Social and Personality Psychology Compass 9/12 (2015): 645–660, 10.1111/spc3.12224

Positive Psychological Functioning and the Biology of Health

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Abstract

Most research considers both psychological and physical health with a disease perspective by focusing on poor psychological functioning or disease outcomes. However, identifying attributes that support adaptive functioning may inform approaches to achieving health beyond what we learn from studying risk factors that accelerate deterioration. Recent evidence suggests that positive psychological functioning contributes to attaining optimal physical health. We evaluate the current state of knowledge on the relationship between positive psychological functioning and physical health, defining health beyond solely the absence of disease. We further consider when positive psychological functioning begins to exert effects on health, whether it has direct effects on biological processes or serves primarily to buffer the effects of stress, and whether it is associated with health outcomes and biological processes beyond those that reflect the absence of deterioration and disease. We propose some key directions for future research including the assessment of positive psychological functioning, positive biological functioning, and optimal health, the value of multi-system measures, and the potential of "omics" to provide novel insights into biological mechanisms underlying associations between positive psychological functioning and physical health.

Introduction

Psychological health and physical health are closely intertwined. Research has documented consistent associations between poor psychological health (e.g., depression, anxiety, stress) and increased risk of chronic conditions and diseases such as obesity, hypertension, diabetes, and cardiovascular disease (Luppino et al., 2010; Steptoe & Kivimaki, 2013; Suls & Bunde, 2005). Moreover, individuals diagnosed with health problems often show an increased risk of subsequent psychological problems (Luppino et al., 2010), which may further exacerbate declines in health (Moussavi et al., 2007). Most work has considered both psychological and physical health from a disease perspective by focusing on poor psychological or impaired physical functioning, but recent evidence suggests that positive psychological functioning may also matter for physical health. To gain greater insight into these findings, we evaluate what is currently known and consider outstanding issues regarding whether and how positive psychological processes shape trajectories of health and well-being across the life course.

We begin from the premise that the absence of disease does not necessarily translate into the presence of health, just as the absence of depression or other indicators of poor psychological functioning does not guarantee positive psychological functioning. This is consistent with the World Health Organization's definition of health as "a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity" (World Health Organization, 1948). Recent theorizing has further proposed that greater insight into processes that maintain and promote health may be gained when health is conceptualized as an attribute of all living beings that promotes thriving and survival (Forrest, 2014).

Identifying attributes that support adaptive functioning may inform approaches to achieving health beyond what is learned from studying risk factors that accelerate deterioration. From this perspective, due diligence to the full spectrum of psychological and physical functioning (i.e., from happiness to misery; from physical vitality and longevity to physical disease and mortality) is necessary for a complete understanding of health and how it might be fostered and maintained. However, research has historically neglected factors that may promote positive health (sometimes called health assets). Here, we explore whether healthy psychological functioning and positive well-being, which we refer to as positive psychological functioning (PPF), may promote physiological thriving.

PPF encompasses multiple indicators of psychological well-being and can be characterized as the positive feelings and cognitions of individuals who evaluate their lives favorably and function effectively. Relevant constructs of PPF include eudaimonic well-being (e.g., purpose in life, environmental mastery, personal growth), life satisfaction, experienced well-being (e.g., positive emotions), and others (e.g., optimism, emotional vitality). Eudaimonic well-being has been defined as fulfilling one's potential and identifying meaningful life pursuits (Waterman, 2007) while experienced well-being has been defined in relation to the pursuit of pleasure and happiness (Waterman, 2008). PPF is also tied to social relationships, with largely separate (but parallel) lines of research showing that both have important relationships with physical health. Historically, more research has focused on the positive benefits of social relationships than of PPF. For the present article, we highlight research on psychological aspects but note that it is also important to consider how being socially connected informs our understanding of positive health.

We consider three lines of inquiry that could further our understanding of PPF in relation to health. The first has the most empirical support and consists of testing the effects of PPF on health outcomes related to disease risk. The most convincing evidence evaluates whether associations are independent of psychological ill-being to show that PPF's associations do not simply reiterate known effects of poor psychological functioning. Consideration of the empirical evidence also points to important new directions for research. These include when PPF begins to exert effects on health, whether PPF directly influences biological processes or primarily buffers effects of stress, and whether there are "positive" versus "negative" forms of biological functioning that reflect processes likely to enhance versus harm health or signal deterioration. Thus, a second line of inquiry considers how the effects of PPF play out developmentally or in the context of stressful circumstances. A third focuses on whether PPF is associated with health outcomes and biological processes beyond those that reflect the absence of deterioration and disease.

PPF, Health, and Disease

PPF and disease. We have proposed that PPF may be a health asset (Boehm & Kubzansky, 2012). To date, distinct indicators comprising the broad construct of PPF have been investigated separately. Whether some attributes promote successful adaptation more strongly than others remains to be evaluated. Moreover, while research regarding psychological states and physical health often considers findings from healthy and patient populations interchangeably, this is inappropriate. Even when biological and behavioral (biobehavioral) pathways leading to the first occurrence of disease are similar to those leading to disease recurrence or subsequent death, correlates and effects may differ for the onset versus progression of disease. Failing to separate disease stage or healthy from unhealthy individuals may be particularly problematic when identifying biological signals of optimal health versus deterioration. Thus, we discuss research in these domains separately.

In the most rigorous empirical work regarding PPF and disease development, PPF is assessed when individuals are disease-free, variables that might indicate a spurious association between

PPF and disease (confounders; e.g., family history of the relevant disease) or help to explain why PPF might influence disease (mediators; e.g., physical activity) are considered. Finally, whether effects of PPF occur over and above any effects of ill-being is evaluated. Most research has considered PPF's associations with cardiometabolic disease (see Boehm & Kubzansky, 2012 for a comprehensive review), although there is work on other outcomes. Other research has considered whether PPF slows progression of disease among older individuals with existing health conditions by considering rate of cognitive decline, disability, and secondary events (Tilvis, Laitala, Routasalo, Strandberg, & Pitkala, 2012).

PPF has been linked with reduced risk of disease, disability, and mortality in studies evaluating purpose in life, positive emotions, life satisfaction, optimism, and emotional vitality (e.g., Boehm, Peterson, Kivimaki, & Kubzansky, 2011; Boyle, Buchman, & Bennett, 2010; Chida & Steptoe, 2008). The protective PPF-health associations these studies demonstrate are consistently independent of effects of ill-being, suggesting PPF promotes health beyond simply marking the absence of poor psychological functioning. Here, we describe some of the strongest findings with PPF constructs, including emotional vitality, purpose in life, and optimism.

Emotional vitality. Emotional vitality has been defined as a multidimensional construct incorporating a sense of energy, positive well-being, and effective emotion regulation (Kubzansky & Thurston, 2007). In a nationally representative sample of adults, high levels of emotional vitality predicted reduced risk of coronary heart disease over 15 years of follow-up after holding constant traditional risk factors, health behaviors, and psychological distress (Kubzansky & Thurston, 2007). Findings suggested that relative to individuals with the lowest levels of emotional vitality, those with the highest levels had 23–30% lower hazard (risk) of developing disease over the study period. This reduction in risk is comparable in magnitude to the increased risk conferred by traditional risk factors such as physical inactivity (Shiroma & Lee, 2010). Other studies have also shown that higher emotional vitality and life satisfaction are associated with reduced risk of developing diabetes and hypertension (Boehm, Trudel-Fitzgerald, Kivimaki, & Kubzansky, 2015; Trudel-Fitzgerald, Boehm, Kivimaki, & Kubzansky, 2014).

Purpose in life. Purpose in life, which has been defined as having goals in life and finding meaning in what one does (Ryff & Keyes, 1995), has demonstrated consistent associations with better health. Typical items for a purpose in life scale might include "I have a sense of direction and purpose in my life" or "I am an active person in carrying out the plans I set for myself". In longitudinal studies of older adults, greater purpose in life is associated with reduced likelihood of having a stroke (Kim, Park, & Peterson, 2011), experiencing cerebral infarcts (Yu et al., 2015), developing Alzheimer's disease and mild cognitive impairment (Boyle, Buchman, Barnes, & Bennett, 2010), and becoming disabled (Boyle, Buchman, & Bennett, 2010). Another prospective study of older U.S. adults demonstrated that individuals with higher purpose are more likely to receive preventive health screenings and spend fewer nights in the hospital, suggesting that life purpose may activate important health-related behaviors (Kim, Strecher, & Ryff, 2014). Similarly, recent prospective studies using diverse cohorts (e.g., Finnish women, British civil servants, U.S. older adults) have found that higher levels of life satisfaction are linked to greater use of preventive health care services and reduced risk of diabetes, heart disease, and bone loss (Boehm et al., 2011; Boehm, Trudel-Fitzgerald, Kivimaki, & Kubzansky, 2015; Kim, Kubzansky, & Smith, 2014; Rauma et al., 2014).

Optimism. Optimism has been defined in several ways, either as having positive expectancies for the future (Scheier, Carver, & Bridges, 1994) or based on attributions for past events (Schulman, Castellon, & Seligman, 1989). Studies have provided a consistent picture regardless of which measure of optimism is used (Rasmussen, Scheier, & Greenhouse, 2009). For example, optimism's association with cardiovascular disease was examined using data from the Women's Health Initiative, which included approximately 97,500 White and Black postmenopausal women from diverse socioeconomic backgrounds who did not have cardiovascular disease or other major illness (e.g., cancer) at study entry. In this sample, the most optimistic women had 26–30% lower risk of developing myocardial infarction and heart disease-related mortality after adjusting for conventional risk factors (Tindle et al., 2009). In fact, in a systematic review that more specifically compared relationships between different indicators of PPF and cardiovascular disease, optimism seemed to be most robustly associated with reduced risk of both first and secondary cardiovascular events, independently of ill-being (Boehm & Kubzansky, 2012). The consistency of findings with optimism has been noteworthy, although optimism has been investigated more systematically than other PPF measures (Boehm & Kubzansky, 2012).

PPF, self-regulation, and adaptation. Findings on optimism and health, together with studies reporting associations between optimism and health-protective behaviors (Giltay, Geleijnse, Zitman, Buijsse, & Kromhout, 2007; Kelloniemi, Ek, & Laitinen, 2005), has led to speculations that effects of optimism are due in part to its regulatory component (Rasmussen, Wrosch, Scheier, & Carver, 2006). Optimism reflects a confidence about the future that supports effortful goal engagement, problem-focused coping with challenges, and goal-adjustment when goals become unattainable (Rasmussen et al., 2006). Self-regulation involves responding appropriately in the cognitive, affective, and/or behavioral domains in any given situation and in the context of one's larger goals (Carver & Scheier, 1998; Vohs & Baumeister, 2004). In the affective domain, self-regulation may take the form of emotion regulation (e.g., changing an emotional response by reinterpreting the meaning of the emotion stimulus); in the cognitive domain, attentional control; and in the behavioral domain, resisting impulses or delaying gratification. These qualities of self-regulation provide the means with which to confront and adapt effectively to life's challenges and relate to adopting more health-protective behaviors (Baumeister & Tierney, 2011; Kubzansky, Winning, & Kawachi, 2014). Most people wish to be healthy, but being able to regulate behavior is critical to achieving that goal (e.g., choosing to eat salad when French fries are more appealing). Empirical evidence is converging on the importance of self-regulation for health, with studies reporting associations with reduced risk of heart disease, less inflammation, healthier cardiac functioning, and healthier behavior (e.g., Appleton, Buka, Loucks, Gilman, & Kubzansky, 2013; Hagger, Wood, Stiff, & Chatzisarantis, 2009; Kubzansky, Park, Peterson, Vokonas, & Sparrow, 2011; Segerstrom, Hardy, Evans, & Winters, 2012).

Regulating appropriately in a given context further brings to mind adaptation and flexibility (Kashdan & Rottenberg, 2010), capacities that may also underlie PPF. Less empirical work has operationalized flexibility (Westphal, Seivert, & Bonanno, 2010) or investigated it rigorously in relation to physical health, yet the ability to adapt may help to explain why PPF serves as a health asset. For example, purpose in life refers to having a sense of meaning and direction in one's life, which may guide goals and behaviors and permit redirection when goals are not met (McKnight & Kashdan, 2009). Thus, an important question is whether positive states do in fact lead to more effective adaptation and if such effects manifest biologically.

Pathways to reducing risk

Given the empirical findings described above, testing when and how PPF leads to better health is an appropriate next step. We propose mediation models to address *how* and moderation models to address *when* PPF might influence health. Important to note, however, is that relations of PPF with biological and behavioral processes are almost certainly bidirectional with reciprocal influences. Understanding the reciprocity of these effects will also provide important insights.

A commonly proposed pathway is through health behaviors, whereby PPF reduces the likelihood of engaging in risky behaviors like cigarette smoking or increases the likelihood of engaging in preventive health practices (e.g., Boehm, Vie, & Kubzansky, 2012; Kim, Kubzansky, et al., 2014). Currently, most of the research is either cross-sectional or examines whether altering behavior (e.g., increasing physical activity) leads to higher PPF (e.g., Mata et al., 2012; Reed & Ones, 2006). Given that effects are likely bidirectional, it will be important for future research to ascertain the extent to which changes in PPF are causally linked to improvements in health behavior. If such causal links are established, research can then examine the extent to which PPF may be malleable (and at what points in the life course) so it could serve as a target for intervention.

There is also growing interest in underlying biological pathways. Most research has been based on models derived from the study of stress and ill-being (see Kubzansky, Seeman, & Glymour, 2014) and has drawn on clinical indicators of cardiovascular health. For example, in a longitudinal study of British men and women, higher baseline happiness was associated with lower ambulatory systolic blood pressure 3 years later after controlling for potential confounders and negative affect (Steptoe & Wardle, 2005). Other work has demonstrated an inverse association between PPF (measured as optimism or the frequency of daily positive experiences) and markers of inflammation, a strong predictor of heart disease risk (Roy et al., 2010; Sin, Graham-Engeland, & Almeida, 2015). A more controversial proposition is that PPF operates through underlying biological pathways that are relevant for enhancing health and less involved in promoting or initiating disease-related processes (Center for Research on Experience and Wellbeing, 2013). That is, PPF may promote the maintenance and activation of restorative behavioral and biological processes that facilitate rapid recovery from challenge or stress, as well as capitalize on opportunities for healthy development and growth.

PPF in Context

Developmental context

Most research on PPF and health has been conducted with adults, for whom many aspects of PPF are likely to be relatively stable. Many PPF constructs are considered traits, and as a result partly heritable (Diener, Oishi, & Lucas, 2003; Plomin et al., 1992). For example, prior research has suggested that dispositional optimism is approximately 25% heritable (Plomin et al., 1992), with estimates for life satisfaction and purpose in life ranging from 32% to 47% (Bartels, 2015; Gigantesco et al., 2011). However, all studies agree that there is substantial environmental influence on the development and course of PPF. In addition, recent research has demonstrated that PPF can change (quite substantially) in adulthood and into old age (Roberts & Mroczek, 2008). For example, several studies have demonstrated that changes in life circumstances (e.g., problems at work) or in social resources (e.g., social network size) were associated with changes in optimism over time, and that these changes were associated with changes in health (Atienza, Stephens, & Townsend, 2004; Segerstrom, 2007). Moreover, PPF appears to be amenable to modification by the social environment. For example, social factors pattern PPF such that among middle-aged U.S. adults, more versus less optimistic individuals tended to be White and highly educated, had an educated parent, belonged to higher occupational classes, and had higher incomes (Boehm, Chen, Williams, Ryff, & Kubzansky, 2015). Other work has described how family dynamics and the larger social context early in life influence emotion response, optimism, and self-regulatory capacity throughout the life course (e.g., Eisenberg, Duckworth, Spinrad, & Valiente, 2014; Evans, Gonnella, Marcynyszyn, Gentile, & Salpekar, 2005; Repetti, Taylor, & Seeman, 2002). Much of this work has focused on effects of adversity (e.g., high family conflict). Although less research has considered whether and how positive social environments establish healthy trajectories, the studies to date strongly suggest the value of exploring these issues (cf. Appleton, Buka, Loucks, Rimm, Martin, & Kubzansky, 2013; Eisenberg, VanSchyndel, & Hofer, 2015; Pulkki-Raback et al., 2015).

Exploring PPF as a health asset may be more interesting if it can be modified and serve as a means for improving health. Building on work demonstrating a variety of methods that have successfully induced personality change (Chapman, Hampson, & Clarkin, 2014), Mroczek (2014) has argued that such traits are moderately plastic and can change, although they may not change quickly. There is also some direct but limited evidence to suggest PPF is modifiable, with strategies ranging from expressing gratitude to practicing kind acts to meditating to engaging in cognitive behavioral or well-being therapy (Boehm et al., 2012; Ruini & Fava, 2012). Few population-level interventions have been developed and tested with the goal of altering PPF, so this is a rich area for further exploration.

Taken together, this work suggests PPF may provide a good target for intervention efforts, recognizing that the success of such interventions may depend on when during the lifespan the intervention is offered. To date, little work has considered whether PPF earlier in life establishes a healthy biological foundation that enables individuals to be more robust and resistant to illness, or if biological effects of PPF may differ at various periods in the life course. Such research will also inform the point in the life course at which PPF may be most malleable and amenable to promotion and/or intervention. For example, the capacity to self-regulate emerges in early life, but many clinical therapies target adults with psychopathology or substance abuse aiming to alter aspects of self-regulatory capacity. While the degree to which PPF is amenable to intervention outside of the psychotherapeutic context and the optimal timing for interventions has not been fully explored, there is work that suggests non-therapeutic interventions are possible and worthy of greater investment (Boehm et al., 2012).

Stress context

An important unresolved issue is whether PPF has direct effects on biological function and health or if it operates primarily via stress buffering (i.e., reducing the harmful cascade of biochemical responses occurring in response to stressful stimuli) (Pressman & Cohen, 2005). These models are difficult to disentangle because much of the research on PPF and health has been conducted in the shadow of the dominant stress-and-health research paradigm, with positive states considered in the context of stress or stressful environments (Papousek et al., 2010). However, the conceptual framework of stress may not provide a sufficiently broad umbrella for investigating the biology of PPF or other positive states. Thus, while stress buffering is likely one important pathway by which PPF influences health, other pathways are also likely.

Conceptualizations of stress and health posit that threatening or challenging experiences activate a neurobiological cascade that can impose long-term damage if the response is frequent, occurs at high intensity, or fails to shut down (McEwen, 1998). Individual differences in stress reactivity (or biological sensitivity) to difficult circumstances vary on a continuum ranging from blunted (should react but does not) to hyper-responsive (should not react but does) (Balodis, Wynne-Edwards, & Olmstead, 2010; Boyce & Ellis, 2005; Chida & Hamer, 2008). One effect of PPF is more rapid or efficient recovery from stress-related biological activation (Fredrickson & Levenson, 1998; Ong, Bergeman, Bisconti, & Wallace, 2006). Beyond reducing reactivity or speeding recovery, a range of biobehavioral processes at the organismic, tissue, cellular, and genomic level have also been identified as relevant for mitigating the stress response (for a comprehensive review, see Robles & Carroll, 2011). PPF may enhance individuals' capacity to activate such processes (Robles & Carroll, 2011).

According to living systems theory, living beings are constantly interacting with dynamic social and physical environments that demand adaptation (Forrest, 2014), suggesting that other processes related to healthy adaptation are also relevant. PPF may not only facilitate more rapid recovery from stressors but may also confer a greater ability to adapt to environmental demands that are not threatening per se but do require change from steady state. PPF may contribute to establishing a different baseline from which challenging events are experienced (c.f. theories on biological embedding; Hertzman, 1999). Individuals with high PPF may have deeper resources or capacities for managing any single stressful perturbation, resulting in a lower magnitude stress response and greater ability to activate and benefit from restorative processes (Hobfoll, 1989). Over time, this capacity may confer health benefits by reducing physiological wear and tear and enhancing biological systems that support health (Piazza, Charles, Sliwinski, Mogle, & Almeida, 2013).

What Is Positive Biological Functioning?

To designate some biological processes as "positive" versus "negative" is an oversimplification of a dynamic web of interactive processes that includes inhibitory and excitatory processes, as well as homeostatic systems with feedback loops and complex chains of events. However, it may be useful to distinguish processes that are likely beneficial in the context of optimizing health from those that signal harm or deterioration. Positive biological functioning can be characterized in several ways. Some biological processes may primarily distinguish people who are disease-free from those who are not (i.e., markers of the presence or absence of deterioration, like inflammation). Relevant biomarkers can provide information on the degree to which physical deterioration (e.g., aging) is occurring, with healthier levels suggesting less deterioration and likely maintenance of current states of health. Other biological processes may indicate not only the absence of disease but also the presence of superior health (i.e., markers of effective functioning). For these processes, relevant biomarkers signal highly effective functioning and a trajectory of optimal health.

Biomarkers of health

Far less attention has focused on "positive" or restorative biological processes than on biomarkers associated with deterioration and disease (cf. Robles & Carroll, 2011). Similarly, scant attention has been given to the phenotype of optimal health compared with health as defined by the absence of a disease, condition, or risk factor. To address this gap, a workshop on Positive Psychobiology supported by Princeton University's Center for Research on Experience and Well-Being (an Edward R. Roybal Center for Translation Research in the Behavioral and Social Sciences of Aging funded by the National Institute on Aging) explored known and novel biological measures representing processes that underlie and explain why and how PPF may enhance physical health (Center for

Research on Experience and Wellbeing, 2013). With the caveat that few biological processes – whether "positive" or "negative" – are uniformly adaptive or maladaptive, processes discussed included neural pathways involved in reward, effort, and exercise-induced brain plasticity; cardiac autonomic balance (i.e., effective coordination between the sympathetic and parasympathetic nervous systems); aspects of innate and adaptive immunity (immunity that occurs naturally and that is activated by harmful agents that get past natural immune defenses) ; sleep, exercise, and other restorative biobehavioral processes; the microbiome (referring to the array of microorganisms and their genomes that live inside and on the human body); and gene expression.

An important next step is to conduct studies of both the causative factors and downstream effects of biomarkers that signal processes involving rest, regeneration, and repair (Smith & Baum, 2003). These processes could come into play not only in response to challenge but also during steady states. Periods of healthy functioning may serve as times during which resource capacity is built. Processes involved in building and/or "storing" well-being or health may resemble the mechanism of fat storage in times of food abundance or, in another context, "cognitive reserve" whereby individuals with higher versus lower cognitive capacity are more resistant to neurological disease (Whalley, Deary, Appleton, & Starr, 2004). Individuals who build such resources may react and adapt to a changing environment more effectively and have the best chance to survive and thrive. Several interesting candidate biomarkers related to restoration have been proposed, including serum antioxidants, high heart rate variability (measuring the variation in the time interval between heartbeats), high density lipoprotein cholesterol, healthy levels of circulating anti-inflammatory cytokines such as IL-10, or a healthy microbiome.

Primordial prevention

A primordial prevention approach – which focuses on factors that prevent risk from becoming established – may inform efforts to identify biomarkers of restorative or health-enhancing processes and their upstream determinants. In the U.S., 86% of health care dollars are spent treating chronic diseases (Robert Wood Johnson Foundation, 2010). Prevention has generally taken two forms: primary and secondary prevention. Secondary prevention refers to slowing the progression of disease after its inception. Primary prevention refers to delaying onset of disease by mitigating existing risk factors, usually concentrating efforts within high-risk populations. It has become increasingly apparent that by the time risk factors like inactivity or obesity are in place, disease processes may already be underway (Lloyd-Jones et al., 2006). Given that most individuals begin life with good health – but over time such health erodes – an alternative approach to fostering health across the lifespan is to prevent risk factors from becoming established (i.e., primordial prevention; Strasser, 1978). An extension of this approach is to consider determinants of positive biological functioning, and studies have begun to evaluate PPF in this context. For example, in 982 middle-aged men and women, greater optimism was associated with higher (i.e., healthier) levels of carotenoids (but not Vitamin E; Boehm, Williams, Rimm, Ryff, & Kubzansky, 2013a). In the same sample, greater optimism was associated with higher levels of high density lipoprotein cholesterol (the "good" cholesterol), as well as lower levels of triglycerides (Boehm, Williams, Rimm, Ryff, & Kubzansky, 2013b). Other cross-sectional work in older adults found that higher levels of optimism were associated with higher levels of IL-10 (Kohut, Cooper, Nickolaus, Russell, & Cunnick, 2002).

Aging research may provide clues to biomarkers that also fit within a primordial prevention framework. A recent review identified biomarkers that appear during normal aging and can accelerate or ameliorate the aging process when experimentally manipulated (Lopez-Otin, Blasco, Partridge, Serrano, & Kroemer, 2013). These "hallmarks of aging" include processes like cellular senescence, telomere attrition, specific epigenetic alterations, and mitochrondrial dysfunction, which reflect failure to maintain the healthy biological function associated with youth. Conversely, absence of these aging-related processes or presence of antagonist processes could indicate a positive biological state. In one study of approximately 500 older men, those with less pessimism had longer telomere length averaged over measures taken at 3-year intervals across 10 years (Ikeda et al., 2014). If further research confirms that PPF fosters positive biological functioning, then it may be considered a valuable primordial prevention factor.

Future Directions

Research on biological mechanisms underlying the relationship between psychological and physical health has increased exponentially, particularly as biological samples are routinely collected in epidemiologic population-based cohorts. Although most research has focused on biological mechanisms linking poor psychological functioning to poor health, the field is poised to make rapid advances with recent theoretical and technical developments.

Assessment of PPF

Beyond establishing that PPF may promote thriving and identifying underlying biological mechanisms, it will be important to evaluate the extent to which different varieties of PPF (e.g., life satisfaction, experienced affect, optimism) have distinct or overlapping contributions to health. However, much of the research investigating links between PPF and disease or biomarkers has come from large epidemiological cohorts in which assessment of psychosocial factors is rarely a priority. Psychological distress measures are sometimes included but measures of PPF are infrequently available (albeit with notable exceptions, including the Midlife in the United States Study, Health and Retirement Study, the English Longitudinal Study of Aging). As a result, studies thus far have tended to use measures that are not well-validated or derive PPF from distress-oriented scales. Although psychological distress is generally inversely related to PPF, these states are distinct (Keyes, 2005; Norris, Gollan, Berntson, & Cacioppo, 2010). Using items initially developed to assess distress as a way to assess PPF can be problematic. A comprehensive definition of a construct is made by both endorsing items consistent and rejecting items inconsistent with the theoretical construct (Ryff & Singer, 2007). Appropriate measurement of PPF constructs in population-based studies will be essential to advance the research agenda proposed here.

Assessment of biomarkers

Somewhat, uncharted territory is identifying the physiological ranges of biomarkers that might be relevant for positive functioning. Although ranges that impose risk are frequently known (e.g., using established cut-points for blood pressure levels that meet criteria for hypertension), normal or superior ranges are less well understood. Most biomarkers under study have continuums ranging from non-deteriorative to deteriorative (e.g., low to high levels of total cholesterol). Some biomarkers may have continuums ranging from restorative to deteriorative, although they have been investigated primarily to indicate deterioration. For example, heart rate variability may signify good health and regulation at the high end and increased risk of disease at the low end (Thayer, Hansen, Saus-Rose, & Johnsen, 2009). By contrast, some biomarkers are primarily restorative (e.g., circulating antioxidant levels) or primarily deteriorative (e.g., atherosclerosis). Other biomarkers may be nonlinear such that there are restorative or deteriorative effects depending on the exact level. Another approach might be to evaluate dynamic flexibility in biological regulatory systems, rather than single-point biomarkers (see Schaefer et al., 2013). Key tasks for this research area include identifying optimal ranges for enhancing physiological function; determining how different physiological systems balance and adjust each other; and establishing how systems can be modified.

Multi-system measures

Although biological systems are dynamic and interactive, much work has focused on single biomarkers. Single system measures provide interesting but ultimately incomplete information. Other work (particularly research on stress) has developed integrated measures of biological function. For example, McEwen and colleagues (1998) proposed the concept of allostatic load, defined as the "wear and tear" that accumulates in the body when individuals are exposed to chronic stress and repeated activation of stress-related biological responses. By definition, allostatic load cannot provide a measure of positive health; similarly, most existing multi-system indices include markers of physiologic deterioration and do not assess *adaptive* physiological responses. However, a multi-system measure of positive health could provide greater insight into adaptation, plasticity, resilience, and recovery.

The potential of "omics"

Ongoing investment in describing the human genome, transcriptome, proteome, metabolome, and human biome will provide exciting opportunities to evaluate the molecular and cellular mechanisms that underlie associations between PPF and physical health. Although PPF is partly heritable, it is unlikely that single genes or even genes in combinations will account for a substantial amount of the variance in PPF (e.g., Cornelis et al., 2012) or its association with health and longevity. Cellular and molecular mechanisms that are less static may be highly informative. For example, is there a metabolomic profile associated with flourishing? Is there an optimal microbial environment in the gut that is more likely to occur with PPF? Initial studies have suggested that PPF is associated with specific gene expression patterning that signals anti-inflammatory activity (Bhasin et al., 2013; Fredrickson et al., 2013).

Effects of PPF on epigenetic processes (chemical modifications that regulate genetic function via mechanisms independent of inherited DNA sequences) may also be of interest. Recent research has suggested that social and psychological factors can in fact alter epigenetic processes (Szyf, McGowan, & Meaney, 2008; Uddin et al., 2011). While few studies have considered potential epigenetic effects of PPF, the work to date is suggestive. One study examined whether optimism modifies effects of air pollution on DNA methylation of two genes (inducible nitric oxide synthase gene, *iNOS*, and glucocorticoid receptor gene, *GCR*), considering ambient particles ($PM_{2.5}$) and black carbon (Madrigano et al., 2012). Findings indicated that *iNOS* methylation was decreased after acute exposure to ambient particles and black carbon, with effects enhanced in less optimistic individuals. The study did not report if there was a main effect of optimism on methylation. With rapid technological progress, researchers have an ever-increasing capacity to measure a vast array of biological processes from genetics to proteomics, intricacies of transcription and translation, as well as metabolomics (Kubzansky, Seeman, et al., 2014). As a result, work considering effects of PPF on these processes is increasingly feasible.

Conclusion

Emerging epidemiologic research strongly suggests that PPF influences health above and beyond effects of psychological ill-being. Both behavioral and biological mechanisms likely explain how PPF enhances and promotes health, but limited research has considered the role of PPF in health-related behaviors and investigations of the underlying biology remain even scarcer. Moreover, most research focuses on deteriorative biological processes and related disease. Significantly, less is known about restorative biological processes that underlie health-relevant aspects of PPF. We suggest that the biology associated with positive states does not merely mark the absence of deteriorative processes but may in fact set in motion restorative processes that build strength, resilience, and reserves for maintaining health. Understanding how psychological factors may influence health across the full spectrum of psychological functioning ranging from highly maladaptive to highly adaptive has the potential to provide greater insight into processes and mechanisms for improving health and aging over the life course.

Acknowledgement

The authors gratefully acknowledge the wise counsel and helpful comments from Lisbeth Nielsen.

Short Biographies

Laura Kubzansky, Ph.D., M.P.H. is a Professor of Social and Behavioral Sciences and the Director of the Society and Health Psychophysiology Laboratory at the Harvard T.H. Chan School of Public Health. Dr. Kubzansky received her Ph.D. (social psychology) from the University of Michigan and completed a two-year postdoctoral fellowship in social epidemiology as well as a M.P.H. at the Harvard School of Public Health. Dr. Kubzansky has published extensively on the role of psychological and social factors in health. Widely recognized for her work demonstrating that emotions play an important role in the development of a number of disease outcomes including cardiovascular disease, lung function decline, and cancer, her research has been published in public health, biomedical, and psychology journals. She also conducts research on whether stress, emotion, and other psychological factors may help to explain the relationship between social status and health. Other research projects and interests include studying the biological mechanisms linking emotions, social relationships, and health; relationships between early childhood environments, resilience, and healthy aging; and how interactions between stress and environmental exposures (e.g., lead and air pollution) may influence health. She is a Fellow in the American Psychological Association and the Academy of Behavioral Medicine Research. She has served as Senior Advisor to the Robert Wood Johnson-funded Positive Health Research program, as a member of the Healthy People 2020 Health-related Quality of Life and Well-being Workgroup and of the American Heart Association, Science of Well-Being Expert Panel. She is PI or co-investigator on a wide variety of grants funded through the Veterans Administration, Robert Wood Johnson Foundation, EPA, NIH, and others.

Julia K. Boehm, Ph.D. is an Assistant Professor in the Department of Psychology at Chapman University. She received her Ph.D. in Psychology from the University of California, Riverside and was a postdoctoral fellow at the Harvard School of Public Health. Dr. Boehm's research centers broadly on well-being and investigates how people can thrive both mentally and physically. More specifically, her research examines whether positive psychological characteristics such as optimism and life satisfaction are associated with improved cardiovascular health. She authored an extensive review in Psychological Bulletin on this topic and has conducted several prospective investigations of heart disease in epidemiological cohorts. In addition, she is interested in the behavioral and biological processes that are relevant for cardiovascular health. Dr. Boehm's goal is to identify those psychological characteristics that contribute to healthy trajectories of cardiovascular functioning across the lifespan. Her work has been funded by the

National Institute on Aging and featured in many news outlets including Reuters, The Atlantic, The New York Times, and BBC News.

Suzanne C. Segerstrom is a Professor of Psychology at the University of Kentucky in Lexington, where she pursues research, trains graduate students, and teaches courses in personality and health psychology. Her current research includes investigations into the effects of self-regulation, goals, and goal pursuit on psychological health and cardiovascular and immune function, particularly in older adults. Her book *Breaking Murphy's Law* (Guilford, 2006) focuses on how optimism both leads to and follows from more effective goal pursuit. Dr. Segerstrom's work has been sponsored by the National Institutes of Health, the Norman Cousins Program in Psychoneuroimmunology, the Dana Foundation, and the Templeton Foundation. She is also the 2002 recipient of a Templeton Positive Psychology Prize for her work on optimism. Dr. Segerstrom has a B.A. with majors in Psychology and Music from Lewis and Clark College in Portland, Oregon, where she was named the 2004 Outstanding Young Alumna. She received her M.A. and Ph.D. degrees in Psychology from the University of California, Los Angeles.

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