR after termination of exercise has been termed HR recovery and standardized methods have been developed for its assessment. Measures of heart rate variability (HRV) in both the time and frequency domains have also been used successfully to index vagal activity. In the time domain, the standard deviation of the interbeat intervals (IBI), the percentage of IBI differences greater than 50 ms, and the mean square of the successive differences in IBI's (MSD) have been shown to be useful indices of vagal activity. In the frequency domain both low frequency (LF) and high frequency (HF) spectral power have been used as indices of vagal activity (Task Force Guidelines, 1996). In addition, measures of baroreflex sensitivity have also been shown to be useful indicators of vagal function. The literature linking these different indices to morbidity and mortality is extensive. Importantly, whereas there are some differences among studies, the consensus is that lower values of these indices of vagal function are associated prospectively with death and disability (for a review see Thayer and Lane, in press).

For example, resting HR can be used as a rough indicator of autonomic balance, and several large studies have shown a largely linear, positive dose-response relationship between resting HR and all-cause mortality (see Habib, 1999, for review). This association is independent of gender and ethnicity, and shows a threefold increase in mortality in persons with resting HR over 90 beats per minute (bpm) compared to those with resting HRs of less than 60 bpm.

Brook and Julius (2000) have detailed how autonomic imbalance in the sympathetic direction is associated with a range of metabolic, hemodynamic, trophic, and rheologic abnormalities that contribute to elevated cardiac morbidity and mortality. Although the relationship between HRV and cardiovascular morbidity and mortality may be easily comprehensible, the fact that autonomic imbalance and HRV are related to other diseases may not be as obvious. However, links do exist. For example, low HRV has been shown to be associated with diabetes mellitus, and decreased HRV has been shown to precede evidence of disease provided by standard clinical tests (Ziegler et al., 2001). We have recently presented evidence that HRV at night is associated with fasting glucose and hemoglobin A1c (HbA1c) levels (Thayer and Fischer, 2005a). Specifically, HRV was inversely related to fasting glucose and HbA1c levels after controlling a large number of covariates including many traditional cardiovascular disease risk factors.

HRV is also associated with immune dysfunction and inflammation, which have been implicated in a wide range of conditions such as aging, cardiovascular disease, diabetes, osteoporosis, arthritis, Alzheimer's disease, periodontal disease, and certain types of cancers as well as declines in muscle strength and increased frailty and disability (Ershler and Keller, 2000; Kiecolt-Glaser et al., 2002). The common mechanism seems to involve excess proinflammatory cytokines such as tumor necrosis factor, interleukin 1 and 6, and C-reactive protein (CRP). Importantly, increased parasympathetic tone and acetylcholine (the primary parasympathetic neurotransmitter) have been shown to attenuate release of these proinflammatory cytokines, and sympathetic hyperactivity is associated with their increased production (Maier and Watkins, 1998; Das, 2000; Tracey, 2002). We have recently provided evidence for the cholinergic anti-inflammatory pathway in apparently healthy adults (Thayer and Fischer, 2005b). We reported that 24-h HRV was inversely associated with CRP levels and white blood cell counts after controlling a wide range of covariates including urinary norepinephrine as an index of sympathetic nervous system activity. Thus, autonomic imbalance may be a final common pathway to increased morbidity and mortality from a host of conditions and diseases.

Although the idea is not new (Sternberg, 1997), several recent reviews have provided strong evidence linking negative affective states and dispositions to disease and ill health (Friedman and Thayer, 1998b; Musselman et al., 1998; Rozanski et al., 1999; Verrier and Mittleman, 2000; Kiecolt-Glaser et al., 2002; Krantz and McCeney, 2002). All these reviews implicate altered ANS function and decreased parasympathetic

activity as a possible mediator in this link. For example, low HRV is consistent with the cardiac symptoms of panic anxiety as well as with its psychological expressions in poor attentional control and emotion regulation, and behavioral inflexibility (Friedman and Thayer, 1998a,b). Similar reductions in HRV have been found in depression (Thayer et al., 1998), generalized anxiety disorder (Thayer et al., 1996), and posttraumatic stress disorder (Cohen et al., 1999).

An additional pathway between psychosocial stressors and ill health is an indirect one, in which psychosocial factors lead to poor lifestyle choices, including a lack of physical activity and the abuse of tobacco, alcohol, and drugs. Both sedentary lifestyle and substance abuse are associated with autonomic imbalance and decreased parasympathetic tone (Weise et al., 1986; Rossy and Thayer, 1998; Reed et al., 1999; Stein and Kleiger, 1999; Nabors-Oberg et al., 2002; Ingjaldsson et al., 2003). In fact, the therapeutic effectiveness of smoking cessation, reduced alcohol consumption, and increased physical activity rest in part on their ability to restore autonomic balance and increase parasympathetic tone.

In sum, autonomic imbalance and decreased parasympathetic tone in particular may be the final common pathway linking negative affective states and dispositions, including the indirect effects via poor lifestyle, to numerous diseases and conditions as well as increased morbidity and mortality, and it may also be implicated in psychopathological conditions. In Section 3, we will argue that the neural networks that regulate autonomic balance are closely related and partially overlap with networks that regulate goal-directed behavior and adaptability. These intimate functional and anatomical relationships will help to clarify how autonomic dysfunction plays a role in both somatic and psychological disorders.

3. The central autonomic network

Investigators have identified functional units within the central nervous system (CNS) that support goal-directed behavior and adaptability. One such entity is the central autonomic network (CAN) (Benarroch, 1993, 1997). Functionally, this network is an integrated component of an internal regulation system through which the brain controls visceromotor, neuroendocrine, and behavioral responses that are critical for goal-directed behavior, adaptability, and health. Structurally, the CAN includes both prefrontal and limbic structures: the anterior cingulate, insular, orbitofrontal, and ventromedial prefrontal cortices, the central nucleus of the amygdala, the paraventricular and related nuclei of the hypothalamus, the periaquaductal gray matter, the parabrachial nucleus, the nucleus of the solitary tract (NTS), the nucleus ambiguous, the ventrolateral medulla, the ventromedial medulla, and the medullary tegmental field. These components are reciprocally interconnected such that information flows bidirectionally between lower and higher levels of the CNS. The primary output of the CAN is mediated through preganglionic sympathetic and parasympathetic neurons. These neurons innervate the heart via the stellate ganglia and vagus nerve, respectively. The interplay of these inputs to the cardiac sino-atrial node produces the complex variability that characterizes the healthy HR time series (Saul, 1990). Thus, the output of the CAN is directly linked to HRV. As noted above, vagal influences dominate cardiac chronotropic control (Levy, 1990). In addition, sensory informations from peripheral end organs such as the heart and the immune system are fed back to the CAN. This allows HRV to serve as an indicator of central–peripheral neural feedback and CNS–ANS integration.

Other functional units within the CNS serving executive, social, affective, attentional, and motivated behavior in humans and animals have been identified (Spyer, 1989; Devinsky et al., 1995; Masterman and Cummings, 1997; Damasio, 1998). One such network has been termed the anterior executive region (AER) (Devinsky et al., 1995). The AER and its projections regulate behavior by monitoring the motivational quality of internal and external stimuli. The AER network has been called the 'rostral limbic system' and includes the anterior, insular, and orbitofrontal cortices, amygdala, periaquaductal gray, ventral striatum, and autonomic brainstem motor nuclei. Damasio (1998) has recognized a similar neural 'emotion circuit', for which there is considerable structural overlap with the CAN and the AER (Thayer and Lane, 2000).

We propose that the CAN, the AER network, Damasio's (1998) 'emotion circuit,' and related systems (Spyer, 1989; Masterman and Cummings, 1997) represent a common central functional network recognized by different researchers from diverse approaches. This CNS network is associated with the generation of context appropriate responses via prefrontal modulation of bottom-up sensory inputs and serves to regulate psychophysiological resources related to goal-directed behavior (Thayer and Friedman, 1997; Friedman and Thayer, 1998a,b). Additional structures are flexibly

recruited to manage specific behavioral adaptations. This sparsely interconnected neural complex allows for maximal organism flexibility in accommodating rapidly changing environmental demands. When this network is either rigidly coupled or completely uncoupled, the ability to recruit and utilize appropriate neural support to meet a particular demand is hampered, and the organism is thus less adaptive. Given that the default response to novelty and uncertainty is one of preparation for action to deal with a potential threat, dysfunction in this network most often leads to a prolonged state of action readiness, energy mobilization, and an accumulating allostatic load.

4. Autonomic regulation and prefrontal inhibition

We have argued above that autonomically mediated HRV is useful as an index of neurovisceral integration and organismic self-regulation. The interaction of sympathetic and parasympathetic outputs of the CAN at the sino-atrial node produces the complex beat-to-beat variability that marks a healthy, adaptive organism. Vagal activity dominates HR control, and thus HR is under tonic inhibitory vagal control (Levy, 1990; Uijtdehagge and Thayer, 2000). HRV is also associated with prefrontal cortex activity (Lane et al., 2001), and the prefrontal cortex has been inversely related to subcortical activity in structures such as the amygdala, that have been implicated in primitive motivation systems (Davidson, 2000). As mentioned above, several lines of research point to the significance of HRV in somatic and psychological pathology. In the remainder of this article, we will discuss the central role of prefrontal disinhibition and low HRV in these disorders, more specifically in affective and cognitive regulation. This will help to illustrate the links between somatic disease on the one hand and psychopathology, with its attendant affective and cognitive dysregulation, on the other.

A major result of low levels of vagal cardiovascular influence is the disinhibition of sympathoexcitatory influences. Due to differences in the temporal kinetics of the autonomic neuroeffectors, sympathetic effects on cardiac control are relatively slow (order of magnitude seconds) compared to vagal effects (order of magnitude milliseconds; see Saul, 1990). Thus, when this rapid vagal cardiac control is low, HR cannot change as quickly in response to environmental changes. These changes and goal-directed behavior in general, are modulated by the prefrontal cortex. When the prefrontal cortex is taken 'offline' for whatever reason, a relative sympathetic dominance associated with disinhibited defensive circuits is released, which can be pathogenic when sustained for long periods.

Human evidence for the inhibitory role of the frontal cortex comes from a recent study of HR and HRV before and after right- and left-side intracarotid sodium amobarbital (ISA) injection (Ahern et al., 2001). HR changes were similar during each hemisphere's pharmacological inactivation. During the 10-min inactivations of either hemisphere, HR increased, peaked around the third minute, and gradually declined towards baseline values. These data indicate that the frontal cortex exerts tonic inhibition on brainstem sympathoexcitatory circuits. There were lateralized effects: larger and faster HR increases occurred during right-hemisphere inactivation. Moreover, vagally mediated HRV decreases were also greater in the right-hemisphere inactivations, mirroring the hemispheric effects on HR. These results support anatomical and physiological findings that right hemispheric autonomic cardiac inputs are associated with greater chronotropic (rate) control.

The effects of the ISA test are largely restricted to anterior neural structures, which include the orbital and medial prefrontal cortices (Ahern et al., 1994; Hong et al., 2000). These areas are components of the CAN and related circuits and thus are critical for affective, cognitive, and autonomic regulation (Thayer and Lane, 2000). Given our emphasis on inhibition, it should come as no surprise that these structures are related to inhibitory control of behavior in general (Roberts and Wallis, 2000) and cardiac behavior in particular (Verberne and Owens, 1998). Critical to our use of HRV is the fact that direct and indirect pathways connect these areas with vagal motor output regions (Ter Horst, 1999). Many researchers have proposed inhibitory cortical–subcortical circuits (Spyer, 1989; Benarroch, 1993, 1997; Masterman and Cummings, 1997; Mayberg et al., 1999), but our group is the first to tie these circuits to HRV (Thayer and Lane, 2000; Thayer and Friedman, 2002). The ISA test results as well as recent neuroimaging findings (Gianaros et al., 2004) provide compelling evidence that cortical structures tonically inhibit sympathoexcitatory circuits by way of vagal mechanisms.

Taken together, these findings suggest that a common reciprocal inhibitory cortico-subcortical neural circuit may, structurally as well as functionally, link psychological processes such as emotion with health-related physiology, or 'mind' with 'body', for that matter. This circuit and its self-regulatory efficiency can be indexed with HRV. This

neural network permits the prefrontal cortex to inhibit subcortical structures associated with defensive behaviors, and thus promote flexible responsiveness to environmental changes. For example, when faced with threat, tonic inhibitory subcortical control can be withdrawn quickly, leading to sympathoexcitatory survival ('fight or flight') responses. However, when this network is disrupted, a rigid, defensive pattern emerges with associated perseverations in cognitive, affective, and autonomic behavior. This protracted state of action readiness and associated sympathetic activity may be the pathogenic state underlying the increased morbidity and mortality found in chronic negative psychological states and dispositions. Elsewhere we discuss the role of perseverative cognitions in the stress-disease link (Brosschot et al., this issue). The notion that HRV is an index of organismic self-regulation is further corroborated by its role in affective and cognitive regulation, as discussed below.

5. Affective regulation

Affect regulation is a valuable skill that has clear implications for health. Emotions represent a distillation of an individual's perception of personally relevant environmental interactions, including not only challenges and threats but also the ability to respond to them (Frijda, 1988). Viewed as such, emotions reflect the integrity of one's ongoing adjustment to constantly changing environmental demands. When the affective system works properly, it promotes flexible adaptation to shifting environmental demands. In another sense, an adequate emotional response represents a selection of an optimal response and the inhibition of less functional ones from a broad behavioral repertoire in such a way that energy use is matched to fit situational requirements.

Several psychophysiological measures have proven to be useful indices of affect regulation. One is the reflexive startle blink, the magnitude of which can be affected by emotional state. The emotion-modulated startle is a robust phenomenon that has been demonstrated in a wide range of experimental situations, and has been broadly linked to affective and motivational phenomena (Lang, 1995). Similarly, HRV has been associated with a diverse range of processes, including affective and attentional regulation (Porges, 1992; Porges et al., 1994). The relationship between these two important measures of affective regulation was recently investigated (Ruiz-Padial et al., 2003). Ninety female participants viewed pleasant, neutral, and unpleasant pictures while exposed to acoustic startle stimuli. Eye blink strength to startle probes was recorded both during affective foregrounds and intertrial intervals, and the relationship between resting HRV and startle magnitudes was examined. Resting HRV was found to be inversely related to both intertrial interval and emotion-modulated startle magnitude. These findings further support the notion that the prefrontal cortex tonically inhibits amygdala output. In addition, subjects with the highest HRV showed the most differentiated emotion-modulated startle effects, whereas those with the lowest HRV showed significant augmentation of startle to neutral foregrounds and marginally potentiated startle to pleasant foregrounds. Thus, individuals with low HRV reacted to neutral, harmless stimuli as if they were aversive and threatening, and also had a tendency to react similarly to positive stimuli. Individuals with high HRV were able to best match their response to situational demands and thus respond most appropriately to the energy requirements of the situation. The findings are consistent with our model that posits that prefrontal cortical activity modulates subcortical motivation circuits in the service of goal-directed behavior and appropriate energy regulation. Moreover, persons with low HRV showed evidence of hypervigilance and the activation of a defensive behavioral system in response to non-threatening stimuli. This failure to recognize safety signals can lead to prolonged action readiness and sympathetic nervous system overactivity.

6. Attentional regulation and executive function

Attentional regulation and the ability to inhibit prepotent but inappropriate responses are also important for health in a complex environment. Many tasks important for survival in today's world involve cognitive functions such as working memory, sustained attention, behavioral inhibition, and general mental flexibility. These tasks are all associated with prefrontal cortical activity (Arnsten and Goldman-Rakic, 1998). Deficits in these cognitive functions are present in negative affective states and dispositions such as depression and anxiety (Hammar et al., 2003). Stress can also impair cognitive function and may contribute to the cognitive deficits observed in various mental disorders. It is also possible that autonomic

dysregulation contributes to decline in attention and cognitive performance. A recent series of experiments in our lab have been conducted to examine this issue and will be described.

Johnsen et al. (2003) examined inhibitory responses in an emotional Stroop paradigm. Dental phobics were first exposed to recorded scenes of dental procedures and then administered the emotional Stroop test. In addition to the traditional color-congruent and color-incongruent words, phobic subjects were asked to respond to neutral words and dental-related words (e.g. 'drill' and 'cavity') that were threatening to them. All subjects exhibited longer reaction times to the color-incongruent words and the dental-related threat words, and thus displayed a difficulty in inhibiting prepotent responses. However, greater HRV was associated with faster reaction times to these words, consistent with the link between vagally mediated HRV, inhibitory ability, and frontal lobe function. These results support the idea that vagally mediated HRV is associated with efficient attentional regulation and greater ability to inhibit prepotent but inappropriate responses.

Subsequent studies further examined executive function and working memory in healthy individuals. In the first experiment, subjects performed a number of tasks involving continuous performance, including a simple reaction time task, a choice reaction time task, and three tasks that involved delayed responding, working memory, and executive function (Johnsen et al., 2002; Hansen et al., 2003). These latter tasks involved the presentation of a sequence of digits that required a response when a digit was identical to one that appeared either one or two back in the series, and have been shown to be associated with prefrontal activity (Goldman-Rakic, 1998). HRV and cortisol responses were recorded, and subjects were grouped into low and high HRV groups based upon their resting HRV levels. Performance on tasks involving simple and choice reaction times did not differ between these groups. However, on tasks associated with executive function and prefrontal activity, subjects in the low HRV group performed more poorly in terms of both speed and accuracy than those in the high HRV group. In addition, the groups did not differ in baseline, morning, or evening cortisol, but the low HRV group showed larger cortisol responses to cognitive tasks that lasted into the post-task recovery period. Stress is associated with an increased cortisol release, and cortisol plays a major role in immune function through its association with proinflammatory cytokines (Kiecolt-Glaser et al., 2002). Cortisol is also known to impair function on cognitive tasks associated with prefrontal cortex (Lupien et al., 1999). Thus, the low HRV group is less stress tolerant as indexed by cortisol responses and more impaired cognitively than the high HRV group.

In another study (Hansen et al., 2004), HRV was manipulated by having half of the subjects in a physically active group undergo mild detraining for 4 weeks. Aerobic capacity and HRV were significantly reduced in this group compared to those who maintained their fitness and HRV levels. All subjects again performed the above cognitive tasks: once before the 4-week detraining period, and once after. The detrained, lower HRV group failed to show the expected learning effect associated with repeated performance of the cognitive tasks, and thus did not reap the typical benefit of previous task exposure.

Taken together, these results support the usage of HRV to index efficient allocation of attentional and cognitive resources needed for efficient functioning in a challenging environment in which delayed responding and behavioral inhibition are key. In addition, these data show that low HRV marks increased risk to stress exposure. Significantly, these results provide a connection among stress-related cognitive deficits, high negative affect, and negative health consequences via the common mechanism of autonomic imbalance and low parasympathetic activity.

7. Conclusion

Autonomic, cognitive, and affective regulation assist an organism in facing the challenge of an environment in constant flux. From a systems perspective, inhibitory processes can be viewed as negative feedback circuits that permit the interruption of ongoing behavior and redeployment of resources to other tasks. When these negative feedback mechanisms are compromised, positive feedback loops may develop as a result of disinhibition. These positive circuits can have disastrous consequences by promoting hypervigilance, perseveration, and continued system activation, thereby limiting resource availability for other processes. This state of affairs can provide a chronic pathogenic substrate for psychological processes and emotions to negatively impact health. Thus, autonomic imbalance, as an index of disinhibition of sympathoexcitatory neural circuits that are normally under tonic inhibitory control via the prefrontal cortex, may be the final

common pathway linking psychosomatics and psychopathology.

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