Chapter 21
Salivary Bioscience Research in Health Psychology and Behavioral Medicine

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Abstract Since their inception, the fields of health psychology and behavioral medicine have largely adopted a biopsychosocial approach to understanding health and the manner in which psychological and social factors "get under the skin." Facilitated by advances in salivary bioscience, great strides over the past several decades have been made in understanding the biological processes by which such factors influence health and disease. Health psychology and behavioral medicine research have integrated advanced clinical and laboratory assessments of relevant immune system and neuroendocrine markers in saliva to identify mechanisms, stress processes, and evaluate the impact of clinical intervention on physiological systems. This chapter highlights contributions of salivary bioscience to health psychology and behavioral medicine with an emphasis on research related to understanding adjustment to chronic illness and the influence of psychological and social factors on disease processes. Research utilizing salivary markers of hypothalamic–pituitary–adrenal axis activity, sympathetic nervous system activation, as well as other neuroendocrine and immune processes has greatly contributed to our understanding of psychological adaptation to illness and the composition of clusters of adjustment-related symptoms such as fatigue, pain, and depression. In addition, documented changes in salivary levels of health-relevant biomarkers in response to behavioral interventions have contributed to a new definition of intervention efficacy. This broad synthesis of the literature emphasizes a more integrated biopsychosocial framework for understanding health and well-being.

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D. A. Granger, M. K. Taylor (eds.), *Salivary Bioscience*,
https://doi.org/10.1007/978-3-030-35784-9_21

Keywords Salivary bioscience · Health psychology · Behavioral medicine · Chronic illness · Stress · Cortisol

21.1 Salivary Bioscience Research in Health Psychology and Behavioral Medicine

The quest to understand the interactions between psychological and physiological factors in human health can be traced across ancient and modern civilizations. Catalyzed by advances in salivary bioscience, the past several decades have brought significant progress in psychosomatic medicine, psychoneuroimmunology, neuroscience, and in our understanding of the health impact of psychological and social stress. The fields of health psychology and behavioral medicine have made vital contributions to this knowledge base and have increasingly become more interdisciplinary as a more complete biopsychosocial model actualizes. This chapter highlights contributions of salivary bioscience to health psychology and behavioral medicine with an emphasis on research related to understanding adjustment to chronic illness and the influence of psychological and social factors on disease processes. As a nexus between health psychology and behavioral medicine, the focus will be on pertinent studies of conditions that comprise significant causes of morbidity and mortality such as cardiovascular and pulmonary diseases, cancer, HIV/AIDS, and rheumatic diseases. The emphasis is on building from empirically supported conceptualizations of psychological adaptation to these conditions, to present an expanded biobehavioral model that emerges, in part, from contributions from salivary bioscience. This includes understanding the management of illness across the disease trajectory as well as influences on its progression. Although this chapter concentrates on chronic illness, it should be noted that salivary bioscience also exerts influence across a variety of areas in health psychology and behavioral medicine including studies of general health promotion and prevention (e.g., Tomiyama et al., 2014), experimental health psychology (e.g., Dickerson & Kemeny, 2004), social processes and relationships (e.g., Kornienko, Schaefer, Pressman, & Granger, 2018; Robles, Slatcher, Trombello, & McGinn, 2014; see also Chap. 22), health disparities (e.g., Le-Scherban et al., 2018), and basic stress processes (see Nater, Skoluda, & Starhler, 2013). We call upon mostly studies of adults with chronic illness; however, relevant literatures exist with a focus on the health of children and adolescents (e.g., Jessop & Turner-Cobb, 2008; see also Chap. 26).

Noncommunicable disease accounts for 70% of worldwide mortality (World Health Organization [WHO], 2017). At the same time, compared with past decades, individuals are living long periods of time following a diagnosis (Centers for Disease Control and Prevention [CDC], 2017). There are thousands of studies to show that the experience of chronic illness can cause significant disruption across life domains. Thus, health psychologists and others have devoted intense empirical and clinical attention to identifying psychosocial and biobehavioral contributors to, and

consequences of, chronic illness and to developing approaches to reduce physical and psychological morbidity (see Hoyt & Stanton, 2018). Hoyt and Stanton (2018) articulated a model of psychological adjustment to chronic illness in which interrelated contexts of risk and resilience (e.g., disease/treatment factors, social processes, personality, socioeconomic factors, and gender) exert influence on various domains of psychological adjustment by way of cognitive, affective, and behavioral responses that include coping strategies.

Although this and other (see Helgeson & Zajdel, 2017) models of disease adjustment possess significant utility, more recent research utilizing salivary markers of hypothalamic–pituitary–adrenal axis activity, sympathetic nervous system activation, as well as other neuroendocrine and immune processes has greatly added to our understanding of the biobehavioral pathways by which psychological processes influence adaptation to illness; relate to the composition of clusters of adjustment-related symptoms such as fatigue (e.g., Bower, Ganz, & Aziz, 2005), pain (e.g., Fischer et al., 2016), and depression (e.g., Weinrib et al., 2010); and possess potential to influence progression of disease (e.g., Spiegel, 2012). For instance, emotional responses to acute and sustained stressors contribute to the modulation of neuroendocrine activity that may provide a link between stress responses, suppressed immunity, and disease-related processes (Fagundes, Murdock, Chirinos, & Green, 2017).

21.2 Measuring Stress to Understand Adjustment

Since the advent of the field, health psychologists and behavioral medicine professionals have been searching to understand how stressful experiences impact human health (Friedman & Adler, 2007). The growth of biological knowledge by the 1970s and a new demand for rigorous research methods that incorporated both behavioral as well as biological science gave way to a new research zeitgeist which included understanding links between external stressors and organic illness. However, new methods of inquiry that integrated and measured biological processes were needed for behavioral scientists.

Salivary bioscience has provided an accessible window into physiological stress processes. This has included access to a broad range of salivary biomarkers, with health psychologists and behavioral medicine professionals being largely interested in understanding how psychosocial experiences relate to physiological stress. Stress is the dynamic response that takes place in both the central nervous system and the periphery of the body that one experiences when demands are perceived to exceed one's personal resources. The involvement of two distinct physiological systems has been identified. The sympathetic adrenomedullary system prepares the body's *flight or fight* response through activation of the sympathetic nervous system. This involves the secretion of epinephrine and norepinephrine by the adrenal glands leading to an increase in heart rate and more rapid metabolization of glucose. The hypothalamic–pituitary–adrenal (HPA) axis is also involved in the stress response. Activation of this system involves increased secretion of corticotrophin-releasing

hormone and stimulation of the pituitary gland. The pituitary gland secretes adrenocorticotrophic hormone inducing an increased release of glucocorticoids by the adrenal cortex. In humans, the glucocorticoid cortisol prepares the body for responding to stressful demands and has been implicated in delaying the body's innate immune response. These systems work in tandem to direct energy from nonessential processes to those necessary to overcome stressors, such as increases in cardiac and respiratory activity, energy consumption, and mental activity.

Although a broader array of salivary analytes is gaining prominence in the health psychology and behavioral medicine literature, salivary cortisol (as a marker of HPA activity) has been a dominative focus. Consistent with findings in individuals who experience chronic stressors (e.g., informal caregivers; Leggett, Liu, Klein, & Zarit, 2016), relationships of both blunted (e.g., flatter diurnal cortisol slope) and elevated cortisol (e.g., higher daily cortisol output or greater area under the curve) responses have been documented in chronic illness groups. Salivary cortisol also has documented associations to health outcomes known to greatly impact quality of life including functional disability (Weinrib et al., 2010), pain exacerbations (Yeung, Davis, & Ciaramitaro, 2016), fatigue (Bower et al., 2005), and sexual dysfunction (Hoyt, Gaffey, Wang, & Lawsin, 2018). The HPA system is often considered to be a mediating system of acute and chronic psychosocial states and disease processes. It is also shown to be particularly sensitive to laboratory stressors (Dickerson & Kemeny, 2004).

Increasingly researchers have been utilizing measures of salivary alpha-amylase (sAA) as a reliable marker of autonomic nervous system (ANS) activity (Granger, Kivlighan, El-Sheikh, Gordis, & Stroud, 2008; Nater & Rohleder, 2009). sAA increases with ANS activation via a release by acinar cells which are innervated by both sympathetic and parasympathetic activity. During periods of psychological stress, sAA level is predominantly influenced by SNS activity in the cervical sympathetic pathway, and sAA levels rise in response to stress (Bosch, de Geus, Veerman, Hoogstraten, & Nieuw Amerongen, 2003; Nater, Rohleder, Schlotz, Ehlert, & Kirschbaum, 2007). Studies that have included measures of both salivary cortisol and sAA have been able to distinguish associations between HPA and somatic nervous system involvement. SAA shows distinct patterns from salivary cortisol in response to stress and might better capture anxious versus depressive reactivity (Yoon & Weierich, 2016). For instance, in fibromyalgia patients Fischer and colleagues (2016) found that cortisol, but not alpha-amylase, impacted momentary pain in a 14-day ambulatory monitoring study.

21.3 Salivary Bioscience and Adjustment to Chronic Illness

21.3.1 Depressive Symptoms After Chronic Illness

The onset or worsening of depressive symptoms following the diagnosis or treatment of chronic illness is an important indicator of adjustment to chronic disease. In

fact, although heterogeneity exists, large prospective studies demonstrate that individuals with chronic illness are at elevated risk for depressive symptoms (Polsky et al., 2005). Cancer survivors have the highest risk of depressive symptoms within 2 years after diagnosis (hazard ratio [HR] = 3.55), followed by chronic lung disease (HR = 2.21) and heart disease (HR = 1.45), versus those with no incident disease. Researchers have been successful in identifying psychological and social predictors of symptom onset; however, research to understand the neurobiological risk factors and mechanisms is emerging. Relationships of dysregulation in salivary cortisol and depressive symptoms have been documented. Studies outside of chronic illness groups have pointed to dysregulation in HPA axis as underpinning elevations in depressive symptoms (Bhagwagar & Cowen, 2008; Stetler & Miller, 2011). It appears that HPA axis over-activation, at least initially, dampens prefrontal inhibition of a sustained stress response, which yields adrenal overstimulation in a feedback loop that terminates in anhedonic states (e.g., Gold, 2015), though notable variation exists across groups and individuals.

Depressive symptoms have been associated with dysregulation in multiple indices of salivary cortisol including morning levels, evening values, and the pattern of cortisol levels across the diurnal cycle in samples of individuals with cancer (Jehn et al., 2006; Lutgendorf et al., 2008; Sephton et al., 2009), cardiovascular disease (Nikkheslat et al., 2015), and HIV (Barroso, Burrage, Carlson, & Carlson, 2006). In some cases, salivary cortisol is more strongly related to depressive symptoms than are treatment factors (see Bower, 2008). However, more longitudinal research is necessary to establish a mechanistic role of cortisol dysregulation. For instance, Kuhlman et al. (2017) found that a higher cortisol awakening response predicted greater increases in depressive symptoms across 6 months in women with early-stage breast cancer.

It is notable that the HPA axis is implicated in regulating inflammation. In depressed patients, cortisol's role in the negative feedback loop leading to anti-inflammatory effects is impaired (Pariante & Miller, 2001) and depressed individuals can experience chronically elevated nocturnal cortisol (Deuschle et al., 1997). Thus, excessive inflammation resulting from impaired glucocorticoid receptor sensitivity is observed with greater depressive symptomatology (e.g., Carvalho et al., 2015). In a study of coronary heart disease patients, Nikkheslat et al. (2015) document that in the presence of low salivary cortisol output, depression is accompanied by elevated levels of inflammation and glucocorticoid resistance. Such findings provide insight into the role of inflammation and salivary cortisol in the etiology of depression in chronic illness patients, and evidence of possible inflammatory pathways to the progression of the disease.

21.3.2 Coping with Chronic Illness

Evidence exists that diurnal cortisol rhythm may be influenced by individual coping strategies in chronic illness groups (e.g., Diaz, Aldridge-Gerry, & Spiegel, 2014).

However, relatively few studies have sought to identify the possibility that specific strategies for coping with illness-related stressors can shape salivary biomarkers (e.g., diurnal cortisol). In this context, coping constitutes behavioral and cognitive efforts to manage the illness-related demands (Lazarus & Folkman, 1984). Coping responses, often categorized as either approach-oriented (e.g., active planning) or avoidance-oriented (e.g., disengagement), modulate the negative consequences of illness-related stressors and impact adjustment and quality of life (Baldwin, Kellerman, & Christensen, 2010). In prostate cancer patients, cancer-related avoidance-oriented coping, and not approach-oriented coping, is associated with more blunted cortisol slope over time (Hoyt et al., 2014).

Identification of the mechanistic salivary biomarkers that influence adjustment and overall health outcomes holds promise for the identification of modifiable coping behaviors useful for the development of tailored interventions. A strong example comes from work on coping processes relevant to goal pursuit. As disease-related demands are perceived as threatening to central goals, the greater the perception of stress, and the more coping processes are engaged. Self-regulation theories highlight the importance of perceived goal blockage in shaping coping and adjustment (e.g., Leventhal, Halm, Horowitz, Leventhal, & Ozakinci, 2005). To the extent that an individual expects those goals are obtainable despite illness, or to the extent that one perceives the ability to identify and engage in alternative goal pursuit, then initiation of approach-oriented coping strategies is likely (Hoyt, Gamarel, Saigal, & Stanton, 2016). However, if a person expects unremitting goal blockage and does not engage in new goals, disengagement might ensue. Likewise, continued pursuit of unobtainable goals will likely exert a negative effect on adjustment (Wrosch, Scheier, Miller, Schulz, & Carver, 2003). The ability to disengage from unattainable goals is associated with better self-reported health and more normative patterns of diurnal cortisol secretion (Wrosch, Miller, Scheier, & de Pontet, 2007). In breast cancer patients, reengagement in meaningful goals following goal blockage appears to buffer against elevated daily cortisol secretion associated with negative affect (Castonguay, Wrosch, & Sabiston, 2017).

Research utilizing salivary biomarkers can also uncover patterns of resilience. In a study of 111 cancer survivors, Costanzo, Stawski, Ryff, Coe, and Almeida (2012) observed that relative to a matched non-cancer comparison group, cancer survivors showed less pronounced changes in cortisol output in response to interpersonal conflict. Similarly, higher mean daily cortisol is associated with poor disease-related social support (Turner-Cobb, Sephton, Koopmanm, Blake-Mortimer, & Spiegel, 2000). Observations that salivary markers are sensitive to variation in coping behaviors, resilience factors, and coping resources provide a strong rationale for targeted intervention development.

21.3.3 Behavioral Medicine Interventions and Salivary Bioscience

The many associations between salivary biomarkers and health indicators suggest that modulation of salivary biomarkers via behavioral interventions may play an important role in influencing health and long-term adjustment to disease. Targeted interventions that aim to modulate HPA axis function or autonomic nervous system regulation hold significant promise, though more randomized controlled trials (RCTs) are necessary. Cortisol is the most widely studied salivary marker in behavioral medicine intervention research. However, reviews of this literature are inconclusive in determining whether such interventions render meaningful changes on salivary diurnal cortisol (Ryan, Booth, Spathis, Mollart, & Clow, 2016). This is in large due to significant heterogeneity across studies in regard to saliva collection procedures and reported cortisol parameters (i.e., cortisol awakening response, area under the curve, diurnal slope, etc.).

Broad variation exists in the design and results of behavioral medicine interventions with identified salivary biomarkers outcomes. Several studies have focused on the use of mindfulness-based stress reduction (MBSR). In an RCT with 271 distressed breast cancer survivors, Carlson et al. (2013) observed more flattened cortisol slopes over time in their control group, but the maintenance of slope in those receiving MBSR plus yoga (as well as those receiving supportive-expressive therapy). However, MBSR was not associated with changes in salivary melatonin in breast and prostate cancer patients (Carlson, Speca, Patel, & Goodey, 2004). However, null findings of cortisol parameters have been documented after mindfulness-based intervention trials including fibromyalgia patients (Cash et al., 2016) and cancer patients with sleep disturbance (Lipschitz, Kuhn, Kinney, Donaldson, & Nakamura, 2013). Although Lipschitz et al. (2013) did not observe effects on cortisol, they found lower sAA activity in the morning after a sleep hygiene education group compared to those in a sleep-focused mind–body intervention.

Group-based cognitive behavioral stress management (CBSM) interventions have also demonstrated a salutary impact on HPA regulation. In a study of HIV+ gay men, baseline cortisol levels decreased across 10-week CBSM participation (Cruess, Antoni, Kumar, & Schneiderman, 2000). Moreover, cortisol reductions had associations decreases in distress, perceived stress, and more frequent at-home relaxation practice. Salivary biomarkers have also been used in pharmacologic trials (e.g., Chaborski, Bitterlich, Alteheld, Parsi, & Metzner, 2015) and integrative medicine trials (e.g., Tornhage et al., 2013).

As discussed by Ryan et al. (2016), little guidance exists on the use of salivary measures in intervention research. To avoid bias and error in RCT design, researchers must consider their hypothesized mechanism of change when identifying *primary* intervention outcomes a priori. For instance, the diurnal profile of various salivary markers renders a host of measurement parameters (e.g., cortisol awakening response versus diurnal cortisol slope) that signal different aspects of the biological mechanism of interest. They also warn that researchers should consider long- and

short-term stability and reliability of the marker of interest when considering intervention interval and follow-up periods.

21.4 Salivary Biomarkers, Disease Processes, and Progression

In addition to the contribution of salivary bioscience to identifying the biological pathways to domains of disease adjustment, the past several decades have yielded groundbreaking strides in our understanding of the multiple biological pathways by which psychosocial and behavioral factors can also affect the progression and symptoms of chronic illness. Long-term epidemiological studies demonstrate that higher cortisol levels (in men) and higher evening cortisol (in women) are associated with increased mortality risk and chronic disease onset (Schoorlemmer, Peeters, van Schoor, & Lips, 2009).

To the degree that salivary bioscience allows researchers to measure aspects of physiological stress patterns, it facilitates the discovery of how stress precipitates, exacerbates, or maintains physical symptoms. As discussed, cortisol dysregulation is linked to pain (Crofford et al., 2004) and mood disturbance (Deuschle et al., 1997), with some evidence that cortisol dysregulation may precede symptoms. However, despite that psychological models have emphasized its role in physical health, evidence linking cortisol to specific disease outcomes has been mixed. As evidence builds for HPA dysregulation underlying physical symptoms such as fatigue, results across studies are not always consistent. More research examining the contextual moderators of cortisol's impact on physical symptoms is warranted. Wrosch, Miller, Lupien, and Pruessner (2008) showed that higher cortisol levels were associated with increases in physical symptoms in older adults, but only among those who reported relatively high negative affect and poor sleep.

Strides are being made to not only understand influences on physical symptoms but also on disease progression. This association has been evidenced across chronic disease and illness populations including cancer, cardiovascular disease, asthma, HIV, and pain conditions. For instance, asthmatics with poorly controlled asthma (a signifier of progressed disease) presented with significantly lower levels of morning salivary cortisol than those with greater symptom control (Shin et al., 2014). Similarly, in cardiovascular disease patients, intima media thickness (a measure of atherosclerosis or arterial plaque buildup) is associated with a greater cortisol awakening response in women (Eller, Netterstrøm, & Allerup, 2005). In the case of HIV, elevated cortisol levels (measured in saliva and serum) have been linked to markers of disease progression, including increased viral load (see Ironson et al., 2015; Schneiderman, Ironson, & Siegel, 2005). Flatter diurnal cortisol slopes evidenced in patients with metastatic breast cancer (Abercrombie et al., 2004) have been linked to early mortality (Cohen et al., 2012; Schrepf et al., 2015; Sephton et al., 2013) leaving researchers to discover in what ways cortisol might be

influencing tumor dynamics. Early work in animal models suggested that experimentally induced impairments in cortisol feedback enhance tumor growth (Sapolsky & Donnelly, 1985). Similar patterns are evident in human studies. Blunted diurnal slopes of salivary cortisol observed prior to surgery have been associated with markers of inflammation in the tumor microenvironment in ovarian cancer patients (Lutgendorf et al., 2008; Weinrib et al., 2010) and appear to play a role in the upregulation of tumor inflammation (Schrepf et al., 2015).

Research has found that sleep is vital to slow disease progression and conversely, that without adequate sleep an individual with a chronic health condition may be at risk for worsened disease progression. Moreover, the assessment of salivary measures has helped to identify the mechanisms of the impact of sleep on disease progression. Although Cash et al. (2015) did not find support for an association of psychological distress and tumor progression among breast cancer patients ($n = 43$), they did find that elevated cortisol awakening responses and circadian activity rhythm disruption (i.e., poor sleep quality) were related to tumor progression and immunosuppression markers (i.e., VEGF, MMP-9, and TGF-b). It may be that increased nighttime cortisol impairs adequate biological restoration during sleep.

Although melatonin is known to modulate the sleep–wake cycle (Zhdanova, Lynch, & Wurtman, 1997), few behavioral medicine studies have examined salivary melatonin, particularly in the context of chronic illness. More research examining salivary melatonin in chronic illness groups might help to better understand changes in sleep quality, as well as the impact of sleep disruption on disease outcomes. For instance, work in patients with chronic renal failure suggests that disease-related disruptions in nocturnal production of melatonin might underscore sleep problems (Pinto, da Silva, & Pinato, 2016). Research in this area is limited; however, similar patterns have been documented in pregnant women with gestational hypertension or diabetes (Shimada, Seki, Samejima, Hayase, & Shirai, 2016).

Identifying mechanisms of how stress-related pathways influence the disease process is a new frontier for research in health psychology and behavioral medicine, but more longitudinal studies in this domain are warranted. Most studies to date highlight significant differences between groups at different stages of disease severity. However, a stronger contribution will be made with within-subject studies that track changes in salivary markers overtime. Further, more research that address salivary biomarker's predictive capabilities of disease progression will help elucidate causal chains.

21.5 Conclusions and Future Directions

This chapter called upon research on psychological adaptation to chronic illness to highlight the contributions and potential of salivary bioscience to develop new and expanded conceptual models that underscore research and practice in health psychology and behavioral medicine. What emerges is an expanded model of adjustment to chronic illness that includes biological mechanisms and physiological

pathways connecting stress and psychosocial determinants of adaptation, as well as a framework for inclusion of relationships with disease processes and progression. Future research should continue to test and refine this emergent biobehavioral model.

The progression of knowledge about biological stress processes is intertwined with the advent and growth of behavioral medicine and health psychology. Understanding how external factors impact health via stress-mediated physiological pathways has marked progress in these fields for decades. It follows that research to date has centered on the assessment of salivary cortisol and alpha-amylase. This work has made vital contributions to the field, and now more studies are emerging examining other salivary biomarkers. These new frontiers hold promise for strengthening the biobehavioral model. For instance, salivary oxytocin has been linked with enhanced feelings of empathy and social connectedness, anxiety reduction, better pain tolerance, and increased attention to positive stimuli in depressed patients (Cochran, Fallon, Hill, & Frazier, 2013; Domes, Normann, & Heinrichs, 2016; Rash, Aguirre-Camacho, & Campbell, 2014) and has been shown to be sensitive to behavioral intervention (Fancourt et al., 2016). Despite these observations, studies of those with chronic illness are only beginning to emerge. In a prospective study, craniopharyngioma patients showed a blunted salivary oxytocin-release compared to controls and this was associated with higher anxiety (Gebert et al., 2018). Continual advances in the measurement of neurotransmitters, cytokines, and analytes that signal such processes as sleep (e.g., melatonin) and metabolic activity (e.g., uric acid) will yield more sophisticated biobehavioral research and more targeted behavioral interventions.

Notably, research designed to understand the mechanistic potential of pro-inflammatory cytokine activation in unique relationships of psychosocial factors and disease processes has been fruitful (see Irwin & Slavich, 2017). The preponderance of this research has relied on the measurement of circulating levels of immune markers in the blood. Acquisition of blood in health psychology and behavioral medicine research impairs ecological assessment and presents logistical challenges and undue participant burden in studies that rely on observations across time or at multiple moments across the day. Salivary measures of inflammation offer the promise of measuring inflammation *in the moment*. However, salivary cytokine studies should be interpreted with significant caution. Across the limited number of empirical studies, salivary markers of inflammation (i.e., IL-1b, TNF-a, and IL-6) have been reliably measured; however, associations with measures of circulating blood levels have been inconsistent (Slavish, Graham-Engeland, Smyth, & Engeland, 2015). Salivary measures of inflammatory markers appear to better reflect activity in the oral mucosa immune environment rather than systemic inflammation (Riis, Granger, DiPietro, Bandeen-Roche, & Johnson, 2015).

Several challenges remain that challenge the progression of salivary bioscience in health psychology and behavioral medicine. Foremost is a need for training across disciplines. Few health psychologists and behavioral medicine professionals receive training in laboratory procedures or research design related to the assessment of salivary biomarkers. In addition to pairing with professionals across disciplines,

researchers are encouraged to seek training experiences and guidance when designing sample collection and analysis protocols (see Adam & Kumari, 2009; Nicolson, 2008). It is imperative that investigators understand the dynamics of measured markers, including any diurnal rhythm, sampling strategy considerations, storage and handling recommendations, and potential within- and between-individual factors confounding measurement. Finally, researchers will need to ensure that all laboratory results are inspected for quality assurance.

Behavioral science researchers should apply principles of high-quality research design used in studies of psychosocial variables to studies including salivary biomarkers. This begins with having clearly defined study objectives and hypotheses. Health psychology and behavioral medicine research are predicated on theory-driven hypotheses. The integration of salivary biomarkers should fit within sound conceptual underpinnings. Studies that relegate biomarkers to exploratory measures run a greater risk of Type I error. Relatedly, studies should be adequately powered for planned analyses. The collection of saliva from a mere sample subset might render inadequate statistical power or contain systematic bias.

Research in salivary bioscience continues to expand our collective knowledge of biobehavioral processes and health. Perhaps more than ever before we are unlocking the secrets of mind–body relationships. However, this can only be achieved when researchers adhere to fundamental principles of the careful study design including vigilant quality control and utilization of informed laboratory procedures, careful data analysis, caution in the interpretation of research findings, and sufficiently powered replication of research results.

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