From the psychologist’s standpoint the psychology of medical [practitioners] is crude; from the medical standpoint the pathology and physiology of the psychologist are out of date.

(Franz, 1913, p. 1062)

In 1913, psychologist Shepherd Ivory Franz published reports in the *Journal of the American Medical Association* and *Science* advocating cross-training between psychologists and physicians, including the need for psychology to incorporate understanding biological processes related to health. Decades later, the biopsychosocial model (Engel, 1977) emerged in response to reductionist biomedical models of disease and became the foundation of health psychology. Accordingly, understanding “pathology and physiology” is implicit in the biopsychosocial model. In this chapter, we survey biological pathways that connect psychosocial factors to the pathophysiology of disease, with a focus on neural and neuroendocrine mediators as shown in Figure 5.1. We then review biological mediators of the pathophysiology of chronic disease (namely cardiometabolic conditions like cardiovascular disease and cancer), from cellular and molecular mechanisms common to all systems (Figure 5.1, lower right) to the system level (immune, metabolic, and cardiovascular systems in particular as shown in Figure 5.1). Understanding the basic biology underlying chronic disease will help readers “reverse engineer” disease pathophysiology to identify biological plausible connections between psychosocial factors and health (Miller, Chen, & Cole, 2009).

### What Is Health? Conceptualization and Measurement

Before surveying the systems, clarifying when biological measures or “biomarkers” are directly relevant for physical health is a key conceptual issue. In 2001, the NIH Biomarkers Definitions Working Group distinguished between *clinical* and *surrogate endpoints*. Clinical endpoints are the “most credible characteristics used in the assessment of the benefits and risks of a therapeutic intervention in randomized clinical trials” and constitute “how a patient feels, functions, or survives” (Biomarkers Definitions Working Group, 2001, p. 91). That definition can include patient-reported outcome measures like health-related quality of life (Cella et al., 2007) or physical functioning and activities of daily living (Schalet et al., 2016); objective ratings of physical function; or observed events like hospitalization and mortality. Importantly, clinical endpoints are directly relevant to health care providers and patients.
Figure 5.1 The Neural Mediators, Neuroendocrine Mediators, and Mediators of Pathophysiology Reviewed in This Chapter

Abbreviations: ACTH = adrenocorticotropin hormone, AVP = vasopressin, FSH = follicle stimulating hormone, LH = luteinizing hormone,
Surrogate endpoints are a small subset of biomarkers that the evidence base suggests can “substitute for a clinical endpoint in clinical trials” (Biomarkers Definitions Working Group, 2001, p. 91). For example, resting blood pressure can indicate benefit in clinical trials of anti-hypertensive medications when clinical endpoints like a heart attack may take decades to emerge. Most biomarkers that measure activity or function in the systems reviewed in this chapter are not surrogate endpoints. Instead, they can be considered biological mediators that explain links between psychosocial factors and underlying biological processes of disease (Miller et al., 2009), but cannot substitute for clinical endpoints. In other words, biological mediators should not be construed as measures of “health.” Mediators like cortisol or norepinephrine have multiple effects across multiple tissues and systems, with little specificity for disease states (with the exception of neuroendocrine or autonomic disorders). Table 5.1 describes biomarkers relevant to the systems reviewed in this chapter, and distinguishes between biological mediators and surrogate endpoints. As biomarkers become more readily available to incorporate in research, distinguishing among clinical endpoints, surrogate endpoints, and biological mediators is important for conceptualization, study design, measurement, and dissemination to practitioners, policymakers, and the public.

Neural and Neuroendocrine Mediators Linking Psychosocial Factors to Disease Pathophysiology

This section reviews signaling from the brain to different target organs and systems within the body; while there is significant cross-talk across these systems and pathways, due to space limitations...
we review each system separately. “Top-down” neural circuits communicate information about the external environment to the body to direct adaptation (Erickson, Creswell, Verstynen, & Gianaros, 2014). Regions within the mesolimbic dopaminergic system, ventromedial prefrontal cortex, and orbitofrontal cortex (shown in the inset on the top right of Figure 5.1) encode the reward value of experienced stimuli (like food) and update expectations of future reward. The insula and anterior cingulate are implicated in encoding and representing uncertainty, and decision-making engages parietal and frontal cortical regions. Medial-prefrontal circuits implicated in processing social contexts and emotions also regulate signaling from the hypothalamus to the rest of the body via the endocrine and autonomic nervous systems (ANS; Erickson et al., 2014; Lane & Wager, 2009; Ulrich-Lai & Herman, 2009). Thus, autonomic and neuroendocrine signals represent processing at multiple layers within medial-prefrontal, limbic (e.g., hypothalamus and amygdala), and brainstem circuits (Ulrich-Lai & Herman, 2009).

The solid gray line pointing back at the brain in the figure indicates that internal bodily states like energy state and inflammation inform the brain about how the external environment impacts the organism’s internal environment (Ulrich-Lai & Herman, 2009). For instance, your motivation to fight an assailant will be impacted by whether you are experiencing pain and drops in blood pressure (from bleeding), which are detected by sensors throughout the body and processed by sensory and affective circuitry in the brain. In addition, the hypothalamus contains receptors for gastrointestinal (GI) tract signals (Berthoud, Munzberg, & Morison, 2017) and products of the immune system (Irwin & Cole, 2011). Ultimately, the circuits that process information about the internal and external environment overlap (e.g., social pain; Irwin & Cole, 2011; Peirs & Seal, 2016), and communication between the brain and the body has numerous implications for health. In the next section, we review brain to body communication which has been primarily studied in the context of stress exposures (reviewed in the previous chapter, Gruenewald & Yang, 2018). As described next, much of the communication from brain to body takes place through messages transmitted via the neuroendocrine system (see Figure 5.1).

**Neuroendocrine Signaling**

**HPA Axis**

Stimuli perceived as uncontrollable, unpredictable, or socially evaluative, activate the hypothalamic-pituitary-adrenal (HPA) axis (Dickerson & Kemeny, 2004); a hormone cascade that hinges on production of corticotropin releasing hormone (CRH) in the hypothalamus and culminates in production of the steroid hormone cortisol by the adrenal gland (Sapolsky, Romero, & Munck, 2000). Cortisol binds to two types of receptors, the high affinity mineralocorticoid receptors that modulate basal functions, and the low affinity glucocorticoid receptors which modulate neuroendocrine stress functions throughout the brain and body (Gunnar, Doom, & Esposito, 2015). Cortisol is also released in a pulse-like fashion every one to two hours, with high morning levels following awakening and low evening levels (Young, Abelson, & Lightman, 2004). Superimposed on this diurnal rhythm is the cortisol awakening response, a sharp increase in cortisol from awakening to 30–45 minutes post awakening (Clow, Hucklebridge, Stalder, Evans, & Thorn, 2010). Due to cortisol’s widespread effects, disruption of HPA functioning through frequent activation, failure to shut off, or inadequate responses, may contribute to disease progression (McEwen, 1998).

**Oxytocin and Vasopressin Pathways**

The neuropeptide oxytocin and the related peptide vasopressin are produced in specific regions of the hypothalamus (Gainer, 2012), and are co-released with CRH into the brain and peripheral
Oxytocin and vasopressin have greater than 85% similarity in their receptors, which are abundant in the amygdala, HPA axis, and the ANS (Neumann & Landgraf, 2012). Oxytocin may also act to suppress HPA axis activity (Churchland & Winkielman, 2012), suggesting that oxytocin may be part of an adaptive response to challenges (Neumann & Landgraf, 2012).

Oxytocin and vasopressin have wide-ranging effects in the body that vary throughout the lifespan, beginning with childbirth and lactation for both mothers and infants (Anacker & Beery, 2013). Both neuropeptides have continuing influence on interpersonal attachment processes in the context of intimate relationships and caregiving during adulthood (Insel & Young, 2001). Oxytocin pathways have been implicated in behaviors that when viewed collectively, may motivate and mediate relationships between people, including mother–infant pairs, romantic partnerships, and kin and community groups (Carter, 2014; Crespi, 2016).

**Autonomic Pathways**

The ANS and its branches (shown in Figure 5.1), the parasympathetic nervous system (PSNS) and sympathetic nervous system (SNS), regulate energy expenditures and other body functions during and after stress exposures (Berntson, Sarter, & Cacioppo, 2006). The key neurotransmitters involved in direct signaling to target tissues and organs are acetylcholine for the PSNS and norepinephrine in the SNS. The PSNS and SNS can exert reciprocal, co-activation, or co-inhibition effects on their target organs, which makes measuring PSNS and SNS signaling separately important (Berntson, Cacioppo, Quigley, & Fabro, 1994). However, both branches innervate many of the same organs, and measures of autonomic function often involve measuring function in target organs. Thus, isolating the effects of psychosocial factors on sympathetic or parasympathetic activity independently is challenging but possible. Later, we discuss indices that reflect functioning within a single branch.

The PSNS primarily exerts its effects on peripheral organs through the vagus nerve. PSNS-mediated control of the heart is indexed by respiratory sinus arrhythmia (RSA), variation in heart rate occurring during a breathing cycle (Porges, 1992). RSA has emerged as a marker of emotion (dys)regulation, mediating the effect of the CNS on the development of physical health outcomes (Masi, Hawkley, Rickett, & Cacioppo, 2007). Epidemiological studies are currently disentangling whether impaired vagal activity precedes or results from chronic disease.

Markers of SNS functioning include skin conductance, cardiovascular pre-ejection period, and circulating epinephrine and norepinephrine. SNS functioning has consistently been implicated in the development of cardiac disease (Chida & Steptoe, 2010). More recent work has highlighted the role of the SNS in cancer progression through regulation of tumor growth (Cole, Nagaraja, Lutgen-dorf, Green, & Sood, 2015).

**Gonadal Pathways**

While the hypothalamic–pituitary–gonadal (HPG) axis is critical for neonatal and pubertal development (Plant, 2015), for space reasons this section focuses on the HPG axis in post-pubertal adults. In biological females, luteinizing hormone (LH) and follicle-stimulating hormone (FSH) produced by the pituitary (see Figure 5.1) stimulate ovulation, menstruation, and production of estrogens and progesterone to support egg fertilization. In biological males, LH and FSH stimulate sperm and androgen hormone production (e.g., testosterone) in the testes. HPG hormones have numerous effects (Deroo & Korach, 2006; Klomer, Carson, Dobs, Kopecky, & Mohler, 2016) and are protective for some conditions (cardiovascular disease, Alzheimer’s disease); and risk factors for others (breast and ovarian cancers). Moreover, HPG hormones modulate reproduction-related motivation and behavior, respond to environmental changes (e.g., parenting, competition outcomes), and may modulate economic decision making (Motta-Mena & Puts, 2017; Roney, 2016;
Unfortunately, HPG function is not typically assessed in health psychology. In human biological females, multiple estradiol and progesterone measures over time are needed to ascertain ovulatory phase (Jasienska & Jasienski, 2008). However, the challenges are outweighed by the potential to correct pervasive exclusions of HPG hormones in biobehavioral research (van Anders, Goldey, & Bell, 2014).

Mediators of Pathophysiology

Neuroendocrine signals from the brain eventually reach target tissues and cells in our body, and those tissues and cells play direct roles in the pathophysiology of illnesses and chronic disease. In this section, we describe how signals from the brain transmit signals to target cells; discuss key biological systems that are directly involved in the pathophysiology of many chronic illnesses (see Figure 5.1), including the immune, metabolic, and cardiovascular systems.

Cellular and Molecular Mechanisms Common Across All Systems

As shown in the lower right inset of Figure 5.1, in every living organism at any given moment, at the level of a single cell, signaling molecules (hormones, neuropeptides), including those from the neuroendocrine system described, bind to receptors located outside or inside cells. That binding leads to cascades of other molecular events in the cell that culminate in two processes that form the “central dogma” of molecular biology: that information encoded in DNA is transcribed into RNA, which is then translated into protein molecules that act inside and outside the cell (Slavich & Cole, 2013). Another shorthand term for this process is “gene expression,” which typically refers to transcription of a specific sequence of DNA (e.g., a gene that contains assembly instructions for one part of a molecule) to RNA. Ultimately, neuroendocrine signals that provide information about the external environment modify the process of gene expression and protein assembly, thus changing the structure and function of individual cells throughout the rest of the body (Slavich & Cole, 2013), including cells in the systems described in the following sections.

Immune System Pathways

The immune system protects us from harmful organisms including viruses, bacteria, and parasites. The immune system has two branches: the innate immune system and the adaptive immune system (Segerstrom & Miller, 2004). If a pathogen manages to break through surface barriers like the skin and mucosa, cells of the innate immune system rapidly detect and destroy any pathogens within the body. One key process initiated by the innate system is inflammation, which generates physiological and behavioral changes (recruiting more immune cells, increasing blood flow to infected areas, disrupting and “eating” pathogens, elevating body temperature) designed to eradicate pathogens. Key cells in the innate immune system include neutrophils, macrophages; measures of innate immunity include circulating molecules that promote inflammation (Segerstrom & Miller, 2004).

In the case of a more infectious pathogen, the slower-developing adaptive immune system will respond with more specificity for the particular pathogenic threat (Segerstrom & Miller, 2004). Cells of the adaptive system orchestrate the overall immune response and destroy bodily cells infected by pathogens (CD4+ and CD8+ T-cells, respectively), and produce antibodies that neutralize pathogens (B-cells). Memory cells that are specific to the pathogen threat are retained over many years, allowing the adaptive system to rapidly respond in the case of re-infection by the same pathogens.

In sum, the immune system plays a key role in preventing or minimizing harm and damage posed by pathogens. At the same time, dysregulated innate immunity, particularly in the form of chronic and persistent inflammation, can damage surrounding tissues and cells and contribute to several
chronic illnesses related to aging (Kiecolt-Glaser, McGuire, Robles, & Glaser, 2002), such as cardiovascular disease described later in the chapter. Suppressed adaptive immunity can result in increased susceptibility to infection, and auto-immune conditions in which the immune system attacks one’s own tissues can impair normal functioning. Thus, across multiple conditions, immune system function and by extension psychosocial influences on immunity, play important roles in disease pathophysiology (Kemeny & Schedlowski, 2007).

**Metabolic Pathways**

The central nervous and digestive systems, along with bacteria that colonize the GI tract, co-evolved to regulate energy (food) intake and expenditure (Berthoud & Morrison, 2008). The brain monitors and acts on information about short- and long-term nutrient and energy states (shown in Figure 5.1) that is integrated with preferences, learned associations, and information about the food environment (Berthoud et al., 2017). During digestion, food is processed in the GI tract (the mouth, stomach, small and large intestine), and taste, fullness, and nutrient composition signals are secreted by organs and bacteria in the tract (Berthoud & Morrison, 2008). Short-term post-meal signals reach the brain through endocrine signaling and neural transmission via the vagus nerve, which innervates the path virtually all nutrients take: GI tract $\rightarrow$ portal vein $\rightarrow$ liver.

The brain also monitors long-term stored energy by monitoring insulin and leptin levels, which circulate in proportion to energy stores in normal-weight individuals. $\beta$-cells in the pancreas detect and secrete insulin in response to increased circulating glucose levels in the liver. Insulin stimulates glucose and fatty acid storage in liver and muscle cells. Leptin is secreted by fat cells. In the brain, low insulin and leptin stimulate reduced energy expenditure and increased food intake, and high insulin and leptin levels stimulate increased energy expenditure and decreased food intake (Schwartz, Woods, Porte, Seeley, & Baskin, 2000).

Ultimately, the brain integrates metabolic information (Berthoud et al., 2017) with information from neural circuits involved in “liking” (μ-opioid systems) and “wanting” food (mesolimbic dopaminergic system), learning and memory, and executive functions. Considerable integration takes place in the hypothalamus, which regulates energy release during environmental changes. For example, cortisol increases circulating glucose and reduces insulin sensitivity, which, according to “selfish brain” theory (Peters et al., 2004), preferentially directs energy to the brain (and the immune system; Yamagata et al., 2017) to help maintain survival.

**Cardiovascular System**

Primarily acting as a blood transport system, the cardiovascular system delivers the necessary nutrients and oxygenated blood to tissues in the body, and has several regulatory pathways (Dampney, 1994). The heart acts as the pump that distributes oxygenated blood via arteries throughout the body (see Figure 5.1). Internal monitoring of the system is fulfilled primarily by baroreceptors located in the heart and blood vessels that measure blood pressure, and by chemoreceptors located in the carotid arteries that measure oxygen and carbon dioxide levels (see Figure 5.1; Berntson, Quigley, Norman, & Lozano, 2017). Baroreceptors are mechanical receptors that detect changes in pressure, and chemoreceptors are sensory receptors that respond to chemicals in the body. ANS regulation involving PSNS and SNS activity leads to changes in how fast and hard the heart beats, and in dilation of arteries (Steptoe & Kvivimäki, 2012). Much of the interest in biological pathways linking psychosocial factors to the cardiovascular system is in the context of cardiovascular disease, described in the *Implications for basic and translational research* section at the end of this chapter.
Biological Processes of Health

**Conceptual Issues**

### Allostatic and Restorative Processes

All organisms must adapt to environmental changes, from daily weather changes to resource scarcity (e.g., drought, economic recessions). *Allostasis*, initially described by Sterling and Eyer (1988), refers to altering biological setpoints or function to maintain survival. For example, increasing body temperature above the tightly regulated 36–37°C baseline can help the immune system eradicate infection (Best & Schwartz, 2014). McEwen applied the allostasis concept to the systems reviewed in this chapter (McEwen, 1998), noting that during stress exposures, *allostatic processes* like releasing stored energy, increasing the sensitivity of cells to respond to signaling from the brain, and altering blood flow can help organisms maintain survival (Peters et al., 2004; Sapolsky et al., 2000). Over time, repeated activation of allostatic processes may lead to *allostatic load*, which is the chronic wear and tear on biological systems that respond to exposures (McEwen, 1998).

Apart from chronic stress exposures that do not end (e.g., refugee status, persistent exposure to noise), individuals spend most of their time *not* exposed to environmental changes, such as during sleep (Robles & Carroll, 2011). During those times, *restorative processes* throughout the systems reviewed in this chapter help return functioning to pre–challenge states. Such processes promote energy storage and tissue growth, production of antioxidants to combat oxidative stress, and genomic repair. Many restorative processes are inhibited by allostatic processes. Digestion, for instance, is inhibited during fight–or–flight responses to stress exposures. Thus, psychosocial factors more broadly may disrupt restorative processes by slowing the rate of repair/rebuilding (e.g., delayed wound healing), disrupting the integrity of materials used to restore function (e.g., altering enzymes that repair DNA), or disrupting normal restorative processes through overcompensation (e.g., increasing appetite and decreasing metabolism). Ultimately, the conceptual distinction between allostatic and restorative processes can be helpful for researchers interested in incorporating the biological systems reviewed in this chapter into theory and research (Robles & Carroll, 2011).

The allostatic load concept suggests the wear and tear of biological systems has implications for long-term functioning and the onset of disease (McEwen, 1998). Researchers are tasked with deciding whether to examine biological processes in the context of acute psychosocial stimuli and/or apply longitudinal designs to track the development of dysregulation and its role in disease onset. Utilizing psychosocial stressors (e.g., Trier Social Stress Test) allows researchers the ability to capture individual differences in stress reactivity across healthy and clinical populations (Kudielka, Hellhammer, & Wust, 2009). However, to examine whether stress mediators play a causal role in disease progression, longitudinal designs capturing baseline functioning and dysregulation prior to disease onset and intervention studies that modify stress mediators should remain priorities in future health research.

### Gene and Environmental Contributors to Individual Differences

Earlier, we highlighted changes in the structure and function of cells via modifications in gene expression as common mechanisms linking psychosocial factors to the pathophysiology of disease. The expression of specific genes, the function of their associated molecular products, and consequently the structure and function of cells can vary both between people and within people. Between–person differences can be due to variations in the genetic code (*genotype*) between people, such as alterations in a single nucleic acid for a specific set of coding instructions (*a single nucleotide polymorphism* or SNP in a specific gene), or *epigenetic modifications* to an individual’s DNA (Slavich & Cole, 2013). Epigenetic modifications are any changes in the DNA that do not involve changes to
the nucleic acids in the gene sequence itself (Champagne & Mashoodh, 2009). Genotype variations
or epigenetic modifications can result in between-person differences in the degree or amount of
gene expressed and protein produced, or changes in the structure of the protein itself; both can have
important implications for the function of tissues and cells.

At the same time, genotypes exist in environments, and the environment plays critical roles in
regulating gene expression. For instance, individuals with a specific variation in a specific gene may
be more susceptible to harmful or beneficial features of the environment; those factors could include
environmental (pollution exposure, drought, infectious illness exposures) and social (socioeconomic
status, quality of family relationships, stress exposure) factors. When different genotypes have dif-
f erent responses to a specific environmental factor, this is known as a gene X environment
interaction (Champagne & Mashoodh, 2009). In a recent example from two large epidemiological studies
(Multi-Ethnic Study of Atherosclerosis, Framingham Cohort 2), for individuals with a specific SNP
in the EBF1 gene (which codes for a protein involved in gene transcription in B-cells), greater self-
reported exposure to chronic psychological stress was related to surrogate CVD endpoints including
greater waist circumference, fasting glucose, prevalence of diabetes, and a marker of atherosclerosis;
but only among White participants (Singh et al., 2014). Accounting for individual differences due to
genotypes, gene x environment interactions, and epigenetic modifications is a challenging but excit-
ing direction for future work on biological processes related to health and their intersection with
psychosocial factors.

Implications for Health Psychology

Implications for Basic and Translational Research

This chapter began with making key conceptual distinctions among clinical endpoints, surrogate
endpoints, and biological mediators when incorporating biological processes and measures into
health psychology research. For researchers focused on a specific disease population, a highly recom-
mended starting point for making those distinctions is “reverse engineering” the pathophysiology
of that disease to identify points where disease biology intersects with biological mediators (Miller,
Chen, & Cole, 2009). For many chronic health conditions, biologically plausible pathways from
psychosocial factors to biological mediators to disease pathophysiology have been identified and
reviewed elsewhere, including many cancers (Antoni et al., 2006), adverse outcomes in pregnancy
(Dunkel Schetter, 2010), and HIV (Miller et al., 2009). As an illustrative example, we focus on cardio-
vascular disease (CVD): a group of diseases that impacts the cardiovascular system, with heart attack,
stroke, or heart failure as key clinical endpoints/outcomes.

Several psychosocial risk factors are related to CVD, including depression, social isolation, and
hostility (Bishop, this volume), which are in turn related to autonomic and neuroendocrine signaling
to the rest of the body. Those neuroendocrine signals influence immune, metabolic, and cardiovas-
cular function, and one “hub” for those influences is atherosclerosis, which is characterized by the
buildup of fat and inflammation in the lining of arteries (Pasterkamp, den Ruijter, & Libby, 2017).
Metabolic pathways play key roles in the pathophysiology of atherosclerosis and other cardiomet-
bolic risk conditions, particularly type 2 diabetes (Kahn, Cooper, & Del Prato, 2014). Type 2 diabetes
is characterized by insulin resistance in which insulin-sensitive tissues do not effectively respond to
insulin signals. Finally, individuals who show high levels of cardiovascular reactivity to stress show
faster progression of atherosclerosis and increase risk for CVD (Merz et al., 2010). This is due in
part to increased blood pressure and catecholamine surges that can result in damage to the lining of
blood vessels (Steptoe & Kivimäki, 2012), and the increased probability of inflammation occurring
in sites of artery damage (Pasterkamp et al., 2017). While these pathways are now relatively straight-
forward, uncovering them required decades of research, and translating that knowledge into effective
psychosocial prevention and intervention strategies in clinical settings will take additional decades of translational work.

Much of the work delineating pathways involved drawing from animal models, which is an important starting point for basic research. At the same time, there is a dearth of inclusive models because female animals are often excluded from research (Prendergast, Onishi, & Zucker, 2014). An important next step for basic research is incorporating biomarker measurements of the mediators or endpoints of interest that have a high degree of precision (reliability) and validity. Finally, while laboratory studies provide a controlled environment for studying biological mechanisms, assessing biomarkers in naturalistic settings can provide greater generalizability to everyday experience.

For translational and intervention research, the biological mediators in this chapter may represent potential intervention targets or mechanisms of change (Slopen, McLaughlin, & Shonkoff, 2014). In addition, individual differences in genotypes and/or phenotypes related to the biological pathways described in this chapter may serve as starting points for developing precision medicine (tailored) interventions (Belsky & van Ijzendoorn, 2015). Finally, surrogate endpoints can serve as key primary or secondary outcomes in psychosocial intervention studies.

**Biological Processes in Diverse Contexts: Age, Ethnicity**

The biological processes covered in this chapter may be more sensitive to the psychosocial environment during specific developmental stages. In particular, early life adversity is related to poor health later in life, and many of the mechanisms that explain such links include the biological processes described in this chapter (Bush, Lane, & McLaughlin, 2016; Miller, Chen, & Parker, 2011). For example, the HPA axis is more sensitive to the quality of caregiving during early childhood (Hostinar, Sullivan, & Gunnar, 2014), with long-lasting impacts on HPA functioning. Lifespan approaches are critical to understanding how biological mediators facilitate disease progression; unfortunately, existing studies rely heavily on retrospective reports of the early environment emphasizing the need for longitudinal designs in future health research.

Adverse health conditions disproportionally affect racial and ethnic minorities; for example, Hispanic children and African Americans are at greater risk of developing cardiovascular disease (National Center for Health Statistics, 2015). Minorities also report greater exposure to socio-environmental influences that increase the risk of poor health outcomes (e.g., exposure to poverty). Chronic exposure to adversity related to low socioeconomic status may be associated with differences in structure and function in the brain regions described earlier (Gianaros & Hackman, 2013). Such differences may then influence cognition, emotion, behavior, and physiology that then manifest in chronic illness in later life. Group differences in the functioning of biological mediators have also been documented, with psychosocial stress and neuroendocrine functioning being more strongly linked in Hispanic and African American adults (DeSantis, Adam, Hawley, Kudielka, & Cacioppo, 2015). The growing percentage of non-White minorities in the U.S. highlights the need to conduct research on mechanisms underlying racial and ethnic health disparities. For a discussion on determinants of health in underrepresented communities, see part IV in this *Handbook*.

**Conclusion**

More than 100 years after the Franz reports in *Journal of the American Medical Association* and *Science*, biomedical science has made enormous strides in accurately describing the pathology and physiology of disease states. Psychology in turn has incorporated many of those advances into the biopsychosocial models of health and disease that health psychologists use today. Health psychologists working in a particular disease or health condition “space” would be well-advised to learn the state of the science on underlying disease or condition biology, such as through comprehensive reviews
in journals like The Lancet or New England Journal of Medicine, and stay up-to-date with changes in biomedical understanding of disease pathophysiology over time. As psychologists continue to complement their understanding of psychosocial factors and interventions with a better understanding of biological processes related to health, researchers, clinicians, and ultimately patients will benefit.

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