

Neuroimmune Bidirectional Communication

The two major routes for the central nervous system to communicate with the periphery include direct innervation and neuroendocrine pathways. The peripheral nervous system (NS) “hard-wires” or directly connects the brain to immune tissue and cells via the sympathetic NS’s release of norepinephrine and the parasympathetic NS’s release of acetylcholine. Norepinephrine promotes nuclear factor-kappa B (NF-κB) activation. NF-κB is a transcription factor that regulates gene expression of several proinflammatory mediators, such as Interleukin-6 (IL-6) and Interleukin-8 (IL-8). NF-κB activation increases gene expression of inflammatory mediators, which, in turn, enhances inflammation. Acetylcholine, however, “calms” the immune system via the cholinergic anti-inflammatory pathway. Cholinergic stimulation of immune cells impedes NF-κB’s modulation of inflammatory gene expression.

Cortisol, the end product of the hypothalamic-pituitary-adrenal (HPA) axis, produces a wide variety of bodily effects. It is one of the most potent anti-inflammatory modulators of the immune system. Cortisol binds to glucocorticoid receptors within immune cells and inhibits activation and release of proinflammatory cytokines. However, chronically elevated cortisol can induce glucocorticoid insensitivity wherein immune cells down-regulate the expression of glucocorticoid receptors. As a result of prolonged high cortisol levels, inflammation can be increased due to unregulated immune cells producing proinflammatory cytokines.

The immune system provides information to the brain via cytokines. For example, IL-1 receptors are located throughout the brain, especially in the hypothalamus, and can stimulate corticotropin releasing hormone (CRH) secretion from the hypothalamus, leading to increased HPA axis activity. Peripheral cytokines induce behavioral changes that mirror depression. Proinflammatory cytokines can access the brain through a variety of pathways, including the leaky regions in the blood-brain barrier, cytokine-specific transport molecules expressed on blood-brain barrier, and the vagus nerve detecting cytokine levels in the periphery and relaying this information to the brain.

Psychoneuroimmunology has advanced understanding of the complexity of health and provides a framework for examining biopsychosocial factors

influencing physical and mental health issues. As each discipline—psychology, neuroscience, and immunology—continues to make new discoveries, psychoneuroimmunologists will incorporate the new information and continue to be a progressive field—graying the boundaries between health-related disciplines.

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See also Behavioral Health; Chronic Illness, Psychological Aspects of; Coping Strategies; Health Psychology; Neuroendocrine System; Neuroscience as One-Sided Dualism; Stress and Resilience to Life Challenge; Stress Syndromes; Stressors and Stress

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PSYCHOPATHOLOGY AND STRESS

Feeling anxious, sad, and discouraged are universal experiences that afflict nearly everyone from time to time. Such emotional reactions fall within the normal range of human functioning and are common responses to adverse life circumstances, such as preparing for a difficult job interview, failing an important exam, getting fired, or losing a loved one. Indeed, emotional reactions such as these are adaptive insofar as they help people prioritize goals, communicate feelings, and remember important life events. In some instances, however, emotional reactions to stressful situations can become exaggerated or prolonged, leading to

levels of distress that affect social and occupational functioning. Under these circumstances, stress can contribute to the development of different forms of psychopathology.

Specific disorders known to be precipitated by stress include social anxiety disorder, generalized anxiety disorder, posttraumatic stress disorder, substance abuse disorder, schizophrenia, bipolar disorder, and major depressive disorder. Stress can also contribute to the development of traitlike personality disorders, such as antisocial personality disorder and borderline personality disorder, especially if the stress exposure is prolonged or severe. This entry reviews different types of stress that cause psychopathology, vulnerability factors that contribute to individual differences in stress reactivity, mechanisms that link stress with psychopathology, and processes that underlie associations between stress, psychopathology, and physical disease.

Types of Stress

Three types of stress have been found to increase risk for psychopathology: *acute life events*, *chronic difficulties*, and *contextual stressors*. Acute life events are relatively short-lived stressors that include situations such as acute health problems or illnesses, accidents, marriages, divorces, job losses, births, and deaths. They can occur once or multiple times and can vary in impact from being relatively minor to very severe. Breaking up with a romantic partner after 2 weeks of dating is typically a relatively minor acute life event, whereas being physically or sexually attacked constitutes a severe life event.

Chronic difficulties, in contrast, are more prolonged in nature and include circumstances that persist for several months or years, such as ongoing health, relationship, financial, housing, occupational, or educational difficulties. Living in an apartment with limited personal space for 2 months is usually a relatively minor chronic difficulty, whereas taking care of a dying spouse for 5 years constitutes a severe difficulty.

Finally, contextual stressors are societal- or macro-level circumstances that form the general physical, social, and psychological environments in which people live. These stressors include experiences such as poverty, war, undereducation, unemployment, discrimination, crime, poor health care

access, and social isolation. Because of their ubiquitous nature, contextual stressors often give rise to specific acute life events and chronic difficulties. For example, people living in poverty are more likely to experience stressors involving crime and physical danger, and those without access to health care are more likely to experience health- and illness-related stressors.

Stress Exposure and Vulnerability

Although stress is ubiquitous, most people who experience stress do not develop psychiatric disorders. This is due, in part, to the severity and duration of the stress exposure, with longer, more severe exposures being more likely to cause psychopathology. Another critical factor that determines whether people develop psychopathology following stress involves level of vulnerability. Theories that account for both the amount or severity of stress exposure and the extent of personal vulnerability present are called *diathesis-stress theories*. These theories posit that the amount of stress required for psychopathology to develop differs depending on the vulnerability of the person. Theories such as *cognitive theory of depression* focus mainly on cognitive vulnerability to stress that comes in the form of negative views of the self, others, or the future.

Vulnerability can be represented at other levels as well. According to *stress sensitization* and the *kindling hypothesis*, for example, people become more neurobiologically and behaviorally sensitive to stress over time because of prior psychopathology or experiences with stress. As a result, less stress is required for psychopathology to develop in the future. In addition, *neuroticism*, or the tendency to remain in a negative emotional state, has also been shown to increase vulnerability to stress. Finally, genetic factors that influence serotonergic and immune system activity also affect stress reactivity, leaving some individuals more likely than others to develop psychopathology following stress.

Research on psychopathology and stress has also identified mechanisms by which stress affects mental health. In *social signal transduction theory*, for example, cognitive, emotional, neural, physiologic, and genetic factors all play a role in linking stress with psychopathology. From this perspective, stress generates specific negative thoughts

(e.g., “I’m not good enough,” “I won’t get through this,” “This will never end”) and emotions (e.g., anxiety, sadness, shame, humiliation) that produce distress. Stress also upregulates biological systems, including the sympathetic nervous system and hypothalamic-pituitary-adrenal axis, which regulate components of the immune system involving inflammation that have profound effects on mood, cognition, and behavior.

In addition, as revealed by work on *human social genomics*, some types of stress—such as social conflict, isolation, rejection, and exclusion—can reach deep inside the body to influence the activity of the human genome. These biobehavioral changes can be adaptive and enhance survival when they occur intermittently and in response to actual physical threat. But if activation of these systems is frequent or prolonged, substantial distress can develop, possibly leading to psychiatric illness.

Finally, stress can also increase risk for several physical disease conditions that frequently co-occur with psychiatric illness, such as asthma, rheumatoid arthritis, chronic pain, metabolic syndrome, cardiovascular disease, obesity, certain cancers, and neurodegeneration. In fact, one of the discoveries in this area involves the finding that components of the immune system that link stress with anxiety and depression may also give stress the ability to promote the physical diseases just mentioned. The implications of this discovery are profound, as they suggest that stress may be associated with both mental and physical health problems through common, underlying pathways. If this is the case, targeting stress-related biobehavioral processes may reduce risk not just for psychopathology but for physical disease as well.

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See also Anxiety Disorders; Behavioral Perspectives on Psychopathology; Grief and Bereavement; Humanistic Theories of Psychopathology; Mood Disorders; Psychoanalytic and Psychodynamic Theories of Psychopathology; Psychoneuroimmunology; Social Factors in Health; Stressors and Stress

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PSYCHOPHYSICS

Psychophysics is characterized by attempts to determine the functional relationship between perceived or subjective magnitudes and physical magnitudes. Much progress has been made in defining and measuring the physical world, yet controversies abound over defining and measuring the perceived world. Over time, standardized scales of measurement have been developed for the physical world. Although there is not unanimous agreement—for instance, a metric mile and international mile are not the same unit of measurement—at least there is agreement that measures on different scales reflect the same quantities—one international mile (i.e., 1,609 meters) is the same in Tucson, Arizona, and in Burnley, Lancashire.

Measuring perception, however, is not so straightforward. There are two major problems: (a) intraindividual variation and (b) interindividual variability. The first refers to the fact that measures of any one person will likely vary as a consequence of factors other than the physical magnitude of the stimulus. The second problem refers to the fact that measures of any two different people will likely be different even though the same stimulus is presented to both. This entry discusses the classical view of psychophysics and subsequent views.

Consider the physical magnitude of sound intensity and the question of what loud means.