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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 When the prefrontal cortex is taken 'offline' for whatever reason, parasympathetic inhibitory action is withdrawn and a relative sympathetic dominance associated with disinhibited defensive circuits is released, which can be pathogenic when sustained for long periods.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