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The Detrimental Effects of Allostasis: Allostatic Load as a Measure of Cumulative Stress

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Abstract Since its inception in the 1980s, through further developments during the 1990s, and continuing today, the paradigm of allostatic load (AL) has becomed an important paradigm for predicting senescence and mortality. AL is a cumulative measure of the effects of multiple stressors and the process of responding to stressors on the soma. AL measurements of individuals is being tested on various samples and species and being reported across a variety of medical and social science journals. From the ISI Web of Science, all articles published between January 2000 and June 2005 with AL in any default category were obtained and transferred to Endnote. These articles, categorized as theory/review or data-driven, human or animal, and variability in risk factors used to estimate AL, are reviewed here. Only two of 90 reports were published in anthropological journals, likely, at least partly, because research on AL has focused more on western, industrialized populations where data are more easily obtained. From 2000-2005, 12 of 42 data-driven reports focused on elderly humans. Studies of animal models also are common (0 in 2000, but 4 in 2004 covering 21 species). During the last year, multiple additional potential physiological variables have been tested as measures of AL (10 to 20 in any one article). In the past half decade, AL also has been introduced to a wide range of disciplines, including psychology, anthropology, gerontology, veterinary medicine, and medical specialties, as a viable research theme. AL appears to provide a useful method for determining cumulative somatic stress such as that seen with senescence and frailty at older ages. *J Physiol Anthropol 25(1): 133–145, 2006* http://www.jstage.jst.go.jp/browse/jpa2
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Introduction

Biological anthropology, with its Boazian origins in documenting developmental plasticity in United States immigrants, has long been interested in environmental effects on human biology. Moving beyond a focus on short term responses to stress (e.g., Cannon, 1929) and a Livingstonian model of genetic adaptation (Williams, 2003), biological anthropology has rediscovered its roots and begun to examine the *cumulative* effect of stress on humans (Bogin, 1999). Several authors (e.g., Goodman and Leatherman, 1998; Thomas, 1998) have concluded that human variation cataloged during studies of adaptability were in reality examples of prolonged nutritional and disease stress on populations resulting from global capitalism. The concept of allostatic load (AL) was developed to measure the effects of long-term exposure to stress on humans. AL potentially offers a comprehensive measure of long term stress, however it was developed during studies of relatively affluent, high-functioning elderly Western cohorts. Physiological anthropology, focusing on variation between and within populations, is particularly suited to refining the concept of AL and testing its applicability across populations. AL provides a tool for investigating developmental and cumulative effects of life-long stress on human variation and senescence. AL fits a newly emerging paradigm in anthropology examining individual life history, incorporating epidemiology, and using ecological approaches (e.g., Bindon et al., 1997; Ellison, 2001; Panter-Brick and Worthman, 1999; Ulijaszek and Hush-Ashmore, 1997). Since AL does not examine individual genes, but measures responses to stress, it gives researchers a new tool for exploring individual variation in responses to stress (e.g., Bindon et al., 1997; Brown et al., 1998; Crews, 2003; Crews and Gerber, 1999; Decker, 2000; Goodman and Leatherman, 1999; Harper et al., 2001; James and Brown, 1997; McDade, 2001; Panter-Brick and Worthman, 1999).

Allostasis elaborates on homeostasis (Sterling and Eyer, 1988). Homeostasis refers to the processes by which biological organisms maintain their physiological and biochemical functioning. As stressors move organisms from one of multiple homeostatic points, self-regulating physiological mechanisms act to restore lost equilibrium. The ability to change in order to maintain overall stability is allostasis (McEwen, 1998). Sterling and Eyer (1988) and Schulkin (2003) posit that a

series of different equilibria exist at different points in time such that an individual is constantly undergoing allostasis (e.g., Mack and Wasserman, 1992). Though vital to biological functioning, allostatic responses can have conflicting and even deleterious effects, thereby creating an AL.

MacArthur Study on Successful Aging

In 1997, the MacArthur Foundation funded an ongoing study of 1189 individuals aged 70 to 79 years from several eastern, urban, North American cities (Seeman et al., 2001). Original participants were thought to be aging successfully based upon their physical and cognitive functioning. Initial recruitment and measurement took place from 1998–9. This group participated in interviews, psychometric assessments, anthropometric protocols, blood draws and urine samples. These individuals were reexamined in 1991, and in 1996. After several attempts to find predictors of morbidity and mortality, one relatively simple calculation based upon a suite of measures created the best results. This measure of AL was a score calculated by summing the number of these measures (Table 1) in the highest quartile of risk for the sample (Seeman et al., 2001). In the MacArthur cohort, higher baseline AL scores were significantly correlated with mortality risk (Crimmins et al., 2003) and were predictive of both cognitive and physical functioning (Seeman et al., 2001). Since AL was conceived as a measure of cumulative insults to an organism due to constant adaptive responses to both external and internal stressors (Seeman et al., 2001; Berkman, 1993; McEwen, 2000) a successful way to measure this among several systems was created. A conclusion from these initial analyses is that AL may be an even better predictor of future morbidity in the general population since MacArthur Foundation Study of Successful Aging participants initially were high-functioning individuals (Seeman, 2001). Therefore, by extension, AL may be applied to other populations, especially those exemplifying the "human other" foundation of anthropology in which any statement of human nature must take in account groups who are different than those of the original researcher (Pandian and Parman, 2004).

Types of Allostatic Load

Stress is "...produced by excessive environmental or psychological pressures" (Allaby, 1999) that moves an organism from homeostasis. This provokes an allostatic reaction to restore homeostasis (Fig. 1A) (McEwen, 1998). During the 1920s, concepts of stress focused on physical stimuli. In the 1970s, an appreciation that organisms' perceptions of externals events altered stress responses was incorporated into studies on stress and heath (Cooper, 2001). AL fits this modern view of stress and response. After stressors are perceived, a set of behavioral and physiological responses are initiated. Behavioral responses are activities that reduce perceived stress, but can have detrimental effects if chronically used e.g., drinking to help relax. Similarly, physiological responses involve release of a cascade of hormones and amines activating the Hypothalmus-Pitituary-Adrenal (HPA) axis; this may also have detrimental effects by creating an AL (McEwen, 2004). AL can accumulate in at least four ways (Fig. 1) (McEwen, 2003). Stressors can "hit" an organism repeatedly, invoking a response. Each time the response is invoked, damage may occur (Fig. 1B). Second, efficacy of response may diminish as a stress continues (Fig. 1C). An example is an individual who dislikes public speaking but still does it often. This individual will therefore invoke the allostatic response each and every time, with each invocation causing slight damage that accumulates over time (McEwen, 2001a). A third source is failure to halt a stress response once the stress ends and homeostasis is restored (Fig. 1D). For example, depression causes an increase in cortisol even after the depressing stimulus is no longer present (McEwen, 2003c). Finally, some genotypes do not produce enough of a primary response hormone (Fig. 1E). This may cause other, more damaging, mechanisms of allostasis to be invoked.

Table 1 Measures used in MacArthur Fellowship study of successful aging

Highest quartile	Systolic blood pressure
	Diastolic blood pressure
	Waist/hip ratio
	Total cholesterol/HDL ratio
	Glycoslyated hemoglobin
	Urinary cortisol
	Urinary norepinephrine
	Urinary epinephrine
Lowest quartile	HDL cholesterol
	DHEA-S

For each score that an individual was in the highest quartile for the first eight measures and in the lowest quarterile for the last two measures, an individual earned 1 point. The sum of these measures is their AL.

Anthropology, given its history of investigating and cataloging the chronic effects of long-term stress among populations usually not investigated by Western biomedical science, would benefit from investigating this new paradigm. In this review, publications from 2000 to 2005 with "allostatic load" in their title, abstract, or keywords are categorized as theory/review or data-driven, human or animal, and variability in risk factors used to estimate AL. Therefore, this study only investigates publications that have AL as a central topic rather than as a peripheral concept introduced during review or discussion. During data collection, ninety publications were found, electronic versions (if available) were retrieved and classified (Table 2).

Methods

The "Science Citation Index" from the ISI Web of Science "...indexes more than 5700 major journals across 164 scientific disciplines, with all cited references captured," (ISINet.com). This database is updated weekly. A search using the phrase "allostatic load" in the default categories, e.g., abstract, title, key terms, etc. was initiated in June of 2004.

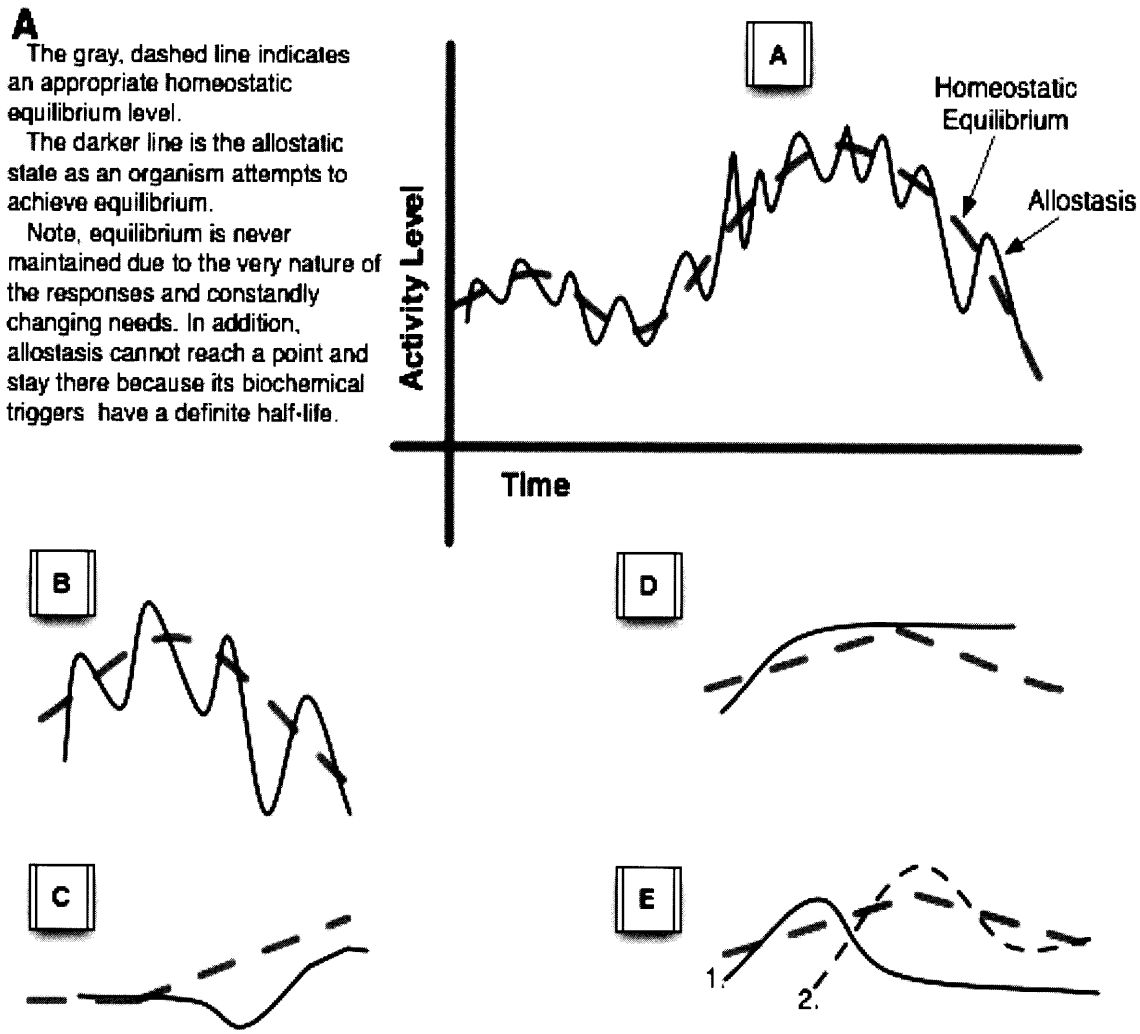

Fig. 1 Mechanisms of allostatic load (after McEwen, 2000c).

Table 2 Allostatic load publications by year

Year	Publications	
	Total	Data-driven
2000	8	3
2001	5	2
2002	11*	4
200	29	13
2004	29	15
Mid-2005	4	2

* Four book chapters (*Annals of the New York Academy of Science*) were indexed in the Science Citation Index in 2002

Table 3 Animal studies of allostatic load

Source	Species	N
Barr et al., 2004a	Macaque	169
Barr et al., 2004b	Macaque	201
Bartolomucci et al., 2003	Mice	42
Bartolomucci et al., 2005	Mice*	
Goymann and Wingfield, 2004	Animals* **	
Hartigan, 2005	Dairy Cows*	
Korte et al., 2003	Rats*	
Pryce et al., 2004	Marmoset	9
Smith and Myburgh, 2005	Rat	40
Tannenbaum et al., 2002	Mice	117
Van der Meer et al., 2004	Mice*	
Zorrilla et al., 2001	Rat	57

*Metastudy

**This article included data from Harris's hawk, Florida scrub jay, White-browed sparrow weaver, African elephant, alpine marmot, dwarf mongoose, spotted hyaena, African wild dog, wolf, ringtail lemur, capuchin, longtailed macaque, savannah baboon, mountain gorilla, and the common chimpanzee

Citations from 2000 to mid-2004 were collected and electronic copies of articles were retrieved during the following two months. Another round of data collection occurred during the first quarter of 2005 to update the data originally collected in Stewart (2004).

Results

In 2000, there were eight publications that satisfied the search criteria. Of these, three (Anderson et al., 2000; Sluiter et al., 2000; Steptoe et al., 2000) were data-driven investigations of humans. These three articles provided insight on early-life sources of AL, adult expression, and relationships with offspring and social support. In a published abstract, Anderson (2000) found that after six hours, infants who lay on their mother's chest have half the cortisol of those removed for one hour. Sluiter (2000) discovered that male, Dutch workers who combine mental and physical work have higher levels of cortisol and slower adrenal recovery than workers who did either mental or physical work. In other words, inconsistency of work environment can increase AL. However, in this group there is no correlation between job demand, locus of control, or social demands and levels of cortisol, adrenaline, or noradrenaline, negating one of the key concepts of AL, social stress. However, this population is notoriously egalitarian with few social divisions and excellent heath care, creating less environmental variation (Bogin, 1999). Steptoe et al. (2000), on the other hand, report that among UK high school teachers, with children, who also believe they have high social support, have a greater decrease in blood pressure during the evening following a workday than others. As with the Sluiter et al. (2000) study, there were no correlations between blood pressure and physical activity, self-perceived job strain, sex, or other variables.

Since a mental process (perception) initiates a physiological response (allostasis) three of the remaining five articles were published in neurological journals, McEwen (2000a, b, and c) proposed several possible uses of AL for *Brian Research*(ers), investigators of neuropsychopharmacological phenomena, and *Neurochemical Research*(ers). The final two articles introduced AL to new audiences, being published in a nursing (Cohen, 2000) and psychological (Fava and Scorrino, 2000) journal.

Four of the five articles published in 2001 focused on humans and, one was data-driven. Seeman et al. (2001) looked at the MacArthur chort again, discovering that AL is a better predictor of senescence and death than metabolic syndrome, which shares many characteristics with AL. This theme is expressed in later research (e.g., Stromvoll et al., 2003). The remaining publications on humans introduced AL to researchers in chemical intolerance (McEwen, 2001a; Bell et al., 2001) and those interested in philosophical discussions of the implications for human biology (McEwen, 2001b).

During the study period, there was an increase in animal studies of AL (Table 3). Advantages of animal models, ability to dissect, addict organisms, and to control environmental and genetic variables, give insights of how cumulative stressors begin to cause AL. For example, both cocaine and alcohol addicted rats have reduced corticotrophin-releasing factor in their brains during addiction. This reduction takes as long as six weeks to increase to baseline levels after withdraw (Zorilla et al., 2001) This provides insight on activation and duration of the HPA axis's response to a stressor.

Of eleven AL articles in 2002, two of the four data-driven publications were from the MacArthur cohort, a trend that persists though the remaining two and one half years under review. Moving beyond morbidity and mortality, Karlmanga et al., (2000) found that AL is a predictor of functional decline on physical measures (balance, lower extremity strength, gait, lower extremity dexterity, and hand dexterity) and mental measures (Boston Naming Test, Roger's Construction Test, Delayed Spatial Recognition Span Test, and a summary measure of the Boston Naming Test and Delayed Recognition test) in both sexes (see Mitinski et al. (2004) for a frailty index drived from AL research). Looking at how long-term social stress can develop into AL in the MacArthur cohort, Seeman

et al. (2002) investigated relationships between social integration and AL. Well-integrated individuals of both sexes aged 50 to 59 years have reduced AL scores. This effect was strongest among 70 to 79 year old men. Such insights may help explain why men over 80 tend to age more successfully (Perls, 1995).

Testing the hypothesis that social class affects AL (e.g., McEwen, 1998; McEwen and Seeman, 1999), Steptoe et al. (2002) studied UK civil servants. Those aged 47 to 58 years of lower socioeconomic status have slower recovery of cardiovascular function after suffering mental stress caused by complex cognitive tasks, demonstrating AL due to inadequate response to a repeated stress (see Fig. 1C). Koopman et al. (2002) also investigated post-traumatic stress disorder among HIV/AIDS individuals, discovering that AL was intensified by psychsocial events.

Neuropeptide and genetic differences among mice of two lineages were investigated by Tannenbaum et al. (2002). Two different strains of mice were exposed to several stressors twice daily over 54 days. Each strain showed significant elevation of corticosterone, dopamine, and serotonin. The degree and persistence, however, depends upon the strain of mouse and type of stressor, which helps to explain individual variation in allostatic responses in humans (e.g., Gold et al., 2003).

Also during 2002, McEwen (2002a, b) published review articles in the medical literature proposing AL as a contributor to the aging process and to post-traumatic stress syndrome. Carroll (2002) reviewed the biochemistry of AL accumulation, Eriksen and Ursin (2002) proposed that AL may be the physiological cause of morbidity usually attributed to psychological mechanisms. Vanitalie (2002) also implicated AL in post-traumatic stress syndrome. A more general review of the psychophysiology of AL was published by Lawler and Wilcox (2002) as well as a review of the effect an individual's personal philosophy has on AL (Ryeff and Singer, 2002). Kudielka et al. (2003) worried that the psychological factors used in AL studies may be overlapping rather than distinct phenomena. However, since many of the measures used in AL studies overlap with syndrome X (Crimmins, 2003) or cardiovascular disease (e.g., Lawler), yet still produce relevant results, this may not be problematic. Finally, Kendall and Hatton (2002) linked AL to attention deficit disorder.

In 2003, there was both a significant increase in publications on AL and a greater frequency of data-driven articles. Of the twenty-nine publications, thirteen were data-driven (twelve on humans, one on mice). The majority of the data-driven publications were on western, industrialized populations experiencing stressors in their social environment. For example, a clinical sample of UK males showed progressively elevated cortisol levels during both alcoholic (intoxicated and not) and recovery phases (Adinoff et al., 2003). In a cross-sectional US sample of individuals aged 20 to 80, AL scores rise nonlinearly as one gets older. All individuals experience a slow increase beginning at age 25. At age 35 these scores rise sharply until age 65, where they tend to level off (Crimmins et al., 2003). Among Germans, age and sex were correlated with AL scores generated from the measures used in the MacArthur cohort. As these individuals aged, especially men, AL score increased. Fitting into the role of perception in creating AL, this cohort's perceived job demands were more correlated with AL scores than age, position, numbers of years employed, social integration and other variables from Atonovosky's salutogenetic theory (Schnorpfeil et al., 2003). Gold et al. (2003) investigated individual differences in susceptibility to increases in AL. Women with a family history of breast cancer secrete more epinephrine and cortisol after psychological stress than the control group, implying that the same stress can produce dissimilar results. An intriguing follow-up project would be to link other genetic diseases with incomplete penetrance to variation in social conditions.

Not all studies use the same AL markers, additional physiological and biochemical measures are used in many, e.g., Kario et al. (2003) (see Table 4). Focusing on cardiovascular measures and personal history, van Kanel et al. (2003) documented increased levels of plasma thrombin/antithrombin III complex, D-dimer vol Willebrand factor, tissue type plasimogen activator and plasmogin inhibitor 1 among caregivers of Alzheimer patients that correlated with increased "negative life events" and stressful caregiving (von Kanel et al., 2003a). College students who practice forgiveness after interpersonal conflicts tended to have lower AL scores and

Table 4 Measures of allostatic load

Source	Measure
Barr et al., 2004	Adrenocorticotropic hormone
	Serotonin
Bierhaus et al., 2004	NF-Kappa B
Carroll, 2002	Glucocorticoid receptor agonist
Crimmins et al., 2004	High fibrogen
Hill et al., 2005	2-arachindonylglycerol
Hogue and Bremner, 2005	Dehydroepiandrosterone
Karalamanga et al., 2004	Low best peak
Kopp et al., 2004	II-6
	C-reactive protein
Kumari et al., 2004	Fibrogen
	von Willebrand factor
Satariano et al., 2003	Creatine
Schnorpfeil et al., 2003	Albumin
Smith and Myburgh, 2004	Corticosterone
Tannenbaum et al., 2002	Corticosterone
Thompson et al., 2004	Corticosterone
van der Meer et al., 2004	Corticosterone
Thompson et al., 2004	Corticotropin-releasing hormone
van Berge-Landry and James, 2004	Creatinine clearance
von Kanel et al., 2003	Thrombin
	Antithrombin III
	von Willebrand factor
	Tissue-type plasminogen activator
	Plasminogen activator inhibitor 1
Wirtz et al., 2004	Monocyte tumor necrosis pressure factor
Zorilla et al., 2001	Corticosterone

Table 5 Human subjects in allostatic load articles

Subject Group	Source	Note
African American	Carlson, 2004	Health disparity
	Crews, 2003a	Compared AL in 3 groups
	Crews, 2003b	Women had higher AL
	Hogue and Brenner, 2005	Maternal stress and premature births
	Kendall and Hatton, 2005	Racism and ADHD
	Lu and Halfon, 2003	Birth outcomes
Amerind	Crews, 2003a	Compared AL in 3 groups
	Crews, 2003b	Women had higher AL
	Stumvoll et al., 2003	Pima Indian hypoinsulinemia
Canadian	Mitnitski et al., 2004	Frailty of older adults
Dutch	Sluiter et al., 2000	Work demands
Germans	Fischer et al., 2003a	Work stress
	Fischer et al., 2003b	Middle-age
	Schnorpfil et al., 2003	Factory work conditions
Japanese	Kario et al., 2003	Cardivascular AL due to an earthquake
Samoan	Crews, 2003a	Compared AL in 3 groups
	Crews, 2003b	Women had higher AL
Taiwanese	Seeman et al., 2004a	Social relationships lower AL
	Seplaki et al., 2004	Middle-age & elderly functioning
	Wagle et al., 2003	Social environment
	Weinstein et al., 2003	Social status and gender differences in AL
UK	Galambos et al., 2005	Injury among athletes
	Steptoe et al., 2000	Civil servants' rank
	Steptoe et al., 2002	School teachers' marriage and children

Note: Other data driven articles can be assumed to be US, with the plurality representing the Macarthur group

faster return to homeostasis (Lawler et al., 2003).

Not all studies published in 2003 were of urbanized or affluent populations. Among rural children in New York state, AL begins to accumulate as they are exposed to psychological stressors of their low SES, e.g., being below the poverty line, having a single-parent, maternal high-school graduation, residential crowding, noise, home quality, family turmoil, having a close family member leave, and exposure to violence. (Evans, 2003). Non-western, industrialized subjects were also studied in 2003. Using a subset of AL measures related to blood pressure and adding additional ones related to atherosclerotic disorders (D-dimer, von Willebrand fastor, and tissue-type plasminogen activator antigen), Kario et al. (2003) reports AL scores are associated with myocardial infarctions among Japanese who experienced an earthquake and with an increased rate of nocturnal ischemic strokes among women. This male/female difference is repeated in many studies (e.g., Seeman et al., 2004). Like Japanese earthquake survivors, among Taiwanese elders' AL is inversely correlated with social status and correlated with "life challenges" (social situations after a loss, e.g., an ill spouse or recent widow (er) hood, death of a child) and were related to perceptions of demands put on them (Crimmins et al., 2003). Relatedly, Wagel (2003) and Wenstein (2003) investigated social factors' associated with AL among Taiwanese seniors.

Several studies of populations of anthropological interest were first published in 2003. Crews (2003), examining AL in samples from three distinct populations—Samoans, Yanomani, and African Americans—published the first abstract on AL to appear in the anthropological literature. Also, AL, as measured by insulin resistance in Pima Indians is a type of allostasis illustrated in Fig. 1D (Stumvoll et al., 2003).

Other than Bartolomucci et al.'s (2003) metastudy on mice that noted that social stress causes an increase in AL and an alteration of behaviors, there were three, nonhuman, data-driven publications in 2003. Looking at psychological and neurological stress on two strains of mice, Tannenbaum and Anisman (2003) observed different behavioral and biological responses to stress, depending upon ancestry. This also provided an insight into the physiological causes of AL. Differences in serotonin and norepinephrine activity after stress is correlated with behaviors akin to depression and anxiety in humans. This can help explain individual differences in AL created by the same stressor. Using lack of exploratory activity as an indicator of fear, Korte et al.'s (2003) metastudy examined rats's behavior after different kinds of stressors.

AL was introduced to those interested in the "gradient between socioeconomic status and health" (Adler and Snibbe, 2003). More directly, Lu and Halfon (2003) suggested that AL is implicated in the greater morbidity and mortality rates of US African American infants. A general overview was presented by McEwen and Lasley (2003). McEwen and Wingfield (2003) presented an energy balance perspective on AL, proposing two types of AL. McEwen (2003a) reviewed the relationship of AL to care-giving experienced in infancy and childhood, focusing

on critical periods in development. He (2003b) also proposed more research on the relationship of psychological disorders to AL. Von Kanel et al. (2003b) reviewed AL and suggested new applications and possible psychological and sociological correlates to it. In addition, several papers that appeared in foreign language journals cataloged by the Web of Science (Esch, 2003: Tiedje, 2003; Fischer et al., 2003a,b), suggests that since studies of the AL caused by smoking, hypertension, and high cholesterol only partially explain differences in health, more work needs to be done. As in 2003, two studies examined AL in elderly Taiwanese. Seeman et al. (2004a) examined social relationships of Tiawanese elderly and "near elderly …(aged 54–70)," by looking at perceived quality of life. AL scores increased depending upon one's perception of events. Notably, men with living wives have lower AL scores. This is not the case with women who live with their husband, prompting questions on whether this phenomenon is cross cultural. If so, it could suggest that some cultural environments (e.g., the duties and expectations of a female) produce different allostatic effects on males and females, a research paradigm already proposed for investigation racial differences in AL (Carlson and Chamberlin, 2003; Lu and Haflon, 2003). Among Taiwanese elderly, women have a more diverse set of markers of senescence and extremes of the ten measures initially used on the MacArthur cohort. However, self reports of health and additional biomarkers such as insulin-like growth factor and interleukin 6, morbidity and mortality are more accurately predicted than just the summary AL score used for the MacArthur cohort (Seplaki et al., 2004). Mitinitski et al. (2004) proposed their own frailty index and tested it on Canadians aged 65 and older. They discovered that this population's frailty index increased at a rate of 3% per year, which suggested to them that this increasing frailty could be the result of the load caused by allostasis. Pruessner et al. (2004) discovered that as individuals get older, mental and physical senescence is faster among individuals with low self-esteem.

Since AL became refined as a measure of senescence, much of the work has focused on those who work with the aged. Like von Kanel et al. (2003), Geiger-Brown et al. (2004) looked at U. S. female nursing assistants working in resting homes. A social condition (stressful work schedule) is correlated with mental health issues (e.g., depression rates quadrupled in these individuals). Since activation of the HPA axis can be associated with adverse mental health conditions, e.g., depression, AL increases in these individuals while their patients have relatively stable scores (Crimmins et al., 2003). An interesting follow up study would be to examine if male workers accumulate AL more slowly than female workers, even if they are married (Kario et al., 2003; Seeman et al., 2002; Seeman et al., 2004a; Seplaki, 2004; Mellner, 2005; Smyth and Myburgh, 2004).

Both van Berge-Landry and James (2004) and Wirtz et al. (2004) looked at hypertension and AL. Male "industrial workers" with hypertension, have more proinflammatory circulating monocytes (Wirtz et al., 2004). For men with mild or borderline hypertension, increased salt intake significantly increases serum electrolytes and proteins, suggesting high salt diets contribute to AL (van Berge-Landry and James, 2004).

A predictor's value is enhanced if there is some kind of treatment. Believing that allostatic damage can be treated before it occurs, Perras et al. (2004) injected ANP to inhibit HPA axis activity. Paradoxically, Hellhammer et al. (2004) discovered that individuals with *hypo*cortisol have lower allostatic load scores, however these individuals have higher depression and scores of "perceived stress" and "physical complaints."

Also in 2004, there were several nonhuman, data-driven studies of AL. These examined the onset of AL early in life, ways to reduce AL, and lifestyle analogues for westerners. Early life experiences and allelic variation in the serotonin transporter gene create different levels of AL, suggesting that experiences modulate the expression of some genes (Barr et al., 2004a,b). Living in full light conditions increases cortisone levels and aggression in male mice, even in enriched environments (van der Meer et al., 2004), suggesting that living in an industrialized society may contribute to AL. Smith and Myburgh (2004), reduced cortisol levels (hence reducing future AL) by giving regularly-immobilized rats the herb *Sutherlandia frutescens* ssp microphylla. Among marmosets who were separated from their parents daily for two years, systolic blood pressure and norepinephrine levels increased after undergoing automated neuropsychological tests (Pryce et al., 2004). In addition, these animals learn at a slower pace and have a greater frequency of responses to environmental stimuli that emulated human major depressive disorders. In a metastudy, Goymann and Wingfield (2004) found that type of dominance system is correlated with corticosterone, GC metabolite, and cortisone.

Hartigan (2004) reviewed AL for veterinarians, however the majority of review articles on AL focus on humans. Chiapelli and Cajulis (2004) link stress to oral ulcers via AL. Angeli et al. (2004) suggest that AL may cause reduced performance in athletes following a rigorous training regimen. Bierhaus et al., (2004) implicated NF-Kappa B as the protein that causes the organ damage associated with AL. Cameron (2004) proposed that the social and hormonal stresses of adolescence contribute to AL while Carlson and Chamberlin (2004) did the same for racism. Kopp (2004) went even further, suggesting that the Eastern European Health Paradox can be explained by AL. Taylor et al. (2004) linked childhood experiences to age-related decline and McEwen (2004) suggested that mental decline, often associated with aging, is due to AL. However, Lupien (2004) warns us against bringing ageism into studies of the aged. Finally, Ursin and Erikson (2004) proposed a cognitive activation theory of stress to endocronologists.

The five articles cataloged and collected in 2005 included two introductions to allostasis and allostatic load (Wingfield, 2005; Korte et al., 2005) to readers of the *Journal of Mammalogy* and *Neuroscience and Biobehavioral Reviews.* Hartigan (2005) suggested applying AL to dairy cows. A

metastudy of mice demonstrated that lower ranked male mice have elevated HPA activity, reduced immune functions, and changed cardiac histology accompanied by altered behaviors (Bartolomucci et al. 2005). Testing McEwen's (2002b) suggestion that AL causes medically unexplained conditions which are more frequent in women. Mellner et al. (2005) looked at 43-year-old Swedish women and found elevated cortisol and heart rates, but no correlation with high AL scores and this symptoms of these diseases. They concluded that though AL score may not be informative in an otherwise healthy 43 year old Swedish women, but certain components may be. Goodman et al. (2005) investigated Midwestern US High School black and non-hispanic white students using the standard MacArthur sets of measures, along with parent education, household income, as well as demographic measures such age, sex, race/ethnicity, family structure, and household size. As in the case of children (Evans, 2003) parental education was correlated with AL (as determined by risk cumulative risk scores). Finally, Galambos (2005), like Angeli et al. (2004), looked at AL in athletes, however, they focused on psychological predictors of injury, suggesting that AL may be the cause behind them.

Discussion

The expansion of AL as a paradigm can be seen in the number of publications and unique first authors. There were sixty-one different first authors during the study period. Certain names were fairly common, though. Table 6 lists the three most common.

Cumulative wear and tear theories are not new (Crews, 2003c). What is new to AL is the recognition of the role of chronic perceived stress and a simple way of assessing it. AL fits into both life history and ecological paradigms. Though it has been 30 years since Damon's *Physiological Anthropology* (1975), AL can be a major component of future work because it is a holistic measure of dysfunction. It would do well to investigate the seemingly contradictory results that some studies have yielded in order to isolate genetic and environmental influences on AL measures.

AL offers an intriguing way of studying chronic stress on multiple systems with a simple test that uses a set of measures associated with stress. It creates a proxy measure accumulation of stress-induced damage and can be modified to fit other investigative paradigms (e.g., van Kanel et al., 2003). Thus, work to link AL with senescence and mortality has been done, but is only beginning. More populations need to be studied and anthropology is well-suited for this task. The MacArthur cohort and Taiwanese elderly, though important studies, are end-of-life cohort of relatively affluent individuals. More intriguing would be examination of AL as it develops through and *even before* the lifespan. Lu and Halfon (2003) propose that research should begin by taking account of maternal life history to look for predictors of "racial and ethnic disparities in birth outcomes." Thereby, expanding Barker et al.'s (1993) work on diabetes and maternal environment during pregnancy. The consequences of AL on development of the offspring's offspring, as documented in rats, must also be addressed (Zambrano et al., 2005). Moving on to postnatal environment, Hogue and Bremmer (2005) propose looking at how early life experiences of mothers may lead to variability in allostasis during their pregnancy. In rodents, glucocorticioid receptor gene expression is influenced by minor elevations in cortisol during childhood (Anderson and Wood, 2000). These effects are stronger in females than males (Anderson and Wood, 2000), and may outweigh sex-based effects on other physiological functions over the life span (Barr et al., 2004a, b). Anthropology is positioned to expand this work beyond intra-populational variation and apply these methods to inter-populational and nonhuman samples.

Table 6 First authors publishing on allostatic load

Top publishers		
First Author	Rank	N
McEwen	1	13
Seeman	2	4
Fischer	3	3
First Authors with two publications		
Gold		
Karlamanga		
Lawler		
Tannenbaum		
Von Kanel		

Note: This is a count of first author only

Moving beyond the perinatal environment and into childhood. Pryce et al. (2004) establish marmosets as an effective animal model for humans. Deprivation of parenting leads to behaviors that mirror those in humans diagnostic of major depressive disorders. McEwen (2003a) proposed a mechanism, and noted (2000) that childhood abuse is significantly correlated with increased cardiovascular disease and AL. Evans' (2003) reported that environmental conditions during childhood correlate with greater AL. Anthropologists are prepared to apply this model to other industrialized populations with public schools and, with modification, to other populations with different cultural or socioeconomic structures. For example, does Japanese style education create similar correlations of AL in their children as US? Could AL accumulated during childhood education be used to investigate differences in life expectancy among Japanese and US citizens? Are there other cultural variables with analogous effect, e.g., does divorce in polygynic households have the same impact as having a close family member leave did in rural New York? Do children below the Federally defined poverty level in New York have AL scores comparable to the poorest children in Taiwan? As individuals move into adolescence stressors change. Cameron (2004) discusses the interrelationship between affect, behavior, and the dramatic change in hormones that accompanies adolescence and using Goodman et al.'s (2005) work on hispanic and white US high

school students, anthropology can look at intra-societal variation in AL. Investigating relationships of social mobility and AL in samples with fluctuating adolescent hormones in different environments, may provide another perspective on generational change over time (e.g., Freedman/Mead controversy). Like studies of maternal environmental effects (Barker et al., 1993), and possibly grand-maternal (Zambrano et al., 2005), on glucose metabolism, the social environment of one's grandparents may impact one's health as social mobility is low for the poor.

AL can be applied to adulthood as part of life history approaches and is being reported more frequently in anthropological settings. One could look at younger adults (students) (Gaab et al., 2003; Lawyer and Younger, 2003) or athletic adults (Galambos et al., 2005) and compare their AL scores to disparate groups (e.g., Crews, 2003a, b; Crews 2004). Cultural factors, such as stress mediation strategies, may reduce AL or while psychological ones may increase injury risks. Following a recent traumatic event, such as a natural disaster (e.g., Kario et al., 2003), US, Pakistani, or Japanese may show different AL responses. Cross-culturally, women have higher AL scores. Examinations of psychological and familial disease, such as among female caretakers and care-recipients in New York (Gold et al., 2003, 2004), would be informative as well. AL among workers in several industrialized nations have been studied, e.g., Geiger-Brown et al., 2004; Kumari et al., 2004; Schnorpfeil et al., 2003; Steptoe et al., 2002; Sluiter et al., 2000, but we still do not know how variable work demands affect Somali workers in Columbus, Ohio or if this stress is comparable to Dutch workers? Does perception of stress among German factory workers have the same impact on AL as Mexican workers in US auto plants? Would AL predict three-year health decline among UK civil servants as well as Zimbabwe civil servants? Or, given differences in life expectancy, would it be greater?

AL also has been studied among non-healthy adult cohorts. In regions without the alcohol dehydrongenase allele, does alcoholism (or abuse of indigenous intoxicants) have the same effects on cortisol as among Westerners (e.g., Adinoff et al., 2003)? Do individuals sampled from other populations have decreased AL associated with hypocortisolism, but increased depression as Hellhammer et al. (2004) documented (see also Decker this volume). Does post-traumatic stress disorder among HIV/AIDs sufferers in Africa show the same correlation with over-reaction to non-traumatic events as Koopman et al. (2002) discovered among a US cohort? Several studies have looked at treatments and interventions, e.g., Smith and Myburgh (2004), Lawler et al. (2003), and van Berge-Landry James (2004). Would these have cross-cultural efficacy? Are there socio-cultural analogues for these treatments in other groups?

It is evident that AL offers a new way to describe stress. Anthropology's unique human-other centered approach is well-suited to expanding current knowledge on AL. With Anthropology's biocultural paradigm and long history of investigating stress, AL offers a research paradigm that will enhance and unite life history and senescence work.

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