Allostatic Load: A Mechanism of Socioeconomic Health Disparities?

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Abstract

Although research on health disparities has been prioritized by the National Institutes of Health, the Institute of Medicine, and Healthy People 2010, little has been published that examines the biology underlying health disparities. Allostatic load is a multisystem construct theorized to quantify stress-induced biological risk. Differences in allostatic load may reflect differences in stress exposure and thus provide a mechanistic link to understanding health disparities. The purpose of this systematic review is to examine the construct of allostatic load and the published studies that employ it in an effort to understand whether the construct can be useful in quantifying health disparities. The published literature demonstrates that allostatic load is elevated in those of low socioeconomic status (SES) as compared to those of high SES. The reviewed articles vary in the justification for inclusion of variables. Recommendations for future research are made in the contexts of measurement, methodology, and racial composition of participants.

Keywords

health disparities; allostatic load; stress

Prospective cohort studies have demonstrated that mortality rates are higher for those of low socioeconomic status (SES) relative to those of high SES (Bucher & Ragland, 1995; Howard, Anderson, Russell, Howard, & Burke, 2000; Smith, Neaton, Wentworth, Stamler, & Stamler, 1996). Traditional risk factors do not explain this difference in mortality (Lantz et al., 2001; Sorlie, Backlund, & Keller, 1995). As a specific example, disparities in cardiovascular disease (CVD) in the United States have increased in the past 30 years (G. K. Singh & Siahpush, 2002) and are only partially explained by the prevalence of CVD risk factors (Adler & Newman, 2002; Lantz et al., 2001). Many published studies relate stress to individual risk factors for disease (Bosma et al., 1997; Carroll, Davey, Sheffield, Shipley, & Marmot, 1997; Steptoe, Cropley, & Joekes, 1999; Stoney, Bausserman, Niaura, Marcus, & Flynn, 1999). However, both theory and data from the literature on stress suggest that additional explanatory power may be obtained by examining the effects of stress using a multisystem measure. Despite a strong and consistent link between low SES and incident disease, there have been few studies investigating such multisystem mechanistic links.

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Differential exposure to stressors may explain a portion of health disparities. Allostatic load is a construct theorized to quantify stress-induced biological risk. Differences in allostatic load may reflect the accumulation of physiological changes induced by differences in exposure to stressors and thus provide a mechanistic link to understanding and studying health disparities. This article reviews the construct of allostatic load and synthesizes evidence from published studies that employ it in an effort to understand whether allostatic load can be useful in quantifying health disparities.

History of Allostasis, Its Relationship to Homeostasis, and Allostatic Load

The multisystem approach to the construct of allostatic load is a descendant of the work of Hans Selye (1976), who proposed that stress-reacting "agents" had "a general effect on large portions of the body" (p. 38). There is no scientific consensus on the definition of *stress* (Pacak & Palkovits, 2001). For the purposes of this article, we will define *stress* as an actual or perceived threat to homeostatic and allostatic functioning. We define *stressor* as the threat itself (e.g., the aggressor, the test, and the job strain). *Stress exposure* is defined as exposure to a threat that initiates the allostatic responses. Selye's orientation toward general effects was crucial to the multisystem approach of subsequent stress researchers, such as Sterling and Eyer (1981), who developed the concepts of allostasis and allostatic load. *Allostasis* comes from the word *allo*, which means change, and *stasis*, which means stability. Further refined by B. S. McEwen and Stellar (1993), the concept of allostasis refers to the body's adaptation to stressors. In contrast to homeostatic systems, which must be maintained within narrow ranges, allostatic systems do not depend on set-point mechanisms and therefore have ample boundaries. Healthy functioning requires ongoing adjustment by physiologic systems' fluctuations that respond to such stressors as isolation, hunger, danger, and infection (B. S. McEwen, 1998). These systems are the sympathetic nervous system; the neuroendocrine system, in particular the hypothalamic-pituitary-adrenal axis; and the immune system. Together, their actions constitute the physiologic stress response. The stress response temporarily subjugates internal needs in response to external ones (Porges, 1995), which is essential for survival. In his refinement of the concept into a framework that can be used in a research context, B. S. McEwen (B. S. McEwen & Stellar, 1993) theorized that a person exposed to multiple acute or chronic stressors would suffer physiologic consequences from this continued subjugation. Thus, multiple recurring stressors leave a physiologic stamp on the body (Seplaki, Goldman, Weinstein, & Lin, 2004), which is reflected in biomarkers and in derangement of the body systems they have affected. This physiologic stamp is the allostatic load, and it impairs the body's ability to adapt to future stressors. Variables used in the measurement of allostatic load and their relationship to the physiologic stress response are depicted in Table 1.

Following the method of Seeman et al. (2004), a summary index of allostatic load is created in the following way: The number of variables for which the participant's scores fall in the quartile of highest clinical risk are added together to create a summary number. For example, if a participant's blood values rank in the highest quartile for HgA1c, the lowest for high density lipoprotein (HDL), and the middle two quartiles for all the other variables, the resulting allostatic load score for that participant is 2. Allostatic load has been operationalized differently in some studies, and because of this, there is no one accepted set of markers used to formally measure it. However, all studies reviewed used multiple measures that represent comprehensive biologic functioning (see Table 1).

Relevance of Employing Allostatic Load to Examine SES Disparities

There is evidence that people in lower SES groups experience greater chronic stress exposure than more advantaged groups (Baum, Garofalo, & Yali, 1999; House et al., 1994; Marmot & Siegrist, 2004; Pickering, 1999; Steptoe & Marmot, 2003). People of low SES experience lower

perceived control at work (Warren, Hoonakker, Carayon, & Brand, 2004), lower levels of social support (Taylor & Seeman, 1999), and more events considered by them to be stressful (Brunner, 1997) than people of high SES. These differences in chronic stress exposure may result in differing biologic risk for chronic diseases (Steptoe et al., 2003). Stress exposure can affect health both directly, such as through increased fibrinogen (Steptoe & Marmot, 2003), and indirectly, such as through stressors' effects on health behavior (Adler & Newman, 2002). If people of low SES have more exposure to stressors, then using a construct such as allostatic load could be useful in measuring the intermediate biological dysregulations that could contribute to heath disparities.

Method

The literature search for this article consisted of two strategies. The first was a computer-based search for the word *allostatic* in the abstract databases Medline, CINAHL, and EMBASE. The second was to follow references in journal articles and book chapters. There were two broad categories of allostatic load studies. The first type (Type 1) consisted of observational studies that assigned allostatic load scores to each study participant based on multisystem indicators and subsequently used those scores to predict health outcomes (Crimmins, Johnston, Hayward, & Seeman, 2003; Karlamangla, Singer, McEwen, Rowe, & Seeman, 2002; Schnorpfeil et al., 2003; Seeman et al., 2004; Seeman, McEwen, Rowe, & Singer, 2001; Seeman, Singer, Rowe, Horwitz, & McEwen, 1997; Seeman, Singer, Ryff, Dienberg, & Levy-Storms, 2002; Seplaki et al., 2004; Singer & Ryff, 1999; Weinstein, Goldman, Hedley, Yu-Hsuan, & Seeman, 2003). The second (Type 2) comprised experimental stress studies in which a stressor served as an independent variable and a biological parameter served as a dependent variable (e.g., effect of stress on blood pressure). This review solely addresses Type I studies encompassing multiple regulatory systems. As such, the literature on stress examining one particular variable (e.g., cortisol) is beyond the scope of this review. Rather, the multi-system or general stress effect that Selye (1976) noted is its focus. Of the 63 articles found that referred to allostatic load, only 11 defined allostatic load using at least 10 biological parameters from at least 3 organ systems. The authors, populations, designs, and key variables of the 11 reviewed articles are summarized in Table 2. Articles mentioning allostatic load were excluded if the researchers used animal models (3 articles) or if the articles were not written in English (2 articles), were solely conceptual reviews (36 articles), or described research with children (2 articles). Multiple articles on the same cohort were included because they provide insight into methodological issues.

Allostatic Load and SES

We located four articles that specifically addressed allostatic load and SES. The most recent investigation of the relationship between SES, allostatic load, and all-cause mortality examined a group of 1,189 initially high-functioning older men and women (Seeman et al., 2004). The authors found that higher allostatic load explained 35% of the difference in mortality risk between those of higher SES and those of lower SES. Allostatic load retained independent explanatory power even after adjusting for established risk factors and diagnosed disease. Another analysis of allostatic load and SES in Taiwanese elderly found that higher SES predicted lower allostatic load ($p = .02$; Weinstein et al., 2003). The third of these studies examined allostatic load and hostility in men 42 to 88 years old. The authors found that lower SES was associated with higher allostatic load scores ($p < .05$), as was hostility ($p < .01$; Kubzansky, Kawachi, & Sparrow, 1999). The fourth study was of 84 people selected from a large longitudinal study for variance in SES and social relationship factors (Singer & Ryff, 1999). In this analysis, people with lower incomes were more likely to have a higher allostatic load. Low-income adults who had had a higher income as children also had a high allostatic load. It is interesting that positive relationships with parents and spouse were protective against

high allostatic load scores even in the context of low income. Conversely, high income was protective against high allostatic load scores despite negative parental or spousal relationships.

Variable Issues

None of the reviewed studies included measurement of the parasympathetic nervous system, which could further refine allostatic load measurement. The parasympathetic and sympathetic nervous systems are both part of the autonomic nervous system and work to balance each other. The parasympathetic nervous system functions to return the body to homeostasis following the cessation of a stressor by decreasing heart rate, relaxing blood vessels, and clearing away metabolic waste products, such as adrenaline and lactic acid. If the body cannot accomplish this task, cardiovascular risk may increase through sustained high blood pressure and continued stimulation of the cardiac muscle (R. B. Singh, Kartik, Otsuka, Pella, & Pella, 2002), which may increase IL-6, thus resulting in increased inflammation (Owen & Steptoe, 2003). Parasympathetic stress can be measured by heart rate variability, which is a gauge of cardiac vagal tone (B. L. E. McEwen, 2003). Heart rate variability can be measured by examining the distances between the intervals on an electrocardiogram.

Validity of Variables

The validity of the variables that were included in these studies was not always clearly established. Although the original operationalization of allostatic load in the MacArthur Study on Successful Aging was well described, including the validity of the 10 variables that provided the data for the allostatic load count (Seeman et al., 1997), subsequent articles that we reviewed vary in the strength of justification for inclusion of variables beyond the original 10 (as seen in Table 1). For example, indicators of inflammation are valuable and have been shown to be related to both acute and chronic stress (Kiecolt-Glaser et al., 2003; Tracy, 2003), but it is not clear that incorporating overlapping inflammation variables is valid in an additive score. Also, two studies published in the past 2 years included respiratory peak flow and creatinine clearance (Crimmins et al., 2003; Seeman et al., 2004). These variables were described as measures of organ dysfunction but not conceptually tied to the physiologic stress response. Their inclusion thus warrants further explanation. The allostatic load literature is evolving. Further justification of included variables would facilitate this evolution.

System Dynamics

The measurement of allostatic load is constrained by its snapshot nature. Even the longitudinal studies (Karlamangla et al., 2002; Seeman et al., 2001; Seeman et al., 2004) use two measurements at particular moments. This limitation can be reduced by employing dynamic measures of allostatic load variables, such as measures of cortisol, throughout the day or in response to challenge. Adding dynamic measures would be conceptually appropriate as the allostatic model is based on adaptation to challenges.

Methodologic Issues

Calculating the Allostatic Load Score

With one exception (Seplaki et al., 2004), the studies reviewed calculated participants' allostatic load scores by summing the parameters in the high-risk quartile for each variable. In the exceptional study, Seplaki et al. (2004) summed the parameters of allostatic load that were in the highest or lowest 10% on any of the allostatic load variables. This method is intriguing and should be examined further as there is evidence that very low glucose and very low cortisol confer risk or are markers of risk (Sapolsky, Romero, & Munck, 2000). In fact, the researchers (Seplaki et al., 2004) found that both high and low values of variables that comprise allostatic load were associated with functional impairment. However, the top 10% of some parameters

are scores that themselves indicate clinical risk (e.g., the top 10% for systolic blood pressure was 166, which is treatable on its own, whereas the cutoff for the top quartile in Seeman et al. [2004] is 138.) Thus, although there is theoretical strength in using high plus low cutoffs, the drawback to cutting the cohorts at 10% and 90% is that they then represent more extreme values that may indicate true clinical disease.

Intermediate Variables

A second methodological issue is whether to control for smoking, depression, and inactivity in analyses of allostatic load by SES. Higher rates of cigarette smoking (Marmot et al., 1991), depression, and inactivity (Strike & Steptoe, 2004) are each associated with low SES. Each of these risk factors might be termed an intermediate variable in the relationship between low SES and increased mortality. If smoking, depression, and inactivity explain much of the SES variance in allostatic load, then the research implication would be to develop effective, culturally competent interventions for smoking, depression, and inactivity. However, B. S. McEwen (1998) termed these factors an essential part of the load the body carries in adapting to stressors. His conceptualization argues against adjusting for these risk factors. Congruent with this conceptualization, authors addressing SES in the context of allostatic load have noted health risk behavior exclusion from the analysis because these factors are potential mediators of SES differences in allostatic load (e.g., Seeman et al., 2004). However, mediating variables can have health and social policy implications. If future research into allostatic load adjusts for smoking, depression, and inactivity and allostatic load still provides independent explanatory power, then chronic stressors must be addressed directly. Because health and social policy implications differ depending on the outcome, more research and critical discussion is necessary to determine the best analytic methods.

Measuring SES

Of the four articles that addressed the relationship between allostatic load and SES, three used educational attainment as a proxy for SES (Kubzansky et al., 1999; Seeman et al., 2004; Weinstein et al., 2003) and one used income (Singer & Ryff, 1999). Education is a strong measure for older adults as it is stable and generally reflects lifetime resources. The disadvantage of using education as a proxy for SES is that the same educational degree does not result in the same societal advantage for all people. For example, an African American woman who graduated from a high school in North Carolina in the 1940s most likely did not accrue the same economic advantage as a White man who graduated from high school in North Carolina in the 1940s. However, a disadvantage of using the alternative of income in elders to measure SES is that many elders live on a fixed income that is reflective neither of their lifetime income bracket nor of their accumulated wealth. A second disadvantage of using income compared to education is that poor health can cause decreased income, whereas poor health in adulthood does not decrease educational attainment. The study that used income to proxy SES (Singer & Ryff, 1999) had 35 years worth of income data and controlled for the possible reciprocal effect of health on income.

Given the drawbacks inherent in using either income or education as measures of SES in the elderly, the examination of the relationship between allostatic load and SES may be refined by inclusion of an index of neighborhood SES. Including neighborhood indices of SES may improve the specificity of measuring SES. Another reason to include neighborhood data in an SES measure is that recent research has found important relationships between neighborhood and health (Diez-Roux, Merkin, & Arnett, 2001; Diez-Roux, Nieto, & Muntaner, 1997; LaClere, Rogers, & Peters, 1998). These studies have, however, been critiqued for lacking a causal theory for the neighborhood effect on health (O'Campo, 2003). Cumulative stress, measured by allostatic load, may provide a mechanism for the effect of neighborhood on health. Research using measurement of neighborhood-level data can suffer from the ecologic fallacy,

which attributes a community characteristic to an individual without having the data measured on an individual level. When data are collected on both the individual and community level and analyzed using multilevel statistical methods, the research can valuably incorporate both individual- and community-level variables.

Race and Ethnicity of Study Participants

We located no articles that analyzed allostatic load by race and ethnicity. Because allostatic load may be a useful construct in health disparities research, this gap should be addressed. The National Health and Nutrition Examination Survey (NHANES), which over-samples minorities in order to facilitate analysis by subgroup, failed to report differences or similarities according to ethnic group. Two of the articles examined allostatic load in a Taiwanese population sample. Researchers may glean useful information on the interactions between SES and race and ethnicity by studying multi-ethnic, multi-SES samples with appropriate analyses.

Conclusion

Allostatic load is a quantification of prolonged or repeated stress that may be useful in health disparities research. The research using the construct of allostatic load would be strengthened by studies that include additional markers biologically justified in relation to allostasis, analysis of race and ethnicity differences, and neighborhood variables. Allostatic load may be a fruitful theoretical framework in health disparities research and may contribute to the explanation of the biological causes of increased mortality and morbidity. In addition, by indicating the biological causes of increased morbidity and mortality, effective interventions can be designed to address socioeconomic and racial health disparities.

Acknowledgments

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Table 1

Variables Used in the Allostatic Load Literature and Their Relation to Allostasis

Variable	Relationship to Allostasis and Citation	N	%
Physiologic stress response hormones			
Cortisol	Measure of HPA axis activity (Seeman et al., 2004)	9	0.81
DHEA-s	Functional HPA axis antagonist (Seeman et al., 1997)	9	0.81
Epinephrine and norepinephrine	Sympathetic nervous system releases as neurotransmitters to prepare body for "fight or flight" (McEwen, 1998)	10	0.91
Dopamine	Precursor to synthesis of norepinephrine (Seplaki et al., 2004)	1	0.09
Insulin-like growth factor	"Hormonal response to stress" (Seplaki et al., 2004)	1	0.09
Metabolic markers			
Waist-hip ratio	Adipose tissue deposition influenced by cortisol activity (Seeman et al., 1997)	11 of 11	
Hemoglobin A1c	Integrated measure of glucose metabolism during a 90-day period (Seeman et al., 2004)	10	0.91
Postprandial glucose	"Influenced by the HPA axis" (Kubzansky et al., 1999)	1	0.09
Fasting glucose	Defined as part of insulin resistance related to stress hormones (Seplaki et al., 2004)	1	0.09
Cardiovascular			
Systolic and diastolic blood pressure	Indexes of cardiovascular reactivity (Seeman et al., 1997)	11	1.0
High-density lipoprotein and total cholesterol	Influeced by HPA axis and by sympathetic-adrenal-medullary activity (Kubzansky et al., 1999)	11	1.0
Body mass index	Cardiovascular risk influenced by metabolic factors (Crimmins et al., 2003; Schnorpfeil et al., 2003)	3	0.27
Inflammation			
Interleukin-6	Elevated in those experiencing chronic stress (Seplaki et al., 2004)	2	0.18
C-reactive protein	Measure of inflammation (Seeman et al., 2004)	3	0.27
Albumin	"Marker of inflammation" (Seeman et al., 2004); did not expressly state a justification (Schnorpfeil et al., 2003)	2	0.18
Fibrinogen	Marker of inflammation (Seeman et al., 2004)	2	0.18
Tumor necrosis factor alpha	"indicator of inflammation" (Schnorpfeil et al., 2003)		
Organ function			
Creatinine clearance	Measure of kidney function (Crimmins et al., 2003; Seeman et al., 2004)	2	0.18
Respiratory peak flow	Measure of respiratory function (Crimmins et al., 2003; Seeman et al., 2004)	2	0.18
Homocysteine	"Amino acid that has been shown to be related to a number of health outcomes" (Crimmins et al., 2003)	1	0.09

NOTE: *N* = number of reviewed studies that include the variable; % = percentage of the reviewed studies that include the variable. HPA = hypothalamic-pituitary-adrenal; DHEA-s = dehydroepiandrosterone sulfate.

Table 2

Allostatic Load Studies Reviewed

Author, Year	*N*	Population	Design	Key Variables
Seeman, 2004	657	MacArthur Study on Successful Aging; baseline ages: 70 to 79	7-year longitudinal	Original 10 plus, albumin, IL-6, CRP, peak flow, fibrinogen, creatinine clearance
Seplaki, 2004	976	Nationally representative sample Taiwanese elders; mean age: 69	Cross-sectional	Original 10 plus dopamine, IGF-1, IL-6, fasting glucose, body mass index
Crimmins, 2003	22,221	Nationally representative U.S. sample (NHANES); ages 20 to 90+	Cross-sectional	Original 10 minus epi, norepi, cortisol, DHEA, waist/hip ratio; plus albumin, CRP, fibrinogen, peak flow, creatinine clearance, omocysteine
Schnorpfeil, 2003	324	Workers in German airline plant; ages 21 to 60	Cross-sectional	Original 10 plus albumin, TNFalpha, CRP, body mass index
Weinstein, 2003	927	Taiwan; age 65 to 80+; compared to MacArthur cohort	Cross-sectional	Original 10
Karlamangla, 2002	251	MacArthur cohort	7-year longitudinal	Original 10
Seeman, 2002	871	Midlife cohort in Wisconsin; ages 58 to 59; compared to MacArthur cohort	Cross-sectional comparisons	Original 10
Seeman, 2001	720	MacArthur Study on Successful Aging	7-year longitudinal	Original 10
Kubzansky et al., 1999	818 men	Ages 42 to 88; Normative Aging Study	Cross-sectional	Original 10 minus DHEA-s, cortisol and HgA1c; plus post-prandial glucose
Singer & Ryff, 1999	84	Midlife cohort in Wisconsin	35-year longitudinal with cross-sectional allostatic load	Original 10
Seeman et al., 1997	765	MacArthur Study on Successful Aging	2.5-year longitudinal	Original 10

NOTE: CRP = C-reactive protein; NHANES = National Health and Nutrition Examination Survey; DHEA-s = dehydroepiandrosterone sulfate; TNF = Tissue Necrosis Factor. Original 10 variables used in the construction of allostatic load = systolic and diastolic blood pressure, hemoglobin A1c, total cholesterol, HDL, epinephrine, norepinephrine, cortisol, dehydroepiandrosterone sulphate (DHEA-s), and waist-hip ratio.