Bridging the biological and social worlds: neuroendocrine biomarkers, social relations, and the costs of cumulative stress in Taiwan

by

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Abstract

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This work investigates the hypothesis that a possible cause of poor health amongst the socially disconnected is increased stress levels. The relatively new theory of allostatic load (AL) posits that the body's response to stress can come at a cost, which accumulates over time and eventually leads to negative health outcomes. There is increasing evidence that high levels of AL are predictive of poor health states, but few studies have attempted to demonstrate that elevated AL results from a stressful life history.

This dissertation analyzes data from the Social Environment and Biomarkers of Aging Study (SEBAS), a nationally representative survey conducted in Taiwan of those aged 54 and older in 2000. Using neuroendocrine biomarkers and social variables, a combination rarely found in large surveys of this quality, this work tests whether various measures of social disconnection and social stress lead to riskier biomarker levels in an AL construct. Key independent variables I use in the analysis include widowhood status and its duration, living alone, not living with a married son, and subjective responses to a

number of questions probing the respondents' stress history. The dependent variable used here is called neuroendocrine allostatic load (NAL), which is an index combining four neuroendocrine biomarkers (cortisol, DHEAS, epinephrine, norepinephrine). Among other reasons for using this construct is that the included markers are core to the physiological stress response and AL theory, and have hitherto been little studied.

A major finding of this work is that, contrary to expectation, major and enduring stressors appear to have no influence on NAL levels. In contrast, psychosocial reports of *current* stress (amongst women) are associated with measurable increases in NAL, even though AL theory would predict negligible impact (since any additional AL stemming from recent events would be dwarfed by events having occurred over the entire life course). Thus, although baseline levels of the neuroendocrine markers may still be useful in predicting worse health outcomes, this dissertation calls into question whether the levels truly represent accumulated costs of past insults. Indeed, the baseline neuroendocrine markers may well be capturing current, ephemeral states at the time of the interview.

Chair　　　　　　　　Date

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Acknowledgments

With a dissertation and nearly half a decade of graduate student life behind me, I have earned the right to play Oscar award recipient. I would like to start by thanking John Wilmoth, who, many years ago, took a chance on a wide-eyed undergraduate and (along with David Nasatir) exposed me to the thrill of original, quantitative social science research. John, despite our doubts and my stints abroad, which at some point led to emailing drafts out of an Internet café in Saarbrücken, Germany – we published! While I am paying kudos to past professors, I must recognize the irrepressible Ann Swidler for her spellbinding and inspiring lectures. No one else could have so skillfully and with such panache introduced me to the world of Durkheim's anomie, Marx's history of class struggle, and Foucault's panopticon.

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who have gone unnamed) have provided heaps of useful feedback. As they say, all remaining errors are my own.

My dissertation is about contexts, and that of my home department has provided me nourishment to carry out my thesis. I am deeply appreciative of Berkeley Demography for its lively, supportive, and charming milieu. How many graduate students can claim the luxury of typing away (in their own offices no less) in such settings as a bucolic, Julia Morgan designed cottage?

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My dissertation is also about social relations, and I am grateful for having lived nearly all of my college years in the co-ops, where lounge lizards mix with bookworms, chik pattie fiends have dinner with meat lovers, wannabe punks philosophize with wannabe aesthetes, and Jeopardy devotees somehow share the TV with Simpson buffs. The blockish, humble building located at 2527 Ridge Rd., on an ordinary street on the campus' north side, could easily be overlooked by passersby. But it is there where I was privileged to have had the company of the stoop sitters of Stebbins, as we tried to sort out the mysteries and frustrations of life, despite our limited learning and late-teen and twenty-something years. It is also there where during our daily, communal dinners, I discovered jokes aplenty and shoulders to lean on. To those many cool cats who taught a middle-class straightedge how to boogie on a Saturday night, what my body has reaped as punishment, my psyche and soul have reaped as reward. In vino veritas! I promise to fight those forces conspiring to dull, blur, and mute the colorful memories from that place with the great, green hands out front, home to a cornucopia of my life's firsts, and perhaps lasts.

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Chapter 1

Introduction

"Suicide varies inversely with degree of integration of the social groups of which the individual forms a part."

Émile Durkheim

"Solitary confinement is one of the severest punishments which can be inflicted."

Charles Darwin

The biological and social worlds hardly need to be at odds with one another. Indeed, physiology and evolutionary theory have fruitfully been applied to issues as diverse as population fertility levels, sexual orientation, delinquency, and occupational status attainment in both sexes (Livi-Bacci 2001; Freese et al. 2003; Dabbs 1992). This dissertation adds to the burgeoning literature that brings a physiological perspective to bear on social phenomena by analyzing neuroendocrine biomarkers[1], social relations, and stress using data from a Taiwanese population survey.

This work takes as its starting point the established link between social connectedness and health. It then attempts to make progress in understanding one of a

[1] Biomarkers can be generally defined as physiological or anthropomorphic measurements. Examples include height, weight, hand grip strength, cholesterol, and blood pressure. The neuroendocrine markers studied here are cortisol, DHEAS, norepinephrine, and epinephrine. Height was one of the earliest collected biomarkers in social surveys and has proved to be a good measure of health, standard of living, and social differentials (Wachter 2001). More recently, bioindicators have been used to measure "physiological age" in comparison to "chronological age" and to predict mortality (Borkan 1982; Arking 1998).

number of plausible biological mechanisms to explain this finding by asking some of the following questions. How and to what extent can the social milieu impact levels of stress? Are any such effects revealed in neuroendocrine system function, a system important to physical and emotional health? To what degree can the theory that stress causes cumulative "wear and tear" on the body be substantiated by recently available neuroendocrine biomarkers in social surveys?

Social scientists since at least Durkheim (1897) have tried to connect greater social integration to better health. Establishing the link as causal is exceedingly difficult. Reverse causality (e.g. poor health leading to less interaction) and the possibility that a third factor (e.g. optimism and/or a buoyant personality) influences both health and one's social network are just two examples of complexities that must be adequately addressed. Research in the last few decades has produced a number of high quality studies that have attempted to make headway on the challenging topic of integration and health. The strength of these studies lies in the diversity of national and international settings in which they have been conducted, their longitudinal designs and long periods of follow-up, variety in their measures of both social connection and health, and controls for relevant variables (Berkman and Glass 2000; Thoits 1995; Taylor et al. 1997; Knox and Uvnas-Moberg 1998; House et al. 1988). In an influential review of such studies, House and others (1988) claimed that social isolation is a risk factor on par with that of health behaviors like smoking. According to other reviewers of the literature, social connection is consistently and strongly related to health, and especially mortality (Berkman and Glass 2000; Thoits 1995; Taylor et al. 1997; Knox and Uvnas-Moberg 1998).

With populations aging in many parts of the world (US Census Bureau 2004), issues relating to social isolation take on greater salience. Social engagement tends to decrease with age (although there is substantial heterogeneity) in part because of deteriorating health, widowhood, and perhaps due to life cycle transitions like retirement and children leaving the home (Bukov et al. 2002). To the extent that older persons are more susceptible to a variety of health problems, they may differentially bear the costs of social impoverishment.

Health, at the most proximate level, is a biological outcome. So what in particular about social integration may lead to better (or in some cases worse) health? How, in the nomenclature of the field, does the social "get under the skin?" There is an existing gap in the literature, what some researchers have called the black box, which lies between the points of social connection and health: the precise mechanisms explaining the association. For the most part, until recently, potential mechanisms have been tested in clinical experiments. While possessing a number of advantages, these studies are often characterized by limited sample size, lack of representativeness, and having been conducted in laboratory, rather than real world, settings. New social surveys that include biological information now allow researchers to test plausible physiological mechanisms with population level data. This dissertation uses such a survey to investigate how social relations might mediate the deleterious health effects of stress.

The stress response, adaptive in our historical past, is a contributor to modern health problems. Dangers we have faced through most of our two-million-year-long evolutionary history were often capricious: natural disasters, attacks by carnivores, and warfare (Horiuchi 1999; Mayr 2001; Wilson 1998). In an environment of short-term, often lethal dangers it seems quite plausible that a "fight or flight" reaction to potentially harmful events would lead to enhanced reproductive success. Today, however, charged responses are often elicited in situations that are not life-or-death, but psychologically, threatening. Over time, such responses can harm the body; stress is implicated in the onset and development of a number of degenerative diseases that are now predominant in developed countries, including coronary heart disease, diabetes, and cancers (McEwen and Stellar 1993; Sapolsky 2004; Gersten and Wilmoth 2002).

Various arguments that fall under the "stressful life account" perspective propose ways in which those who are socially connected could also experience lower levels of stress (Cacioppo and Hawkley 2003). One theory included in this perspective is that during times of stress one's social network provides coping resources. A number of clinical studies examining cardiovascular, immune, and neuroendocrine system function have supported the stressful life account perspective (Uchino et al. 1996). For instance, significantly lower levels of the hormone cortisol were measured after an anxiety-producing test in those who had had a friend's support compared to those without such aid (Heinrichs et al. 2003).

This dissertation engages a relatively new paradigm about stress and the physiologic toll it exacts. The testing of this theory holds promise for clarifying the factors contributing to, and the mechanisms of, disease onset. *Allostasis*, originally proposed by Sterling and Eyer (1988), is the concept that the body must constantly adapt itself to changing environmental demands in order to achieve *homeostasis*, an "ideal steady state" (Timiras 2003). Allostatic load (AL) develops, according to the theory, when the repeated costs of dealing with stress accumulate to cause "wear and tear" on the body (McEwen 1998). AL supposedly leads to dysregulation in a number of different physiological systems, which is represented by system operation outside of normal ranges. AL can accumulate over the life course and is considered a pre-disease indicator (McEwen 1998).

Appropriate operationalization of AL is a major challenge (Seplaki et al. 2004; Hale 2004; Karlamangla et al. 2002). A key feature of the AL construct is inclusion of multiple biomarkers in a single index. To date, the most commonly used index stems from the MacArthur studies which used 10 individual bioindicators. High baseline levels on the MacArthur construction of AL predicted worse physical and cognitive functioning years later (Seeman et al. 1997). The index has been shown to be more predictive than individual biomarkers alone (Seeman et al. 1997). In many ways the physiological diversity captured by the index is its strength. However, the interpretation of AL is difficult because the entire construction is something of an admixture in that it includes markers representative of many different biological systems. Thus, understanding the dynamics of the index components is also necessary.

The MacArthur index can conceptually be broken down into at least two major sub-indexes, the primary mediators and secondary outcomes (McEwen and Seeman 1999). The latter is comprised of familiar measures such as cholesterol and blood pressure, and is the more thoroughly tested of the two. Primary mediators include such neuroendocrine markers as cortisol, DHEAS, epinephrine, and norepinephrine. This dissertation focuses only on the neuroendocrine markers for a number of reasons. First, as mentioned above, the AL load construction as a whole is predictive of worse health outcomes, but the role of its components has been less intensively studied. Further, the neuroendocrine markers (like the secondary outcomes) are, in the MacArthur studies at least, predictive of worse health outcomes in their own right and thus seem to warrant further study (Seeman et al. 2001). Second, in the experimental literature, the neuroendocrine measures are more clearly linked as outcomes of the stress process. Accurate understanding of the AL construct requires knowledge about these markers. Third, it is rare to have bioindicators in social surveys and it is rarer still to have neuroendocrine measures. Consequently, on the population level, little is known about them.

I analyze in this dissertation the Social Environment and Biomarkers of Aging Study (SEBAS), a population survey conducted in Taiwan in 2000. Despite the cross-sectional nature of the survey, it has a number of strengths. First, it is unusual to have such a survey that is nationally representative. Second, the response rate is relatively high, at over 90% for the interview portion. Third, the age range of 54–91 is wide relative to other studies of similar design. Lastly, the SEBAS has collected neuroendocrine biomarkers, a rarity in population surveys and key for testing of AL.

The analysis here uses an abbreviated AL construct that includes only the neuroendocrine biomarkers. The construct is called NAL, an acronym for neuroendocrine allostatic load. Most generally, the dissertation tests whether a stressful life history, with attention to those aspects of a more social nature, are linked to NAL. Stress is conceptualized both in terms of life events and subjective interpretations. Regarding the respondents' social milieu, I focus on marital status (married compared to widowed) and self reports of stress that stem from different aspects of family life (e.g. conflict amongst members and members' health and financial situations).

A major conclusion of this study is that there appears to be little evidence that the stressful life history measures correlate with NAL measured at the time of the survey. For instance, low education, length of widowhood, and length of a variety of social stressors are not linked with the measure. On the other hand, at least for women, NAL is strongly correlated with report of current stressors. These findings are robust to some alternative scoring schemes of NAL. Thus, there appears to be evidence that the baseline neuroendocrine markers are more reflective of current conditions, rather than any past ones. In other words, it seems that the "noise" produced by current events overwhelms any hoped-for "signal" generated by events throughout the life course. This finding, if supported in further research, would pose a serious challenge to our understanding of AL constructs, which are thought to primarily represent the result of long-term processes.

Chapter 2

Stress and neuroendocrine biomarkers

Summary: Defining "stress" is complicated, but it can be conceptualized as involving each of the environmental, psychological, and physiological domains. While short-term stress is evolutionarily adaptive, over time the stress response can also have damaging effects on the body which contribute to the onset and worsening of myriad health conditions. Two key neurological systems – the hypothalamic-pituitary-adrenal axis and sympathetic nervous system – are involved in the body's stress response. Cortisol and DHEA/DHEAS levels represent activity of the former system, and the catecholamines, the latter. With increasing age (and at rest) cortisol levels stay relatively stable, but the circadian rhythm (pattern over the day) appears to flatten. Older subjects respond as vigorously as younger ones in stress tests, but take a longer time to return to resting levels. Not nearly as much is known about DHEA/DHEAS and its relation to stress. DHEA/DHEAS has attracted more research attention recently partly because of the possibility that it buffers some of the negative consequences of cortisol. In both men and women there are steep declines in DHEA/DHEAS with age under basal conditions. Lastly, in regard to the catecholamines, aging (under nonstressed states) is associated with higher levels of norepinephrine, but not epinephrine.

2.1 Conceptualization, measurement, and health consequences of stress

A particularly useful conceptualization of stress focuses on three different domains: environmental, psychological, and physiological (Cohen et al. 1995). The environmental approach emphasizes stressors, events that occur around us in the world that have the potential to be stressful. The environmental conceptual frame often leads in population surveys to checklists of what are thought to be likely stressful events. Such a list of stressors might include questions concerning personal loss (e.g. death of a spouse, other loved one, or friend), major life transitions (e.g. graduating and entering the workforce or retirement), and other life challenges (e.g. caring for an ill relative or suffering from financial problems). As might be imagined, the psychological approach is concerned more with a person's perception of events as subjectively stressful or not. Such psychological stress might be realized when perceived demands exceed perceived abilities to cope. Lastly, the physiological domain concentrates on understanding short and long-term biological changes that occur with exposure to physical and psychological stressors. Ideally, a survey about stress would tap all these dimensions since none alone is considered the "gold standard." An analyst could be confident that a participant has experienced stress if all three measures are in accord. Combining these approaches into one definition related to a health outcome, stress can be defined[2] as "a process in which environmental demands tax or exceed the adaptive capacity of an organism, resulting in

[2] Other definitions for stress abound. One that takes a positive view of the phenomenon and does not reference any future health outcome states that, "stress is a process which activates a number of physiological responses to maintain an internal equilibrium (steady state or homeostasis) for normal function and survival" (Paola Timiras, personal communication, June 2005).

psychological and biological changes that may place persons at risk for disease" (Cohen et al. 1995).

Figure 2.1 graphically summarizes this definition. In one example illustrating the figure's pathways, it can be imagined that a husband loses his beloved wife of many years. Such a loss would likely test the limits of the widower's adaptive capacities, resulting in a great negative emotional response. Such a reaction might *directly* lead to increased risk of physical disease, for example through a suppressed immune system. As well or alternatively, health could be affected *indirectly*. For instance, the loss might produce changes in behavior, such as poorer sleeping or eating habits that raise the possibility of a negative health outcome. The dotted lines in the figure represent possible feedback loops. For example, reaching out for positive social support would affect early aspects of the chain, which would subsequently ripple downwards.

The body's response to stress helps steel it against a challenge. While stressors in contemporary Western societies are predominantly psychological, during our evolutionary history they often threatened our very survival. The lion suddenly appearing in the savanna ready to attack, kill, and eat his prey is a favorite example of this second case. There is a basket of typical physiological reactions to stress, many more appropriate for such acute, short-term demands of the distant past (Sapolsky 2004; Timiras 2003). For example, the heart pumps harder and blood is diverted to skeletal muscles, improving capacity to flee from the predatory lion. Concentration and alertness improve and so too does memory imprinting, useful for possible future recall of what you did right (or wrong) in a previous, similar situation. Pain sensitivity also decreases, which would prove helpful in the case of injury. When confronting an acute stress, appetite, sex drive, and growth all diminish, a delay of the body's less immediate needs for later (Sapolsky 2004; Timiras 2003).

The short-term mobilization of resources for coping with stressors has proved to be a successful adaptive response. At the same time, however, the response is taxing and the body must recover. Stresses that are too acute, too frequent, or that last too long can have negative effects on heath. These range from a weakened immune system that less vigorously wards off the common cold (Cohen et al. 1991) to more serious illnesses like heart disease and possibly forms of brain damage (Brunner 2000; Sapolsky 2004; McEwen 1998).

In regards to the physiological domain of stress conceptualization and measurement, cardiovascular and neuroendocrine aspects of human biology have been intensely studied. Neurological investigations have mostly focused on two areas, the hypothalamic-pituitary-adrenal (HPA) axis and sympathetic nervous system (SNS) (Cohen et al. 1995).

2.2 Neuroendocrine systems

2.2.1 HPA axis

2.2.1.1 Cortisol

Cortisol is a key hormone in the HPA axis and has long been considered the *sine qua non* of the physiological stress response. In this vein, some have defined stress as "anything that makes your glucocorticoids[3] go up" (Heuser and Lammers 2003). Cortisol is a steroid hormone[4] that eventually is released into the blood by processes that begin in the brain. With stress the hypothalamus secretes a number of releaser hormones, primary among them CRH (corticotropin releasing hormone). In turn, CRH stimulates the pituitary gland, located below the brain, to synthesize and release ACTH (adreno-corticotropic hormone) into the bloodstream. After reaching the adrenal gland which lies above the kidney, ACTH sparks cortisol production (Worthman 2002; Brunner 2000; Tsigos and Chrousos 1996). This sequence is shown in Figure 2.2.

In an effort to obtain the appropriate "set point," the HPA axis uses feedback signals (Timiras 2003; Brunner 2000). The set point can be considered an internal balance the body is trying to achieve to meet environmental demands. Since challenges posed by the environment change, there is constant evaluation and adjustment of CRH, ACTH, and cortisol levels. For instance, after the response to stress which results in the increased production of glucocorticoids, these same hormones can send signals to reduce the output of CRH and ACTH, which in turn lowers glucocorticoid secretion.

Studies of stress using cortisol have examined levels in both non-stimulated (basal) and stimulated situations. Under basal conditions and with healthy subjects, cortisol is released in bursts throughout the day, with maybe 15 in a 24 hour period. Levels also show what is called diurnal variation, or a circadian rhythm. That is, levels in the body display a consistent fluctuating pattern depending on the time of day. Cortisol

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[3] In humans, the primary glucocoricoid is cortisol, whereas in rats it is corticosterone.

[4] A hormone is a chemical substance with particular regulatory functions. These messengers percolate into the bloodstream and can have wide ranging effects. Steroids refer to five different classes of hormones that have a similar chemical structure derived from cholesterol. In addition to glucoccorticoids, the other steroids are androgens (like testosterone), estrogens, progestins, and mineral corticoids.

levels are lowest at night and highest during the morning (Baum and Grunberg 1995; Lupien et al. 1996).

Some studies have examined how cortisol levels change with age. When exposed to a stressor, it appears that older subjects react as strongly as their younger counterparts, but during the recovery phase it takes the aged longer to return to baseline levels. It is believed that this "sluggish" recovery is due to a dysregulation of the negative feedback system that limits glucocorticoid secretion (Seeman and Robbins 1994; Sapolsky 2004). The literature provides conflicting results on any trend of basal, mean cortisol levels with age, with studies having shown mainly stable and slightly increasing values, but also declining ones (Deuschle et al. 1997; Lupien et al. 1996; Seeman and Robbins 1994; Timiras 2003). Part of the difficulty in identifying any pattern is limited sample size, narrow subject age range, and cross-sectional design (Barrett-Connor 2002). In regard to cortisol's typical wave-like pattern, in older persons it may flatten, with the evening nadir delayed and attenuated (Van Cauter et al. 1996; Magri et al. 2000; Ice et al. 2004).

Cortisol can be measured via blood, urine, or saliva, with each method carrying its own pros and cons (Baum and Grunberg 1995; Kirschbaum and Hellhammer 1994). Collecting salivary samples is becoming increasingly popular, largely because it is the least invasive and offers similar results to those found in blood. Both blood and saliva samples measure cortisol levels at one point in time. Hence, to determine levels over a day, for instance, multiple samples need to be taken. These various data points can then be used to determine average levels. Alternatively, to measure a daily average, one could collect urine voided over 24 hours. Urine samples contain cortisol excreted over an entire period and thus represent an integrated measure. Since cortisol levels are related to body size independent of stress, they must be standardized by creatinine, which is excreted in the urine at a steady rate proportional to total muscle mass (Weinstein et al. 2003).

In studies with urine collection, samples are often over 24 or 12 hours, with the latter including night and morning times (e.g. 8pm–8am). It has been argued that the 12 hour collection interval is preferable to a more extended one because study participation rates are improved, and so too is compliance with the experimental protocol. Further, since cortisol levels can be influenced by exercise, levels of exercise should to the extent possible be held constant. The impact of physical activity on biomarker levels is probably limited with an overnight sample where the participant is more likely to be at home and much of the time in bed. Lastly, in a pilot study comparing 12 and 24 hour urine specimens, cortisol, epinephrine, and norepinephrine levels were highly correlated (Crimmins and Seeman 2001).

Cortisol levels in the body are often influenced by other phenomena besides stress, and a researcher should consider controlling for their effects. Some of the phenomena that increase levels include smoking (Meliska and Gilbert 1991; Kirschbaum et al. 1992; Kirschbaum and Hellhammer 1994), physical activity (Kanaley et al. 2001; Kirschbaum and Hellhammer 1994), and eating, especially the mid-day meal (Gibson et al. 1999; Follenius et al. 1982). Meal composition (Gibson et al. 1999; Field et al. 1994) as well as sleep and wake times (Kudielka and Kirschbaum 2003; Caufriez et al. 2002) may also influence cortisol production. Some substances linked to raised levels are caffeine (Lane et al. 2002; Lovallo et al. 1996; Ice et al. 2004) and alcohol (Adinoff et al. 2003; Lovallo et al. 2000).

In a last note on methodology, assays of different quality have been used to analyze urine, blood, and saliva samples. Unlike older assays of the mid-1970s and earlier, modern ones are both sensitive and specific enough to measure cortisol accurately (Baum and Grunberg 1995).

2.2.1.2 DHEA/DHEAS

Compared to cortisol, much less is known about the role of DHEA/DHEAS and certainly the latter has been less intensively investigated as part of the stress response. Interest in the role of DHEA/DHEAS has grown recently with studies showing harmful consequences of high cortisol levels, and cellular evidence suggesting that DHEA/DHEAS could be protective by functioning as a cortisol antagonist (Leowattana 2004; Celec and Starka 2003; Yen and Laughlin 1998). Because of the potential anti-glucocorticoid actions of DHEA/DHEAS, some researchers contend that studying subjects' molar ratio of cortisol to DHEA/DHEAS gives a more accurate picture of adrenal function than both separately. Deciding to examine this ratio is not trivial since it may lead to alternate study conclusions (Goodyer et al. 1998; Cruess et al. 1999; Morgan III et al. 2004).

DHEA/DHEAS is endogenously produced in similar ways as is cortisol. CRH in the hypothalamus stimulates ACTH formation which in turn leads to secretion of DHEA/DHEAS by the adrenal glands. Unlike cortisol, DHEA/DHEAS does not appear to exert negative feedback on the HPA axis and DHEA/DHEAS can also be produced in small amounts in the male testes (Leowattana 2004; Baulieu 1996). Under acute stress, the adrenal glands produce both cortisol and DHEA/DHEAS, with the ratio of cortisol to DHEA/DHEAS increasing because of differential formation (Timiras 2003; Hornsby 1996; Goodyer et al. 2001; Worthman 2002). DHEA/DHEAS is not always produced coincident with cortisol, however (Worthman 2002). Too few studies have carefully examined the connection between long-term stressors and resting DHEA/DHEAS concentrations for conclusions about any link between the two to be made.

DHEA and DHEAS are the abbreviations for dehydroepiandrosterone and its sulfate bound form. They are converted one from the other and seem to perform similar functions (Baulieu 1996; Hornsby 1996; Ferrari et al. 2001). The precise role of DHEAS is not well understood, but it has attracted attention for a number of reasons in addition to its potential cortisol antagonizing properties. First, DHEAS is the most abundant circulating steroid in the body. Second, it is thought to be a precursor (some might grandiosely say "mother hormone") to a number of beneficial androgens and estrogens. Third, on a population level, DHEAS has a dramatic age-related pattern of decline. Men tend to have higher circulating levels of DHEAS than women, but for both sexes, levels are highest between ages 20–30. Thereafter, there are steady declines so that by seventy or eighty years old about 10–20% of DHEAS, relative to peak amounts, is generated (Hornsby 1996; Ferrari et al. 2001; Leowattana 2004).

There are an increasing number of studies investigating DHEAS concentrations and the potential impact of those on a wide variety of health outcomes, including cardiovascular disease, immune function, and depression. So far these investigations have not proven conclusive. While it is believed that having higher levels of DHEAS more typical of a younger person's profile represents lower risk, both high and low levels of

DHEAS have been linked to health problems (Celec and Starka 2003; Allolio and Arlt 2002; Glei et al. 2004; Morrison et al. 2000; Cleare et al. 2004). In the US and in other countries for some years now, DHEA supplements have been available over-the-counter. While some have claimed that DHEAS replacement therapy promises a "fountain of youth," limited high quality trials have yet to establish any potential benefits (Leowattana 2004; Celec and Starka 2003; Allolio and Arlt 2002).

It is possible to measure either DHEA or DHEAS through blood samples. Because of its longer half life and lower metabolic clearance rate, DHEAS shows little within-subject variation over the day (Leowattana 2004). The mild and temporary stressors of the variety given in experimental tests (such as public speaking) or of ordinary daily hassles are unlikely to produce noticeable changes in DHEAS concentrations. However, extreme stress exposure, as is experienced in military survival training, can produce significant increases (Morgan III et al. 2004).

Little work has explored the numerous ways DHEAS levels might be altered by various behaviors. It is unclear in what way alcohol consumption influences DHEAS levels, but it appears that smoking raises them (Leowattana 2004). Also uncertain is the role of exercise and diet on concentrations of the steroid (Corrigan 2002; Field et al. 1994). Because of the proven ability of DHEA replacement therapy and supplement use to substantially increase concentrations of the hormone (Tummala and Svec 1999), the greatest attention should be paid to these potential confounders.

2.2.2 Sympathetic nervous system

2.2.2.1 Catecholamines

The body's autonomic nervous system[5] helps control functions that are more or less involuntary, such as digestion and sweating. The autonomic nervous system is comprised of two parts, the sympathetic and parasympathetic. In response to stress, the former initiates actions important for arousal, like an increased heart rate and blood pressure. At the same time the sympathetic nervous system is activated under stress, the parasympathetic nervous system is suppressed. Under conditions of calm, the parasympathetic nervous system works to promote long-range needs such as digestion, energy storage, and growth (Sapolsky 2004). Some of these competing functions of the sympathetic and parasympathetic nervous systems are shown in Figure 2.3. As described earlier, the HPA axis is also activated with stress. The HPA axis and sympathetic nervous system are very much linked together, interacting with one another in complex ways (Goldstein 2003; Tsigos and Chrousos 2002).

Epinephrine and norepinephrine are major catecholamines produced by the sympathetic nervous system. Epinephrine is secreted by the sympathetic nerve endings in the adrenal medullae, whereas norepinephrine is secreted by all the other sympathetic nerve endings throughout the body. It is possible for different stressors to cause epinephrine and norepinephrine to be disproportionately secreted. For instance, epinephrine release may be more related to emotional stress, whereas norepinephrine

[5] The other half of the body's nervous system is the voluntary nervous system.

release may be more related to physical exertion (McEwen 2003; Goldstein 2003). Further, some stressors will release norepinephrine from some branches of the sympathetic system and not other branches (Sapolsky 2004).

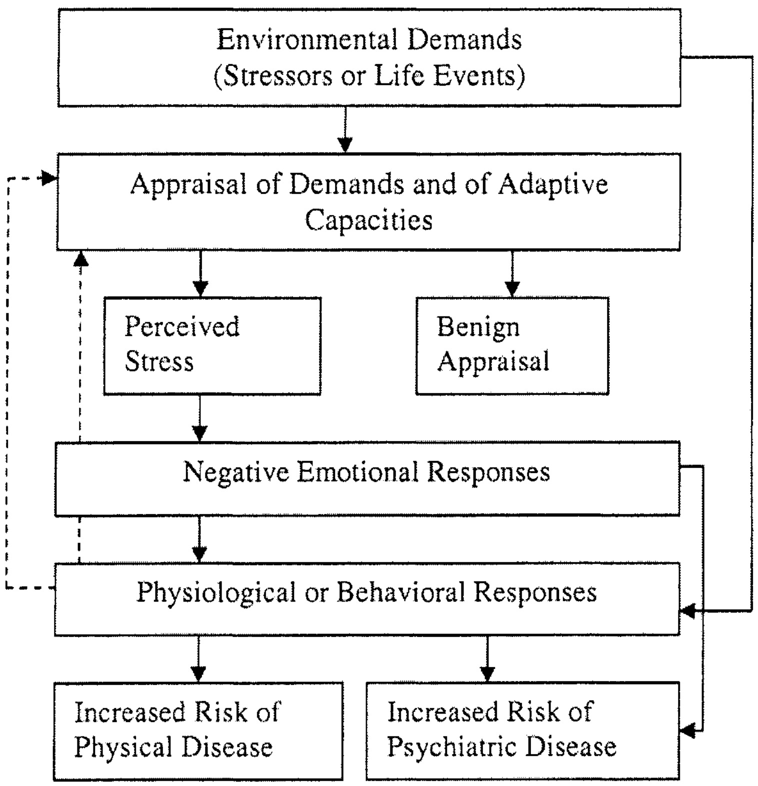
Catecholamines have most often been studied in blood and urine, although other advanced techniques (such as microneurography) are also used (James and Brown 1997). Similar to cortisol, catecholamine levels measured through blood samples reflect more immediate, transient states (such as stress experienced in the last 1–3 minutes). In contrast, urine samples reflect stress levels that have occurred in the period between voids, with the margin of error being about an hour or less (Cohen, Kessler, and Gordon 1995).

Under basal conditions, investigators generally have found that epinephrine levels are slightly lower or do not change over age (Seals and Esler 2000; Ruben et al. 2000). Using "tracer methodology" rather than the usual measurement techniques, however, one study revealed stark declines in epinephrine secretion in older men relative to their younger counterparts (Seals and Esler 2000). Measurement of norepinephrine over age has yielded more consistent results. Its secretion under basal conditions likely increases with age and is region specific, targeting skeletal muscle and the gut (Seals and Esler 2000; Reuben et al. 2000). Regarding stress reactivity, there is some debate whether catecholamine responses to various stressors is different in younger compared to older subjects (James and Brown 1997; Seals and Esler 2000; Sapolsky 2004).

In regard to sex, sympathetic nervous system activity does not appear to be different at baseline for either men or women. Under conditions of stress, however, women may respond with lower urinary epinephrine (James and Brown 1997). As with cortisol, a number of typical health behaviors affect catecholamine levels. These include smoking, drinking, exercise, and aspects of one's diet (James and Brown 1997; Cohen, Kessler, and Gordon 1995). Particular to the Taiwanese context, chewing betel nut is known to increase amounts of epinephrine and norepinephrine. While on the decline, the habit is still popular in Asia with an estimated 300 million users[6] (Chu 2001).

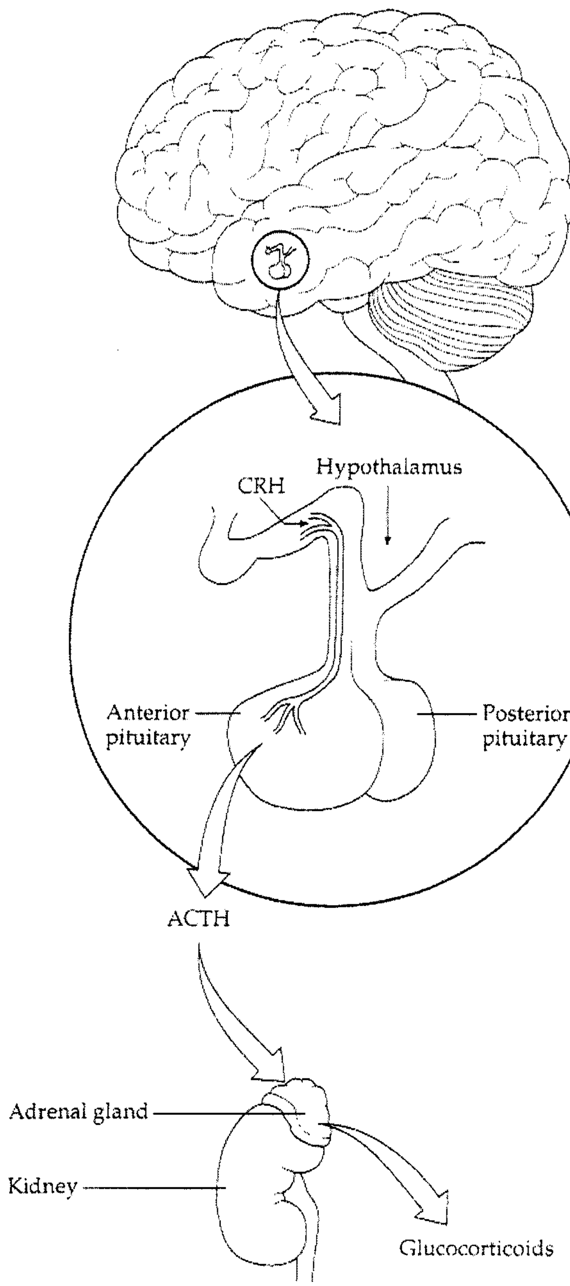
[6] Apparently knowledge of betel nut consumption was slow to reach the West despite its status as an ethnopsychopharmacologic agent of antiquity like the Peruvian coca leaf and Indian hemp. Users report a number of psychosomatic effects such as heightened alertness and a sense of well-being. Betel nut use also has social and cultural dimensions. Chewers point out, for example, that sharing one's betel nut can help initiate conversation and improve interpersonal relations. The technical term for the nut is *Areca catechu* and it is often eaten with lime and wrapped in a plant leaf (Chu 2001).

Figure 2.1 A model of the stress process integrating environmental, psychological, and behavioral factors



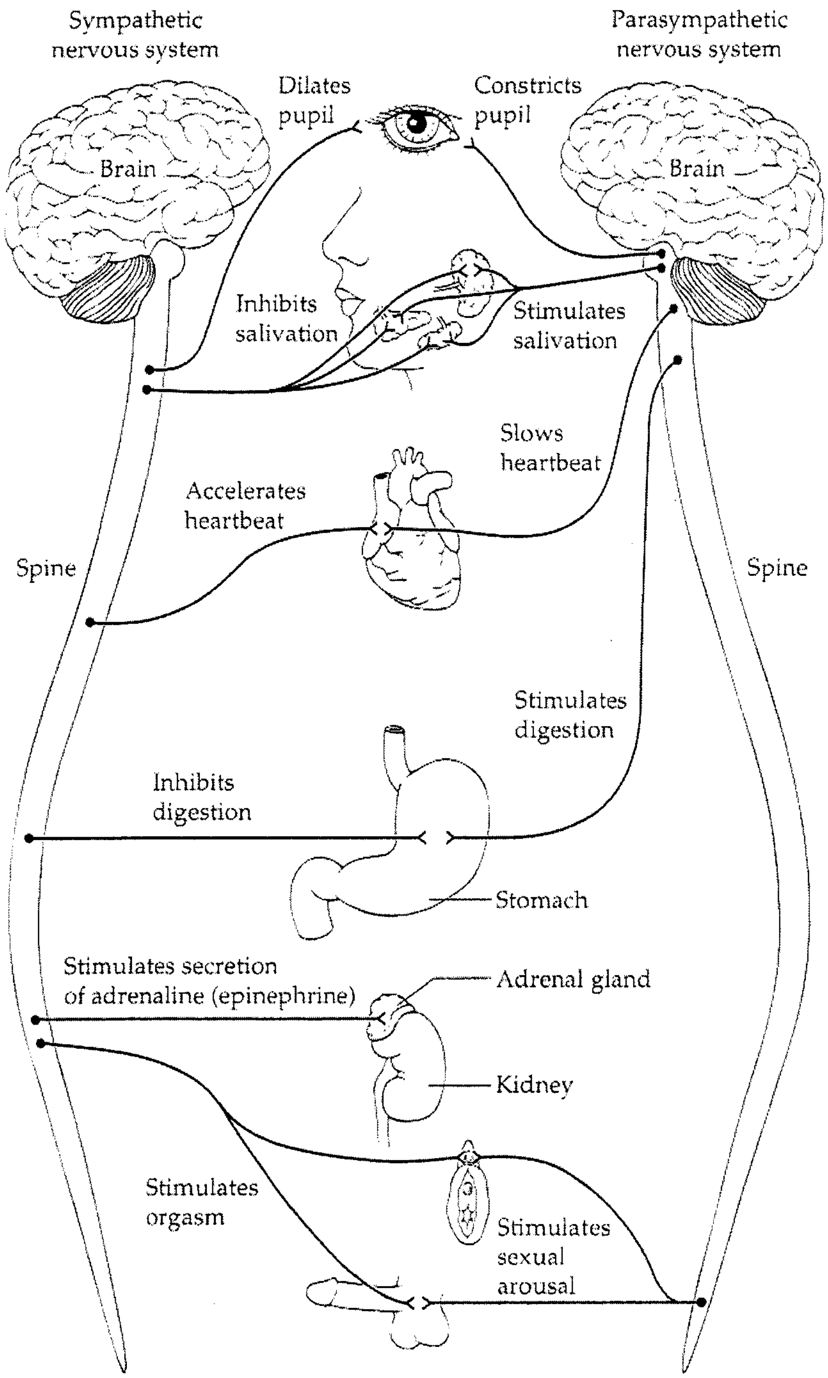
Source: Cohen et al. 1995.

Figure 2.2 The HPA axis, with emphasis on the origin of main chemical signals



Source: Sapolsky 2004.

Figure 2.3 Some functions of the sympathetic and parasympathetic nervous systems



Source: Sapolsky 2004.

Chapter 3

The theory of allostatic load and its measurement

Summary: The relatively new theory of allostatic load (AL) holds that repeated exposures to stress can exact a toll on the body and build up in AL. Load supposedly increases in an incremental and cumulative fashion over the life course, and can eventually harm different physiological systems. Initial operationalizations of AL using a panel of 10 biomarkers have been predictive of negative health outcomes. Researchers are continuing to improve the measurement and predictive power of AL by testing different scoring techniques and considering more biomarkers that could contribute to one's load. Less attention has been devoted to understanding the neuroendocrine components of AL and trying to determine whether AL truly represents a stressful life history.

3.1 The theory of allostatic load

Allostasis, originally proposed by Sterling and Eyer (1988), is the concept that the body must constantly adapt itself to changing environmental demands in order to achieve *homeostasis* (Timiras 2003). Homeostasis is an "ideal steady-state" that is never truly achieved. That is, the body continuously responds to both internal and external challenges in an attempt to reach equilibrium. The theory of allostatic load (AL) emphasizes the optimal *operating ranges* of physiological systems, replacing the homeostatic emphasis on optimal *set points* (Seeman et al. 1997).

In reacting to challenge, the allostatic systems initiate an intricate chemical response that eventually shuts off when the threat has passed. The response is initiated mainly through the autonomic nervous system and the hypothalamic-pituitary-adrenal (HPA) axis, and to a lesser extent the cardiovascular, metabolic, and immune systems are also involved (McEwen 1998). While the activation of these systems can have beneficial short-term effects, it can also take its toll on the body. According to the theory, AL develops from the repeated costs of dealing with stress. Whether AL accrues depends on the nature of the stressors and the body's response to them. For instance, in one case, AL can develop when the body responds normally to stressors, but those stressors occur repeatedly and frequently. In another case, AL can develop when the body's response to a stressor is inappropriate, such as when the stress response does not turn off, although the threat has passed (McEwen 1998).

Stressors that can cause AL are defined broadly and include those of an acute and chronic nature, as well as those physical (e.g. infections and extremes of temperature) and psychological (e.g. feelings of loss and isolation). Importantly, AL represents the *cumulative* wear and tear on the body caused by stress (McEwen 1998). The cumulative nature of AL is highlighted in Figure 3.1 (created by this author) where the experience of some temporary and permanent stressor corresponds to different ALs. In the left panel, some constant and low level stress until time 4 contributes to AL. From time 4 to 6 the temporary stressor leads to an increased slope, but when the stressor has passed, the slope returns to its original intensity. In the case of a permanent stressor (right panel), the slope for the increase of AL is permanently changed, so that by time 10 the AL is greater than that for the previous case.

It is hypothesized that the metabolic, cardiovascular, neuroendocrine and other physiological systems deteriorate with the buildup of AL. A consequence of increasing AL is supposedly a slow, incremental dysregulation of these systems, which eventually manifests itself as operation outside of normal ranges (Seeman et al. 1997). AL theory adopts a life course approach, assuming that AL accumulates from the very earliest ages[7]. AL is considered to be a pre-disease indicator, and as such it is entirely possible that someone could present with no morbidities and yet have high AL (McEwen 1998). AL may also be thought of as a measure of "physiological age," in comparison to "chronological age" (Seeman et al. 1997).

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[7] While the AL literature repeatedly mentions having adopted a life course approach, I have not been able to find a definitive statement for exactly when AL begins to accumulate. It could be from birth, sometime thereafter, or perhaps even prenatally. The exact timing of a stressor during the life course and its affect on AL also seems like a largely ignored (and certainly complicated) topic. It could very well be the case that stress is more deleterious during the "critical periods" where there is the fastest growth and development (the youngest ages) and fastest deterioration (the oldest ages).

3.2 Operationalization of allostatic load

At least two key issues need to be addressed in the search for improved operationalization of AL. The first regards the construct's utility in prediction. For instance, high AL is predictive of which particular morbidities? Would differential weighting of the biomarkers in an AL construct improve its predictive power? What summary, statistical techniques are most efficacious in predicting poor health? The second issue regards whether the AL construct actually represents what it theoretically purports to represent. For example, a construct of AL at baseline may very well be predictive of downstream health outcomes, but not truly represent a stressful life history. Regarding these two sets of issues, the first has by far been the more intensively investigated.

A key feature of the AL construct is inclusion of multiple biomarkers in a single index. To date, the most commonly used index stems from the MacArthur studies which used ten different bioindicators. To create the index they employed the "elevated risk zone" approach, whereby participants were given one point towards their score on each biomarker for which they were at high risk. High risk was determined as being above or below the top or bottom quartile in the study population for both men and women combined. Percentile distribution cut-offs were used because for many of the biomarkers it is simply unknown what values place a person at risk. For the biomarkers where there is a more established clinical literature relating to elevated levels (e.g. blood pressure and cholesterol), percentile distributions were still used because of the idea that AL captures early system dysregulation. Traditional danger zones for blood pressure and cholesterol, since they attempt to gauge more immediate risk, are too high for a measure of AL. The original MacArthur studies biomarkers and their respective cut points are presented in Table 3.1.

The AL construct as operationalized in the MacArthur studies has predicted poorer health. High baseline levels were associated years later with worse physical and cognitive functioning, as well as incidence of cardiovascular disease (Seeman et al. 1997). The essential results were robust to alternative cut points and an alternative method of AL scoring using averaged z-scores. Additionally, the index has been shown to be more predictive than individual biomarkers alone, supporting the idea that risk depends on the function of a number of different physiological systems (Seeman et al. 1997). More recent analysis of the MacArthur study cohort has revealed that high baseline AL is also predictive of mortality (Seeman et al. 2001). The predictive power of the AL construct appears to stem both from biomarkers like cholesterol and blood pressure, that are indicative of the metabolic syndrome, and biomarkers like cortisol and epinephrine, that are indicative of neuroendocrine function.

As alluded to earlier, there are a number of important features regarding the original operationalization of AL. First, the index weights the biomarkers equally. It may turn out to be the case that differential weighting is more ideal and/or that some biomarkers should be entirely dropped from the construct. Second, the original cut points were based on a non-national study population of well-functioning US elderly and one that combined data for men and women. Whether it makes more sense for men and women to have separate AL scores is still unclear and researchers are still investigating what more precise values represent high risk. Third, certain biomarkers that are considered by some to be important indicators of AL were not collected and hence not included in the original index. Biomarkers that could reasonably be collected in population surveys and that would lead to an expanded AL index are shown in Table 3.2. As presented in the table, measures of inflammation and coagulation were among the markers not included in the original MacArthur study operationalization. Fourth, many have criticized the cut point method of scoring as crude.

Researchers are aware of the shortfalls of the original AL measure and are continuing to refine it and develop new approaches. For instance, Seplaki et al. (2004) have attempted a refinement by using the elevated risk zone method of scoring, but considering both high and low biomarker values (a two-tailed versus one-tailed approach) as representing risk. Among the new approaches are those by Karlamangla et al. (2002) who have used canonical correlation analysis, a technique which uncovers latent relationships between two sets of variables (which in their case were biomarkers and functional outcome scores). Also, Hale (2004) has used "recursive partitioning trees" to try and establish separate risk profiles for men and women. In addition to these attempts at methodological advancements, at least one newer survey has collected more biomarkers than the original MacArthur ten. The Social Environment and Biomarkers of Aging Study (SEBAS) has a panel of 16 markers that includes dopamine, IL-6, and IGF-1 (Weinstein and Goldman 2003).

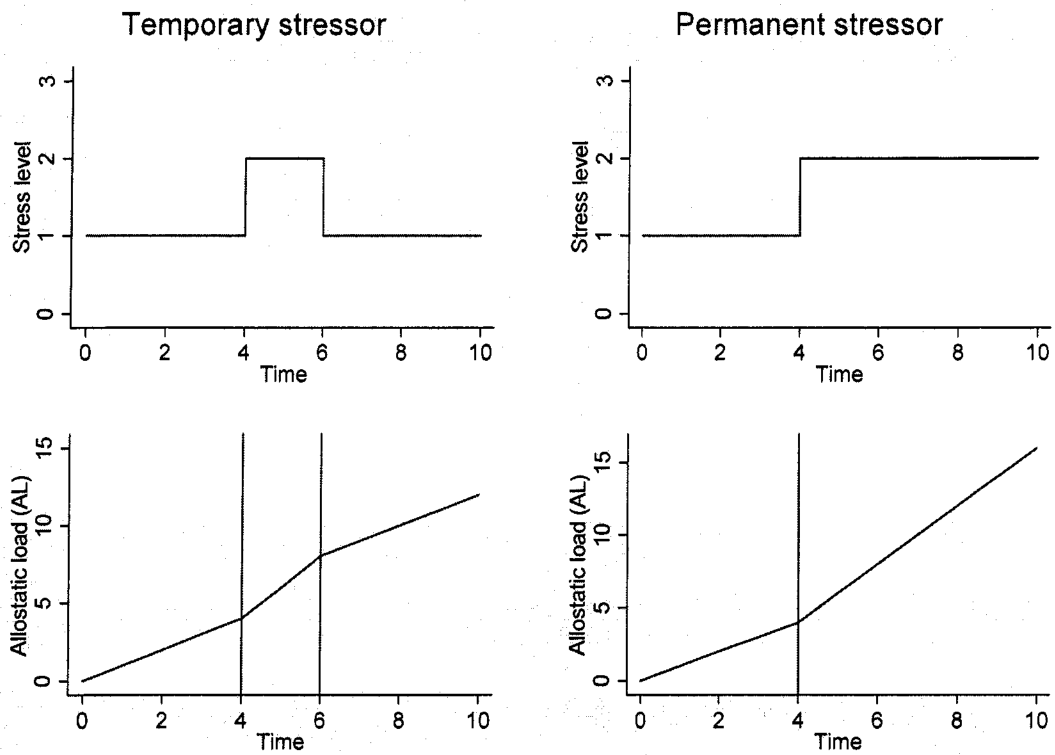
Any future operationalization of AL would surely benefit from a deeper understanding of how the various biomarkers relate to one another both within and across their physiological classes. In many ways the physiological diversity captured by the index is its strength. At the same time, however, the interpretation of AL is difficult because the entire construction is an admixture of markers whose relationship to stress can be quite different from one another. While a thorough discussion of all the biomarkers is beyond the scope of this chapter, it is useful to consider some aspects of the temporal nature of the body's stress response.

Stress begins in the brain, and a possible marker of this earliest process would be an MRI scan. In what might be considered a subsequent and secondary response, the initial brain activity sets off a neuroendocrine reaction, noticeable within seconds to minutes in biomarkers like epinephrine and cortisol. Metabolic, cardiovascular, and immune responses critical for adaptation are triggered by the neuroendocrine system reaction. A typical cardiovascular stress response includes increased heart rate and blood pressure. With stress, target end organs can eventually become impaired, with the impairment manifest in changes in *resting* levels of markers like blood pressure and cholesterol. The deterioration of organs can then lead to various functional declines. In the language of the AL literature, chemical messengers that are released during allostasis are considered "primary mediators," and so far include cortisol, DHEAS, epinephrine, and norepinephrine. "Secondary outcomes" are the markers like blood pressure and cholesterol, and "tertiary outcomes" are diseases or disorders like cancer or heart disease (McEwen and Seeman 1999).

It is important to emphasize that the neuroendocrine and blood pressure markers change under stressful conditions, and basal levels are thought to change over time. With respect to these markers, then, particular care must be made to evaluate the extent to which survey values are due to current conditions, versus accumulated changes in baseline levels. Even at rest (in contrast to an experiment with deliberate challenge) current stress can influence the measures. A well-known example of this phenomenon is "lab coat hypertension," where a patient has higher blood pressure because of the doctor's visit. It is also worth noting that there is quite a range of time over which the AL markers all grouped within the "secondary outcomes" category might reveal an impact of an earlier stressor. For instance, within weeks of a stressful period, basal systolic and diastolic blood pressure levels might change. Changes in cholesterol level, however, might be detectable only after a number of months, and change in waist-to-hip ratio only after some years. Little attention has been given in social science work to these timing differentials, although the discrepancies may be important. For example, it would make no sense to include waist-to-hip ratio as part of an AL construct if the aim of a study is to gauge AL changes to stress occurring within the past year.

As discussed above, much is known about the neuroendocrine system in initiating the stress response. We understand far less, though, about the meaning of neuroendocrine basal measurements. For instance, the length of time that might need to elapse after an initial stress before resting levels of neuroendocrine markers change does not seem known. This gap in our knowledge is obviously important since AL constructs measure the neuroendocrine bioindicators at rest. What is more, as reviewed in the chapter on stress and the neuroendocrine biomarkers, for cortisol and epinephrine it is even unclear how basal levels change over age. Since increasing age yields more exposure to stressful insults whose costs can only accumulate, that biomarker levels become dysregulated over age is a necessary but not sufficient condition for AL theory to hold. For norepinephrine and DHEA/DHEAS, where levels do change over age, research would need to show that stress accelerates the changes.

Figure 3.1 Temporary and permanent stressors and their corresponding allostatic loads over time



Source: Created by this author.

Table 3.1 Final paramaterization of allostatic load in the MacArthur studies

Systolic blood pressure	≥	148 mmHg
Diastolic blood pressure	≥	83 mmHg
Waist-to-hip ratio	≥	0.94
Ratio total cholesterol/HDL	≥	5.9
Glycosylated hemoglobin	≥	7.1%
Urinary cortisol 9	≥	25.7 mg/g creatinine
Urinary norepinephrine	≥	48 mg/g creatinine
Urinary epinephrine	≥	5 mg/g creatinine
HDL cholesterol	≤	37 mg/dL
DHEAS	≤	350 ng/mL

Source: Seeman et al. 1997.

Table 3.2 Recommended biomarkers across different physiological systems to test the theory of allostatic load

Cardiovascular system	Antioxidant profiles
Systolic blood pressure**	
Diastolic blood pressure**	
Metabolic system	Inflamation and coagulation factors
BMI/waist-to-hip ratio**	IL-6, CRP, low cholesterol
Total cholesterol**	Albumin
HDL/LDL cholesterol**	Fibrinogen
Homocysteine	
Glycosylated hemoglobin**	
Hypothalmic pituitary adrenal axis	Sympathetic nervous system
Cortisol**	Norepinephrine**
DHEAS**	Epinephrine**
Renal function	Lung function
Creatinine clearance	Peak flow rate

Note: ** First operational measures of allostatic load in MacArthur studies of successful aging.
Source: Crimmins and Seeman 2001.

Chapter 4

The social milieu's influence on health

Summary: While more research needs to clarify and strengthen the findings, high quality studies over the last two decades have suggested the beneficial and powerful effect of social relations on health. The social world can get "under the skin" to affect health through numerous routes, including those beginning with the most macro of social-structural forces like political unrest and social cohesion. In regard to the benefit of social networks on health, most studied has been networks' potential to provide support (i.e. emotional, instrumental, and appraisal) in times of need. Also, at other periods and in less direct ways, social connections can be salutary, such as through "weak ties" that can bridge to information about employment opportunities, or through group participation that can satisfy psychological needs to be part of a larger community. Perhaps the most direct evidence of the power of social factors to affect biological outcomes come from laboratory studies, where careful manipulations of the social environment have reliably impacted major physiological systems related to health. Lastly, sex and age differences exist in social network structure and in other areas.

4.1 Introduction

Social scientists since at least Durkheim (1897) have tried to connect greater social integration to better health. Trying to establish a causal connection between health and something as multifaceted and nuanced as the social world is clearly difficult. Reverse causality (e.g. poor health leading to less interaction) and the possibility that a third factor (e.g. optimism and/or a buoyant personality) influences both health and one's social network are just two examples of difficulties that must be adequately addressed (Cohen et al. 2003; House et al. 1998). The impact of social relations on health also likely varies by sex, stage of life, race, and socioeconomic condition (Taylor et al. 1997; Kawachi and Berkman 2001). As well, any salubrious effects of social integration may not be linear, so that the avoidance of major deficiencies in a social network could be more important than an increase in connectedness for someone who is already moderately or well integrated (House 2001).

High quality studies addressing these and other complexities have been carried out in the last few decades. The strength of these investigations lies in the diversity of national and international settings in which they have been conducted, their longitudinal designs and long periods of follow-up, variety in their measures of both social connection and health, and controls for relevant variables (Berkman and Glass 2000; Thoits 1995; Taylor et al. 1997; Knox and Uvnas-Moberg 1998; House et al. 1988). In an influential review of such studies, House and others (1998) claimed that social isolation is a risk factor on par with that of health behaviors like smoking. According to other reviewers of the literature, social connection is consistently and strongly related to health, and especially mortality (Krause 2001; Berkman and Glass 2000; Thoits 1995; Taylor et al. 1997; Knox and Uvnas-Moberg 1998). Despite these convincing survey findings, however, randomized controlled studies where the intervention is some form of social support have been somewhat disappointing (Krause 2001; Cacioppo and Hawkley 2003).

Although studies have attested to the overall salutary nature of social networks, interpersonal relations can obviously also be a source of problems. The obligation of being a caregiver, for instance, can be quite stressful and care recipients may not desire or benefit from too much assistance (Epel et al. 2004; Krause 2001). It has also been found that while cohesiveness may protect against depression, repressive social regulation may lead to anxiety disorders (Kawachi and Berkman 2001). As well, negative aspects of social contacts such as criticism, rejection, and lack of reciprocity can, especially if they are with close family members, last for many years (Krause 2001). While usually not a reason to avoid others, casual and more intimate contact can also increase the chances of transmitting various infectious diseases (Berkman and Glass 2000).

4.2 Social factors influencing health

4.2.1 Macro social and structural conditions

Social environments affect health in complex and myriad ways, and disentangling the various mechanisms by which this happens is challenging because of their often overlapping, reciprocal, and subtle nature. Figure 4.1 summarizes a vast landscape of potentially relevant social factors, presenting them in a causal chain from quite upstream to downstream influences. The macro, structural conditions societies impose are the most upstream set of forces, influencing an individual's health in more distal and hard to pinpoint, but nevertheless important, ways. For example, Émile Durkheim explored how societal patterns could affect the decision to commit – what some might consider the ultimate individual act – suicide. Durkheim described different types of suicides related to societal conditions, including an "anomic" type. This particular form, he claimed, stemmed from individuals' sense of normlessness, or anomie, during periods of rapid social change. According to Durkheim, in turbulent economic or political times, the institutions, values, and beliefs that generally could provide people with a set of expectations, sense of place, and meaning, could break down and contribute to increased suicide risk (Durkheim 1897; Berkman and Glass 2000). The former Soviet Union and countries of Eastern Europe might be good examples of nations currently undergoing drastic enough disruptions to provide a context for anomic suicide (Berkman and Glass 2000).

More recent work involving "social capital" follows in the spirit of Durkheim's work. Social capital might be defined as "those features of social structures ... which act as resources for individuals and facilitate collective action" (Kawachi and Berkman 2000). Important to this concept is the idea that communities and societies are not merely the sum of individuals. That is, there are collective characteristics of communities that have power "sui generis," in and of themselves. In theory, since social capital is not lodged within an individual, a community's level of social capital would affect someone who had either a rich or impoverished social network. Social capital has been measured in a variety of ways, including levels of interpersonal trust, perceived reciprocity, and density of membership in civic associations (Kawachi and Berkman 2000; Taylor et al. 1997).

A community high in social capital might improve the health of its members through numerous routes. One, for instance, is that a cohesive neighborhood could be more willing to exert social control over deviant behaviors such as crime and underage smoking and drinking. A second example is that such a neighborhood might also be better able to unite in securing valuable community services, amongst them health services. Finally, it may also be the case that even at the state level, states with more social capital are more likely to pass measures that promote the security of its members (Kawachi and Berkman 2000; Taylor et al. 1997).

4.2.2 Social networks

As shown in Figure 4.1, social networks can be considered mezzo level factors in a causal chain affecting health, downstream from some of the larger social and structural conditions previously discussed, and influencing more micro psychological mechanisms. Social networks can be categorized in a number of ways. In regard to network structure, its size and density (the extent to which members are connected to each other) are important characteristics. So too are its homogeneity and boundedness (the degree to which the networks are defined on the basis of traditional group structures such as work and neighborhood). Key elements of network ties include multiplexity (the number of types of transactions or support flowing through a set of ties) and frequency of face-to-face and non-visual contact. The duration and intimacy of interpersonal relationships are two other important network features (Krause 2001; Berkman and Glass 2000; Thoits 1995).

4.2.3 Psychosocial mechanisms and pathways

One of the potentially key ways in which social networks impact health is through social support, a social "fund" that can be drawn upon in times of stress (Thoits 1995). Main types of social support include emotional, instrumental, and appraisal. The sympathy, caring, and love provided by another are emotional forms of support. Instrumental support includes various types of tangible aid such as help with finances, buying and cooking food, and transportation needs. Lastly, feedback on problems and assistance with decision-making fit under the rubric of appraisal support (Thoits 1995; Berkman and Glass 2000).

In trying to determine the availability of support, researchers have often investigated three measures. The first has been one of embeddedness, the size, density, and other social network characteristics as described in the previous section. Received support (help actually provided by network members) and perceived support (subjective evaluation of supportive exchanges) are the remaining two. It turns out that a straightforward and powerful indicator of social support is the presence of an intimate other (an embeddedness measure), usually a spouse or partner (Thoits 1995; Kiecolt-Glaser and Newton 2001). The most powerful of the three measures, however, is perceived support, which is consistently and strongly linked to health[8]. Respondents'

[8] Interestingly, self-rated health, another measure with subjective evaluation, is also quite predictive of

evaluations of their available support likely come from many sources. Probably, to some degree, respondents consider help received in the past as well as indications by the social network that, should the need arise, assistance will be provided. Subjects may also evaluate their level of anticipated support through observing exchanges by others within their social networks (Krause 2001).

In addition to social support that often is called upon in times of need, interpersonal relations may influence health during other periods and less directly. Social networks, for instance, might help to provide access to resources and material goods (see Figure 4.1). Marriage, as just one example, could allow one partner to take advantage of the better health insurance plan of the other. Combining incomes and sharing goods might also enable the pair to live in a better neighborhood (e.g. safer, greater opportunities for recreation, and closer to desirable services) than they otherwise could (Waite 1995). Classic research by Granovetter (1973) indicates that even "weak ties" that lack intimacy can offer opportunities for mobility. Such ties might be established through participation in organized religion, sports, or other group activities. Contacts generated in these settings, that are often bridges to other networks, might facilitate information exchange about all sorts of matters, including job openings or other professional opportunities.

The mere act of being involved socially could also improve feelings of well-being. Socializing can simply be enjoyable and it can also satisfy deeper psychological needs. Interacting with others, participating in groups, and fulfilling social roles can provide a sense of belonging and community, provide enhanced feelings of self-worth

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future health (Kiecolt-Glaser and Newton 2001).

and self-control, and fill life with a sense of coherence and meaning. Feelings of connection and obligation to others might additionally bring about changes in personal behavior. One could imagine a case, for instance, where a father decides to circumscribe riskier habits after the birth of his first child. Along with social engagement, norms surrounding health behaviors likely exert a measurable, if indirect and difficult to quantify, effect. Wider attitudes about smoking and drinking, gleaned from media and other sources, for example, impact the calculus for starting and continuing those behaviors (Berkman and Glass 2000).

Beyond the ability to affect behavioral and psychological pathways that eventually impact health, social environments are capable of more direct influence on major physiologic systems. Increasing evidence for the capacity of the social to "get under the skin" to cause health outcomes comes from experimental animal and human studies (Taylor et al. 1997; Knox and Uvnas-Moberg 1998; Berkman and Glass 2000). In a comprehensive review of 81 laboratory studies of humans that examined the role of the social milieu on major physiologic systems, Uchino and others (1996) concluded that social support has beneficial effects on aspects of the cardiovascular, endocrine, and immune systems. Most of this research has been conducted on the cardiovascular system and, by and large, social support has been found to reduce cardiovascular reactivity to acute psycho-social stressors (Uchino et al. 1996). Such reduced reactivity, when sustained over long periods, likely decreases the odds of acquiring cardiovascular disease (Knox and Uvnas-Moberg 1998).

The following highlights a representative experiment from the social relation and cardiovascular reactivity literature. Kamarck and others (1990) examined change in cardiovascular state in response to various stress tests, including performance on a mental arithmetic challenge. About half of the female participants were instructed to bring a close, same-sex friend who could provide emotional support during the challenges, while the other subjects came alone and received no social support. The mental arithmetic stress test involved serial subtraction by 17's aloud in front of an evaluator. Respondents performed this challenge in a stressful environment, having been told they would be judged on speed and accuracy, having been given an example of a "model" performance which was much faster than they could reasonably emulate, and having been urged at some point in the challenge to go faster and with improved accuracy. For those with social support, the friend was physically close and touching her on the wrist during the stress task, and it was explained to both that the friend was there to be "a support partner" and to "silently cheer on" the subject. As can be seen in Figure 4.2, as hypothesized, the social support group experienced less heart rate and systolic blood pressure change. The difference in diastolic blood pressure change is corroborative with these outcomes, although not statistically significant.

4.2.4 Sex and age differences

There appears to be some differences between men and women in regard to their social networks and how they give and receive support. It seems that women's networks are less "extensive" but more "intensive" than those for men. That is, women have smaller networks than men but maintain more emotionally intimate relationships. Women tend to provide more frequent and effective social support to others, and in periods of personal stress mobilize more aid. Men are more likely to frequently respond to personal stress by accepting the problem, with problem-solving efforts, or not thinking about the situation (Kiecolt-Glaser and Newton 2001; Thoits 1995).

A common finding in the literature is that women express more psychological distress and experience more depression than men (Kiecolt-Glaser and Newton 2001; Thoits 1995). This disparity may exist in part because women's proclivity for intimate relations could make them more likely to internalize the problems of those with whom they are close (Kawachi and Berkman 2001). Men are also far more likely to drink alcohol, which may temporarily mitigate stressful feelings (Thoits 1995). Another consistent finding in the literature is that men are more physically and mentally hurt by widowhood. It has been suggested that this is the case because men's spouses are often their primary and sole confidant, and sole source of emotional support (Kiecolt-Glaser and Newton 2001; Thoits 1995). While the loss of a spouse is one of the most severe stressors for either sex, women seem less affected because of their greater number of intimate ties. As mentioned before, social support might be thought of as a social fund. To explain the findings that women experience greater everyday distress, but men experience greater distress with widowhood, it seems that the social fund analogy is useful. Greater investment in periods of non-need could result in more strain, but produce a larger return when in need.

In regard to aging, social engagement tends to decline, although the trend exhibits substantial heterogeneity. The decrease partly stems from deteriorating health and perhaps life cycle transitions like children leaving home and retirement (Bukov et al. 2002). The networks of older persons often focus more on core, rather than peripheral, ties and more on kinship, rather than friendship, ones (Krause 2001). To the extent that older persons are more susceptible to a variety of health problems, they may differentially bear the costs of social impoverishment.

Figure 4.1 Upstream and downstream social factors that could influence

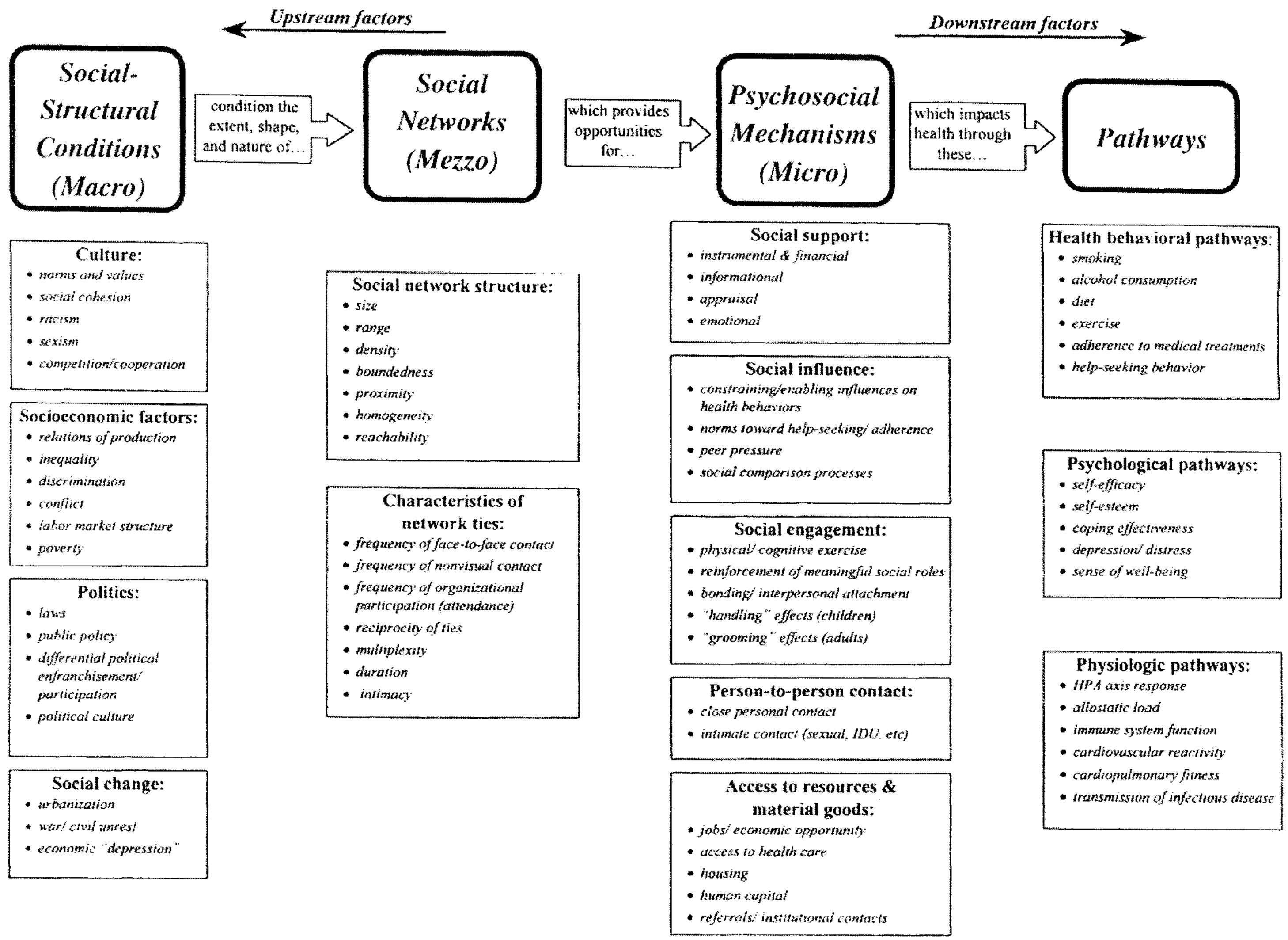
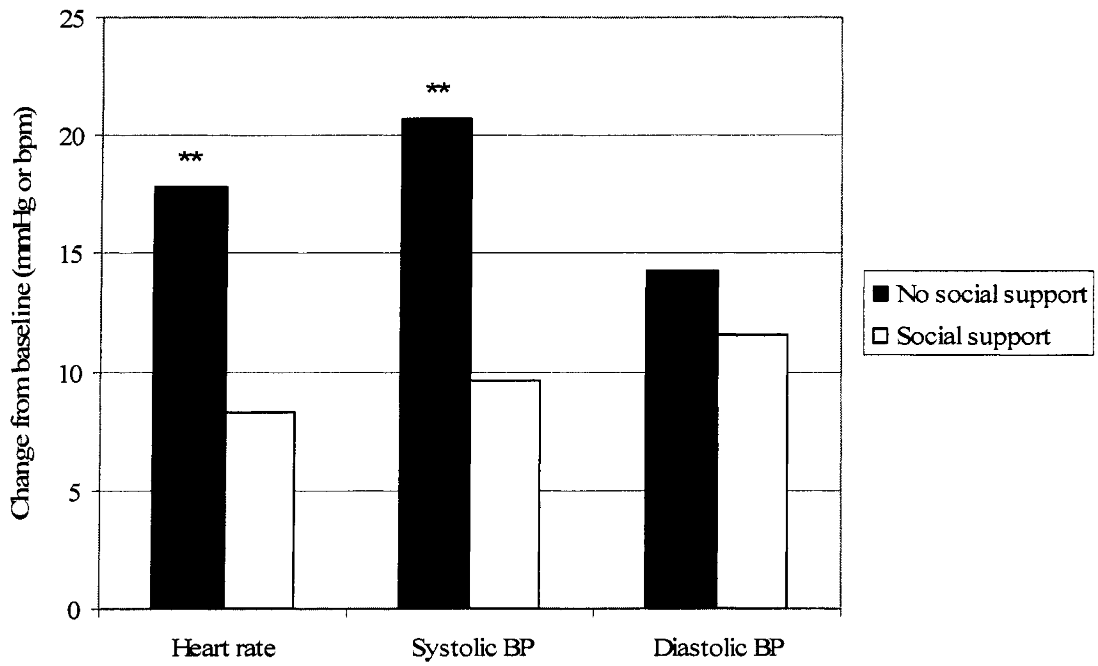


Figure 4.2 Change in cardiovascular activity (from baseline) in response to mental arithmetic stress test, with social support and without



Note: *, **, and *** represent statistical significance at the .05, .01, and .001 levels, respectively.
Source: Kamarck et al. 1990.

Chapter 5

Taiwanese context

Summary: Taiwanese culture has been heavily influenced by Confucianist traditions, which emphasize the importance of interconnectedness, family, and patriarchy. Taiwanese elderly still prefer living with married sons, who, along with their wives, are expected to care for the aging parents. Women have historically been disadvantaged in Taiwan and this reality is revealed in, among other indicators, older women's lower levels of education and literacy. Of the three main ethnic groups on the island, the Mainlanders have had the highest socioeconomic standing and have held the most political power, although ethnic differences are diminishing. Since World War II, Taiwan has experienced dramatic change in areas such as fertility, urban residence, age at first marriage, and economic development. Finally, older age and high levels of education are valued attributes in Chinese culture.

Taiwan, named by early Portuguese sailors as "Ilha Formosa," or beautiful island, was long known as "but a rude outpost in a great [Chinese] empire" (Greenhalgh 1984). After China's defeat in the Sino-Japanese War, this frontier island was ceded to Japan in 1895 and ruled until 1945. As a colonial power, Japan limited the freedom and educational and political opportunities of the Taiwanese. Only Japanese could become bureaucrats or members of the police force, Japanese was decreed the official language, and Taiwanese movement to and from the island was restricted (Grajdanzev 1942). Despite this discrimination, Japan oversaw much in the way of infrastructural improvements, including creation of communication, transportation, and educational systems, and the funding of public health projects (Weiming 1996; Grajdanzev 1942). Perhaps also to Taiwan's benefit, as a colony it was cut off from much of tumult that characterized mainland China in the first half of the 20th century, including collapse of the Empire and a near constant civil war between the Nationalist government and Communist-led armies (Silverman et al. 2000; Gold 1996).

China regained control of Taiwan with Japan's World War II defeat. Shortly thereafter, conflict on the Mainland precipitated an emigration of approximately one million[9] military and civilian supporters of the Nationalist (Koumintang) army to the island. This influx represented practically 15% of Taiwan's population at the time (Mason and Lee 2004). The new arrivals, who were mainly younger and male, assumed positions of power vacated by the Japanese (Weiming 1996; Mason and Lee 2004). To this day, "Mainlanders" (these Chinese immigrants and their descendents) are overrepresented in higher status professions, including "iron rice bowl" jobs in the public

[9] While one million migrants is an often cited figure, larger estimates include one and a half million

sector, and until very recently maintained political power (Greenhalgh 1984; Goldman et al. unpublished manuscript; Gold 1996). Mainlanders are also more likely to live in urban areas, have higher levels of education, and, since they tended to arrive without other kin, less likely to live in extended family arrangements and more likely to rely on formal sources of support (Beckett et al. 2002).

It is important, however, not to overstate the differences between the Mainlanders and other ethnic groups. Owing to intermarriage among older generations and an appreciation of a common heritage from the People's Republic of China, the salience of ethnicity has been much reduced (Greenhalgh 1984). Moreover, since Mainlanders form simple, often two-generation families that draw income from few sources, their families are likely not to be among the wealthiest (Greenhalgh 1984). The other main ethnic group is the Taiwanese, having arrived in Taiwan nearly 150 years before the Mainlanders. The Taiwanese are comprised of both the Hakka and Fukienese (who originated from the Kwantung and Fukien provinces in China, respectively), with little socioeconomic differences now existing between them (Liang et al. 1999; Goldman et al. unpublished manuscript). The third and last ethnic group, comprising only a small fraction of the total population, is the Aborigines. Apparently, so sinicized[10] are the Aborigines that "their cultural distinctiveness is displayed only as an occasional tourist attraction" (Weiming 1996).

Since World War II, Taiwan has undergone rapid economic development. Mean per capita income, for example, has increased by a factor of more than seven (in constant dollars) from 1960 (Beckett et al. 2002). Now considered a newly industrialized society,

(Greenhalgh 1984) and two million (Central Intelligence Agency 2005).

Taiwan has a standard of living in Asia behind that of only Japan, Hong Kong, and Singapore (Central Intelligence Agency 2005; Mason and Lee 2004). Interestingly, Taiwan's sharp growth generated widespread upward social mobility without being accompanied by much increase in inequality, although "red-eye disease" stemming from jealousy of the *nouveau riches* is apparently a budding phenomenon (Gold 1996; Weiming 1996). Other changes have been so dramatic that many of Taiwan's current demographic indicators resemble those of Western nations. For instance, since the late 1950s, fertility has dropped steeply and is now well below replacement level (Population Reference Bureau 2004; Feeney 1994). Also, life expectancy at birth in 2004 for both sexes combined was 76, only one year less than for the United States (Population Reference Bureau 2004). Over the last 50 years or so in Taiwan there also has been a marked increase in age at first marriage, urbanization, levels of education (especially among women), and employment outside of the home and farm (Hermalin and Yang 2004). In a demographic oddity, because most of the immigrating Mainlanders were men, elderly men outnumber their female counterparts despite a female advantage in life expectancy.

Chinese culture has been heavily influenced by Buddhism, Taoism, and especially Confucianism. Training of government officials was based on Confucian texts from 130 B.C. (with some interruption) until the Empire collapsed in 1905, and during the Han dynasty Confucianism essentially operated as the state religion (Smith 1991). Among other teachings of these philosophies/religions is the importance of the familial institution. One researcher on Taiwan in the 1970s went so far as to say that, "Family

[10] Sinicized means modified by Chinese influence.

happiness is by far the most important value in Taiwan. Everything else appears of negligible importance" (Greenhalgh 1984).

Filial piety stresses that children should respect their parents and be loyal to the family, and, indeed, perhaps the greatest shame children can bring upon themselves is abandonment of their parents (Chen 2001; Lee et al. 1994). Parents, for their part, earn their children's respect by having given them the gift of life, support before marriage, and help in finding a spouse (Greenhalgh 1985). Moreover, parents are expected to love their children, provide a model of upright behavior, and work for the good of the household (Chen 2001). Taiwanese culture has placed importance on continuity of the family line through sons, whose filial loyalty was to extend to all preceding generations, as ritualized through ancestor worship (Lee et al. 1994).

Despite changing norms, the preferred living arrangement for Taiwanese parents is still with their children and grandchildren, where "three generations live under the same roof" (Lin et al. 2003). Coresidence with married sons is considered ideal, and it is not uncommon for parents with more than one son to rotate among their sons' residences (Lin et al. 2003). Only about 2% of Taiwanese live in nursing homes and Taiwan's first certified nursing home was established only in 1995 (Wang et al. 2001; Kao and Stuifbergen 1999). A national health insurance system, which includes coverage for the elderly, was also recently established (Lotus et al. 2004). Although there are increasingly state-funded institutions to provide support for the aged, it is still very much expected that children personally care for their parents and provide financial assistance. Sons, and especially the oldest ones, provide most of the various types of support, but daughters will do so if sons are not able to. A new wife will commonly move into the home of her husband and parents-in-law, with the expectation that she takes care of her husbands' parents when they are in need. After her marriage, the daughter-in-law's obligation to her biological parents typically comes to an end, even if she gave substantial support before her union (Lin et al. 2003). Since there has traditionally been few welfare benefits for older persons in Taiwan, researchers have interpreted parents' investment in their children with the expectation of aid later in life as an informal insurance policy (Lee et al. 1994).

China's traditional family system of some 2000 years has been known as quite patriarchal, having included such practices as female infanticide and footbinding (Greenhalgh 1985). While conditions today have shifted dramatically, elderly Taiwanese women alive today still were expected to be subordinate to men throughout their lives, first to men in their biological family, then to their husbands, and then to their sons if widowed (Goldman et al. unpublished manuscript). Among examples of women's inferior treatment, is that they did not receive a portion of the family property when split, and were essentially barred from owning any type of property at all. A strict division of labor demanded that women were responsible for reproductive activities within the household, and women who did work faced occupational segregation and limited access to more prestigious jobs. Relative to sons, daughters also suffered more parental control over job selection, choice of residence, and remittance of income (Greenhalgh 1985).

The primary responsibility of married women was to produce at least one son to continue the family line. If they were not able to do this, besides the practical problem of diminished support that would likely result, community members worried that these women might become "hungry ghosts" who preyed on the living and brought about misfortune of every sort (Greenhalgh 1985). Because it was expected that daughters' support of their parents ended with their marriage, it was commonly thought that daughters did not make good economic investments and, hence, were "goods on which one loses" or "water spilled on the ground" (Greenhalgh 1985). The prevalence of this thinking led parents to invest less in their daughters and as a result older Taiwanese women have lower levels of education and literacy. In one study of Taiwanese elderly, sons were twice as likely as daughters to be the most educated child in the family (Lin et al. 2003). Government statistics also report that elderly Taiwanese women are four times more likely than their male counterparts to be illiterate (Wang et al. 2001).

Notions of the self in relation to others are also influenced by Confucianism, Buddhism, and Taoism. These teachings emphasize the importance of lack of self-centeredness and the importance of connection to others, self-sacrifice for the group and collectivity, as well as social harmony (Chen 2001; Smith 1991). It has been hypothesized that this general sense of interdependence and collectivism mitigates the deleterious effects for the "socially impoverished," as based on Western measures (Seeman et al. 2004).

Another important feature of Taiwanese society is the role of age and generation. Growing old is considered "one of the five great blessings" of life, and respect and deference to the elderly is the norm (Silverman et al. 2000). Increasing age is associated with greater authority, decision-making power, and improved treatment by children and others (Beckett et al. 2002). Huston Smith (1991), when elaborating on this theme in his chapter on Confucianism, relates a story where an aged visitor to Japan is asked how “wise” he is. After the visitor appears befuddled, the Japanese questioner apologizes for his poor English and clarifies that he meant to ask how “old” he was.

Chinese culture has also placed great value on education. Historically, the scholar-bureaucrat topped the social hierarchy, with the soldier at the bottom, and perhaps outside of a few other examples according to Smith (1991), no civilization has so thoroughly tried to engender Plato’s ideal of the philosopher king. In modern-day Taiwan, educational attainment remains a critical component of social status and a vehicle for upward mobility (Weinstein et al. 2003).

Chapter 6

Data and methods

Summary: A general aim of this dissertation is to test whether a stressful life history is linked to higher neuroendocrine allostatic load (NAL). To accomplish this goal, data from the Social Environment and Biomarkers of Aging Study (SEBAS) is analyzed. The SEBAS is a nationally representative survey of Taiwan conducted in 2000 and includes a panel of biomarkers as well as social variables. The dependent variable in the analysis is four neuroendocrine biomarkers (cortisol, DHEAS, epinephrine, and norepinephrine) combined to form an index. Key independent variables include those assumed to be related to a stressful life history and respondents' subjective interpretations of events as stressful or not.

6.1 Data

6.1.1 Overview of the data set

I analyze the Social Environment and Biomarkers of Aging Study (SEBAS), a population survey conducted in Taiwan in 2000 (for a more detailed description of the study consult Weinstein and Goldman 2003). The survey is nationally representative of those 54 and older and includes the institutionalized population[11]. The SEBAS drew its sub-sample of respondents from a larger, ongoing longitudinal study called the Taiwan Survey of Health and Living Status. Among other things, the interview portion of the SEBAS included questions about cognitive functioning, psychological well-being, socioeconomic status, and life stressors. The in-home interviews averaged nearly an hour. With the respondents' additional consent, they were scheduled for lab work and a physical exam several weeks after the interview. Lab work included collection of blood and urine samples to produce a panel of physiological measurements, and the physical exam recorded information such as height and weight, blood pressure, and checked for a number of health problems.

Of those originally contacted for inclusion in the 2000 SEBAS, 92% gave interviews and 68% of these participants consented to the clinical examination, for a total of 1,023 respondents. Analysis reveals that partly because those most and least healthy declined to participate in the clinical exams, with controls for age estimates derived from

[11] While inclusion of the institutionalized population is an advantage, as Chapter 5 mentions, very few Taiwanese elderly reside outside of the community. The survey does exclude the aboriginal population, which is also a small portion of the total.

clinical information are unlikely to be seriously biased (Weinstein and Goldman 2003). In about 4% of all cases proxies helped answer some questions for the respondents. Most often a spouse was the proxy and the reason most frequently given for needing the proxy's assistance was hearing troubles. The survey over-sampled those 71 years and older and urban residents.

It is not possible to conduct a longitudinal analysis using biomarkers since earlier waves of the survey did not contain them. Nevertheless, the cross-sectional SEBAS has a number of strengths. First, it is unusual to have a nationally representative survey that includes biomarkers. Second, the response rate is relatively high, at over 90% for the interview portion. Third, the age range of 54–91 is wide relative to other studies of a similar design. Lastly, the SEBAS has collected neuroendocrine biomarkers, a rarity in population surveys and key to the testing of AL.

6.1.2 Dependent variable

6.1.2.1 The neuroendocrine biomarkers

In this dissertation I focus on a physiologically coherent class of markers representative of the neuroendocrine stress response[12]. The measure introduced here is called NAL, for neuroendocrine allostatic load[13]. Among NAL's greatest advantages is

[12] For an in-depth explanation of why these biomarkers have been selected for analysis please consult Chapters 2 and 3.

[13] In other work, these four neuroendocrine bioindicators have been referred to as non-syndrome X markers. For this analysis this seems like a poor name since it highlights what the markers are not, rather than what they are. In previous research neuroendocrine markers have also been referred to as primary mediators.

its interpretability that stems from grouping markers of a similar level of biological abstraction. NAL includes markers related to two systems: the hypothalamic-pituitary-adrenal (HPA) axis and the sympathetic nervous system (SNS). The HPA axis is key in regulating homeostatic processes in the body, and environmental stressors can lead it as well other regulatory systems to react. Cortisol and DHEAS are indicators of HPA axis activity. The body's "fight or flight" response is in part mobilized by the SNS, and its activity can be measured by norepinephrine and epinephrine levels.

6.1.2.2 Measurement of biomarkers

The survey tried to capture basal (resting or non-stressed) levels of the neuroendocrine biomarkers. This is in contrast, for example, to studies that deliberately stress respondents with an interest in the dynamics of immediate physiological reactions and subsequent return to baseline levels. Also, instead of taking numerous "point in time" measures throughout the day via blood or saliva, integrated measures for three of the four markers were collected in urine samples. That is, for cortisol, norepinephrine, and epinephrine, respondents were asked to void urine at 7pm, which was discarded, and to collect all subsequent samples until 7am the following day. Because dissimilar body size leads to differential concentration of the neuroendocrine markers in the urine, total urine was standardized using grams of creatinine. The subjects fasted from midnight onwards until a study affiliate came to their home to collect the urine sample, and during the same

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Besides being a vague term, primary mediators can also include a number of other bioindicators in addition to the neuroendocrine ones. As far as I know, then, I am the first to use the term neuroendocrine allostatic load, although I follow other researchers in analyzing them collectively.

day blood was also drawn. The amount of DHEAS in the body was determined through the blood sample.

Because biomarkers can vary over the day and be influenced by a host of factors, a few features of the study design likely limited intra-subject variation. The first was use of an integrated measure of certain biomarkers. Also, respondents collected urine samples at home, presumably a less stressful environment than a laboratory setting. As well, the influence of exercise on biomarker values was probably curtailed since from 7pm to 7am the respondents likely spent much of their time sleeping. Lastly, the prohibition on eating after midnight reduced to some extent the variance in meal number, meal composition, and meal times. Unlike some clinical studies, however, the SEBAS did not place any sort of restrictions on the following: the dinner time, type and quantity of the dinner meal, exercise, smoking tobacco, and chewing betel quid. Biomarkers were obtained for all subjects regardless of health condition or medication use.

6.1.3 Independent variables

A general aim of this dissertation is to test whether a stressful life history is linked to higher NAL. Demographic and life event variables are one set by which a stressful life history is operationalized. Variables such as marital status, participation in group activities, and coresidence with a married son tap social connectedness. With the exception of marital status, information for respondents earlier than 2000 is not available. Those never married, divorced, or separated have been excluded (n = 50, 5% of sample) from the analysis. Thus, the sample contains only those who voluntarily entered a union and whose union ended involuntarily through spousal death. The main purpose for the exclusion is to minimize the number who spent time in an undesirable marriage (such as divorcees) for whom the state was more likely to be stressful. The shock of losing a spouse is considered a severe stressor for both sexes, and for men it is considered that and a permanent stressor, much like a chronic illness[14].

The second set of variables of interest is psycho-social stressors. Only questions from the survey that were related to social stressors were included (e.g. stress questions concerning the respondent's own health were excluded). Respondents were asked whether certain situations made them *currently* feel stressed or anxious. If, and only if, a participant answered affirmatively to currently experiencing a stressor was he asked about its duration. One of the six stressors asked about "getting along with family members (e.g. not getting along well, tension, conflict)." Four others probed stress over "family members' or children's" health, financial situation, job, and marital situation. The last question was open ended and allowed the respondent to mention a stressor not already asked in the survey.

Other independent variables serve as controls. As Chapter 2 delineated, levels of the neuroendocrine biomarkers can be influenced by a wide variety of factors independent of stress. Control variables include those pertaining to diet, exercise, smoking, and medications.

[14] As elaborated in Chapter 4, a consistent finding in the literature is that men are more harmed by widowhood.

6.2 Methods

6.2.1 Biomarker index scoring

The most popular approach to operationalizing AL has been to create a score that gives one point for every biomarker for which the subject can be considered at higher risk (i.e. the elevated risk zone approach). The literature most often represents high risk by greater values for cortisol, epinephrine, and norepinephrine, and lower values for DHEAS; this convention will be followed here[15]. Since there is no agreed upon standard for what biomarker values represent different risk levels, it has been most common to define risk as above or below distribution percentiles (e.g. 10^{th}, 25^{th}, 75^{th}, 90^{th}). Since subjects can be assigned 1 point on four biomarkers if they have high risk values, NAL scores can range from 0–4.

The NAL score will be the dependent variable in various regressions (i.e. linear, ordered logit) and will be scored using different cut-off points (i.e. 10^{th}, 15^{th}, 25^{th}, 75^{th}, 85^{th}, 90^{th}). Additionally, a summed z-score is created for respondents, which is the total number of standard deviations from the mean in the direction of high risk for each biomarker. Unlike the cut-off approach, an index using the z-score method allows for unequal weighting of the biomarkers (e.g. a combined z-score of 3 could stem from being 2 SDs above the mean for cortisol, 1 SD above the mean for epinephrine, and the mean for the other two measures). The combined z-score is again the dependent variable in a linear regression and can range from 0 to no pre-determined upper limit.

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[15] For a number of other scoring schemes see Seplaki et al. (2004), Hale (2004), and Karlamangla et al.

6.2.2 The independent variables

The coding of the independent variables is straightforward. One item to note, though, is that the six social stressors asked in the survey are combined to form two indices. One of the indices represents the number of times any one of the stressors is reported. As mentioned before, if a respondent states that he is currently experiencing a stressor, he is then asked for its duration. The second index sums durations across stressors.

6.2.3 Software, weights, and sex stratification

All analysis was conducted using STATA version 8.0 (StataCorp 2003). The bivariate and multivariate analysis use weighted data[16]. Because of potentially important sex differences stemming from biological, psychological, and social factors that could in the end affect NAL levels, analysis of stress reporting, duration, and the multivariate analysis will be conducted separately by sex.

(2002).

[16] In STATA, setting the appropriate weight with respect to SEBAS's survey design involves specifying the survey weight, strata, and primary sampling unit (PSU). Analysis was then conducted with STATA's "svy" commands (i.e. svymean, svyregress, etc.).

Chapter 7

Descriptive statistics and preliminary analysis

Summary: In part because much is still unknown about neuroendocrine biomarkers, section one of this chapter explores how those markers based on data from the SEBAS relate to one another, and their trends over age. I find that the neuroendocrine bioindicators from this survey are weakly correlated across the SNS and HPA axis and, somewhat more strongly, within these physiologic systems; this result is in accord with the clinical literature and engenders confidence in using the neuroendocrine allostatic load (NAL) construct as a dependent variable in further analysis. In regards to biomarker trends over age based on SEBAS data, only DHEAS is consistent with the clinical and allostatic load (AL) literature. Section two of this chapter provides background analysis of the independent variables that will be used in the next chapter. It is notable that nearly a quarter of respondents report currently feeling stressed on at least one of four (out of six) questions that probe subjective, social stress. Far fewer respondents report stress over familial conflict or anything not already asked about in the survey. In regards to different living arrangements of the married and widowed, the widowed, on average, live with nearly as many persons in their household as their married counterparts. However, the widowed are far more likely to exhibit certain indicators of connection (i.e. living with married sons) and lack thereof (i.e. living alone), suggesting that the range of social connectedness of the widowed is wider.

7.1 Biomarkers and the dependent variable

7.1.1 Biomarker distributions

Table 7.1 presents some descriptive statistics for the biomarkers along with the cut-off points that will be used in this analysis. Of the 1,023 persons committing to lab examination, practically all provided adequate urine and blood samples. Only four missing data points for cortisol, epinephrine, and norepinephrine, and two missing data points for DHEAS, were due to problematic samples. As the following sentences explain, in only one case was a respondent who successfully completed the protocol, and for whom there is data, dropped from the analysis. Since cortisol distributions generally have long right tails, extreme values were not unexpected. Nevertheless, a data point that was 25 SDs away from the mean has been excluded since it is very likely an error. Two other cortisol values are trickier to interpret since they are extreme, but not obviously errors (see Figure 7.1 for a plot of cortisol data). These dubious points will be left in the analysis for the cut-point method of scoring, since a "high" or "very high" value both earn a point towards the NAL index. However, analysis will be conducted with and without them when the z-score method of scoring is used because it is sensitive to outliers.

Figure 7.2 shows histograms of the biomarkers. Of the four measures, norepinephrine is closest to obtaining the classic "bell curve" shape, while cortisol is the most right tailed. Epinephrine and DHEAS also have right tails, and the large number of null values for epinephrine is due to the coding of values that read below assay sensitivity as zeros (see Appendix, and Goldman and Weinstein 2003 for a larger discussion).

7.1.2 Biomarker relationships to one another

The literature suggests (see Chapter 2) that the bioindicators studied here should be related in one of two ways. The first hypothesis is that since the HPA axis and SNS systems are interrelated, but somewhat separate, the strongest correlations should be within each system (i.e. higher cortisol should be associated with lower DHEAS and higher norepinephrine associated with higher epinephrine). The second hypothesis is that a history of lifetime stress should activate both the HPA axis and SNS systems such that their markers all are correlated with one another. Should either one (or a mix) of these hypotheses be supported, we would have greater confidence in the neuroendocrine allostatic load (NAL) construct used as the dependent variable in the analysis in the next chapter.

Table 7.2 shows the pairwise correlations (r) between the biomarkers in order to distinguish between these hypotheses. These correlations represent plus/minus the square root of R^2 when some variable y is regressed on only x. Correlations are produced when one is uninterested in the change in y with a one unit change in x (Devore 2000). Results from the table lend support to the idea that the markers are most tightly related within their respective systems, although there is a fair amount of evidence that they are also related across systems. By and large, these results bring about more confidence in the dependent variable. The only anomaly is the positive correlation between epinephrine and

DHEAS. With a stressor, one expects epinephrine, norepinephrine, and cortisol levels to go up, while DHEAS goes down.

7.1.3 Trend of biomarkers over age

As described earlier, allostatic load (AL) supposedly builds up over time when stressors and the body's response to them are of a certain character. Given the cumulative nature of AL, it is a necessary but not sufficient condition that as one ages AL increases. Thus, in reference to the neuroendocrine markers, the AL literature would suggest that DHEAS should decline, while epinephrine, norepinephrine, and cortisol should increase with age (see Chapter 3). The clinical literature, however, does not appear to fully accord with these hypotheses. Clinical studies do support DHEAS and norepinephrine changing in the directions the AL literature would predict, but finds little evidence of increasing cortisol or epinephrine levels (see Chapter 2). What are the trends in this survey?

The SEBAS is not ideally suited to answer this question because it is not longitudinal and does not collect data on anyone younger than 54 years old. Nevertheless, it does seem that some insight from the survey can be gained. A case could be made that the cross-sectional data approximates that that would be found in a longitudinal study. On the one hand, change over age is likely measured conservatively in a cross-section. Since for older respondents there is an effect selecting for good health, they probably have "younger" biomarker profiles. On the other hand, Taiwan experienced increases in standard of living during the lives of these respondents. Older participants probably aged in more stressful times and so might have a worse health endowment coming into their older age. It seems that these competing phenomena tend to cancel one another out.

Figure 7.3 shows the relative fitted values of cortisol, norepinephrine, epinephrine, and DHEAS over age. To obtain this graph, separate linear regressions were fit through the data for each of these four biomarkers (shown in the Appendix). DHEAS declines sharply with age, and at around 90 years old levels are about half that compared to age 54. The change in cortisol, epinephrine, and norepinephrine levels are less dramatic. With the cortisol outliers in the data, the slope is highly significant, but without them the slope is borderline significant at the .05 level. The slope for epinephrine is also nearly significant at the same threshold, while norepinephrine is significant at the .10 level. As an alternative to fitted regressions as a way to capture biomarker trends over age, box plots of separate five-year age groups were analyzed. Among other things, this sort of analysis reduces the weight of outlying data points (Devore 2000). This alternative yielded similar substantive findings (not shown).

Of the results shown here, the trend of DHEAS agrees most closely with the clinical and AL literature (see Table 7.3). From the perspective of the clinical literature, the weak increase in norepinephrine with age is surprising, with the inconclusive results for the remaining two biomarkers less so.

7.1.4 Neuroendocrine allostatic load (NAL)

Figure 7.4 shows the distributions of NAL based on the different cut-points and the summed z-score. Referring to the distributions based on the cut-point method of scoring, even when risk is defined most broadly, few persons have NAL scores of three or four. Linear and ordered logistic regressions will be used to analyze results from the different cut-point methods of scoring, and only linear regression is used to analyze the z-score distribution.

7.2 The independent variables

7.2.1 Demographics

Most of the Taiwanese in this survey were born before the rapid economic and social changes that took place after WWII. This legacy is revealed in some of the sample characteristics (see Table 7.4). Respondents are in part characterized by relatively low levels of urban residence and formal education. Taiwan's population sex structure is unusual in that women have a longer life expectancy, but men still outnumber them in total and even at some of the older ages (Population Reference Bureau 2003; US Census Bureau 2004). Accounting for this demographic exception is the Nationalist army's migration from mainland China shortly after World War II.

7.2.2 Social factors

As Table 7.4 indicates, nearly all study participants have married at some point in their lives and have experienced very low rates of divorce. About 40% of respondents live with a married son and few live alone. The most popular form of group participation is in an elderly club, followed by a religious association. About 45% of all survey participants are active in one or more of such group activities.

7.2.3 Psychosocial stressors

Of the psycho-social stressors examined here, the four most frequently mentioned (i.e. stress about family's work situation, financial situation, health, and marital situation) are reported in similar magnitude of between about 20 and 25% (see Table 7.5). Given the importance of the family and harmonious social relations in Chinese culture, report of direct familial conflict, as might be expected, lags far behind at 6%. When asked to volunteer another type of social stressor, practically none of the respondents did so. A little under half of the respondents reported one or more stressor. Following conventions in the literature, the six social stressors are combined to form an index in the multivariate analysis.

7.2.4 Controls

As described in Chapter 2, most clinical studies that measure the neuroendocrine biomarkers examined here use strict protocols that standardize patient meals, sleep and wake times, amount of exercise, smoking and drinking behavior, and so on. Unlike these studies, the SEBAS places few restrictions on respondents. The extent to which the lack of standardization affects the final results is unclear. First, while certain behaviors can increase biomarker levels, these behaviors would have to impact urine samples collected over a long period of time (12 hours), during which most participants would be sleeping. Second, even if the behaviors did affect the samples, the behaviors would need to be differentially distributed among subgroups to cause bias.

To the extent possible, this analysis tries to control for possible confounders. Ideally, outside of restricting certain behaviors, we would want to know information about those behaviors during the time over which respondents were collecting urine samples. For instance, chewing betel nut is known to increase catecholamine levels, but we do not know if survey participants engaged in the practice during the urine collection period. The next best option is to infer such information. The analysis here assumes that relevant behaviors are worth controlling for if it is known whether respondents engaged in them on a daily basis[17].

Table 7.5 presents relevant controls that met this criterion. In the case of betel nut chewing, as with alcohol consumption, few participants report engaging in the practice on a daily basis. Nearly a quarter of the respondents reported daily smoking and nearly 57% of respondents take medication. Reportedly, almost half have a daily diet rich in fruits and vegetables and about 40% exercise six times a week or every day.

7.3 Characteristics of the married and widowed

Considering that widowhood status figures prominently in this analysis, it is useful to gain some background into differences between the widowed and the currently married. As might be expected, the widowed are slightly older and predominantly female

[17] The variable in the survey gauging exercise is used here, although those who exercise six or seven times

(see Table 7.6). Interestingly, the married and widowed live in households of nearly the same size. The average is deceptive, however. On the one hand, the widowed are more likely to live with married children; on the other, they are less likely to participate in groups and are 15 times more likely to live alone. Perhaps the death of a spouse leads both to an increase in living alone and moving into a child's household. The widow's older age is almost certainly associated with more mobility problems, perhaps explaining the differential in group participation which requires activity outside the home. Married and widowed respondents report psycho-social stressors in much the same magnitude.

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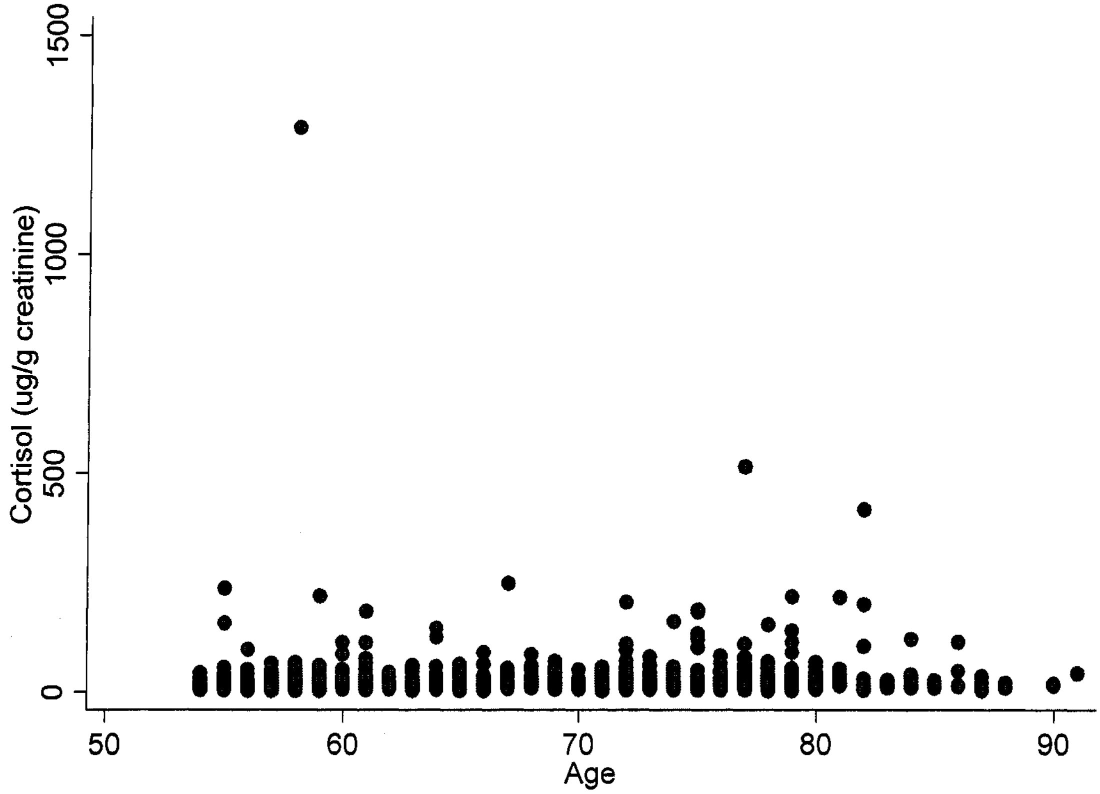
a week were lumped together.

Table 7.1 Descriptive statistics and cut-points for the neuroendocrine biomarkers – sample population, Taiwan (ages 54 to 91, year 2000, both sexes combined)

	Mean	SD	N	Percentile cut-offs					
				10th	15th	25th	75th	85th	90th
System									
HPA axis									
Cortisol	27.1	33.5	1018	--	--	--	29.9	38.5	47.9
DHEAS	80.7	58.6	1021	20.9	28.6	40.8	--	--	--
SNS									
Epinephrine	2.6	2.6	1019	--	--	--	3.7	4.8	5.6
Norepinephrine	21.9	9.9	1019	--	--	--	27.1	31.5	34.7

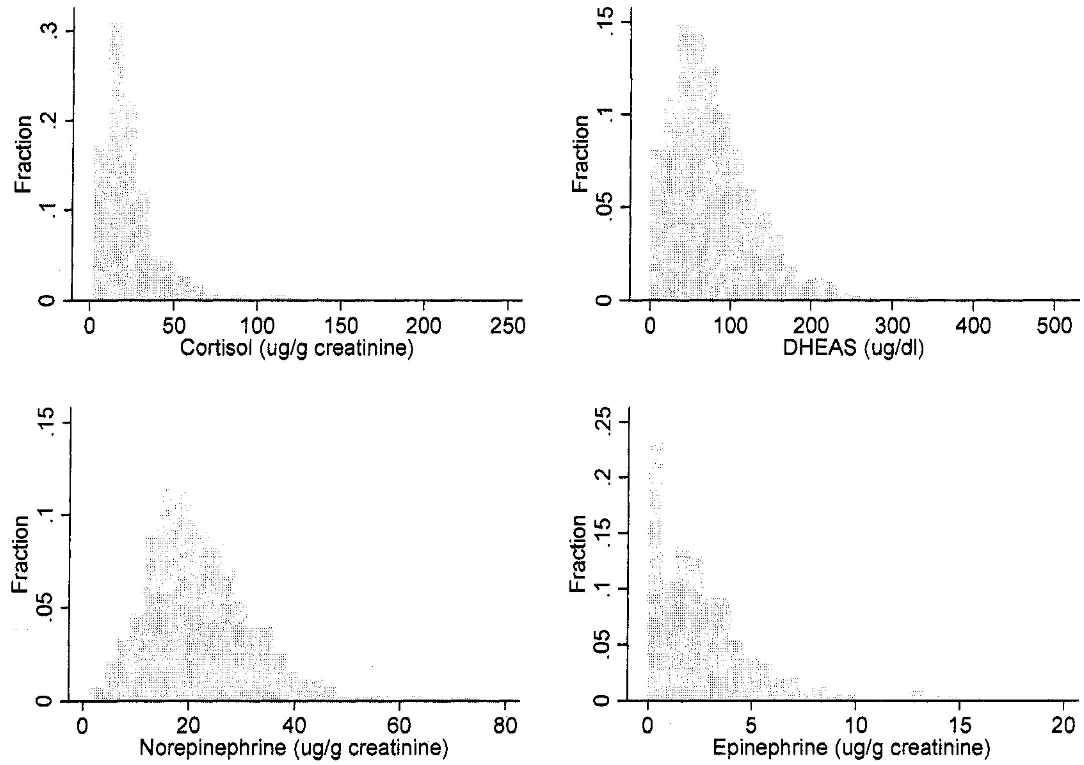
Note: Tabulations based on unweighted survey data.
Source: Author's tabulations based on the 2000 SEBAS (Goldman and Weinstein 2003).

Figure 7.1 Plot of cortisol over age – sample population, Taiwan (ages 54 to 91, year 2000, both sexes combined)



Note: Plot based on unweighted survey data.
Source: Author's plot based on the 2000 SEBAS (Goldman and Weinstein 2003).

Figure 7.2 Histograms of the four neuroendocrine biomarkers – sample population, Taiwan (ages 54 to 91, year 2000, both sexes combined)



Note: For improved readability, the two cortisol outliers were left out of the histogram. Histograms based on unweighted survey data.

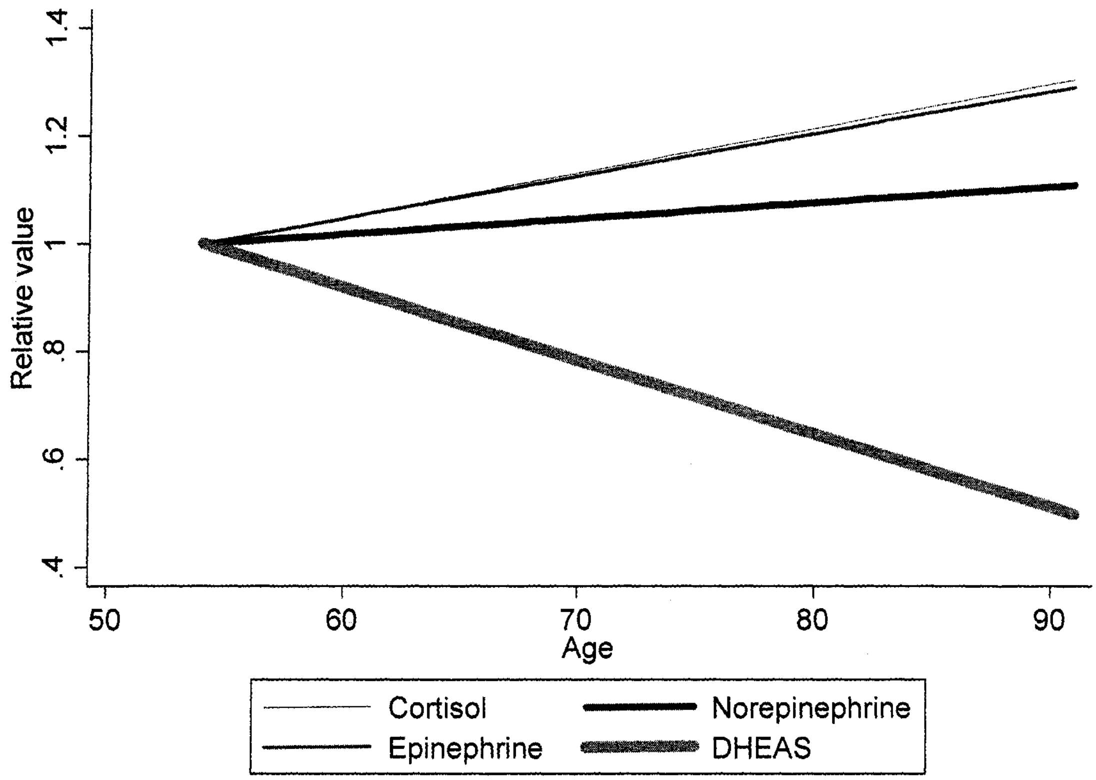
Source: Author's plots based on the 2000 SEBAS (Goldman and Weinstein 2003).

Table 7.2 Correlations between the neuroendocrine biomarkers – sample population, Taiwan (ages 54 to 91, year 2000, both sexes combined)

Within system relationships	*r*	Across system relationships	*r*
SNS		SNS and HPA axis	
Epinephrine and norepinephrine	0.32***	Cortisol and epinephrine	0.06
HPA axis		Cortisol^ and epinephrine	0.09**
Cortisol and DHEAS	-0.10**		
Cortisol^ and DHEAS	-0.09**	Cortisol and norepinephrine	0.03
		Cortisol^ and norepinephrine	0.06
		DHEAS and epinephrine	0.09**
		DHEAS and norepinephrine	-0.10**

Note: *, **, and *** represent statistical significance at the .05, .01, and .001 levels, respectively.
Calculations based on unweighted survey data.
^ These cortisol values do not have the two outliers.
Source: Author's calculations based on the 2000 SEBAS (Goldman and Weinstein 2003).

Figure 7.3 Cortisol, norepinephrine, epinephrine, and DHEAS relative fitted values over age – sample population, Taiwan (ages 54 to 91, year 2000, both sexes combined)



Note: Fitted values were determined by OLS regression equations resulting from regressing each biomarker on just age. The above fitted values are relative to that at age 54. The cortisol regression excludes the two outlying values. Analysis based on unweighted, cross-sectional survey data.

Source: Author's calculations based on the 2000 SEBAS (Goldman and Weinstein 2003).

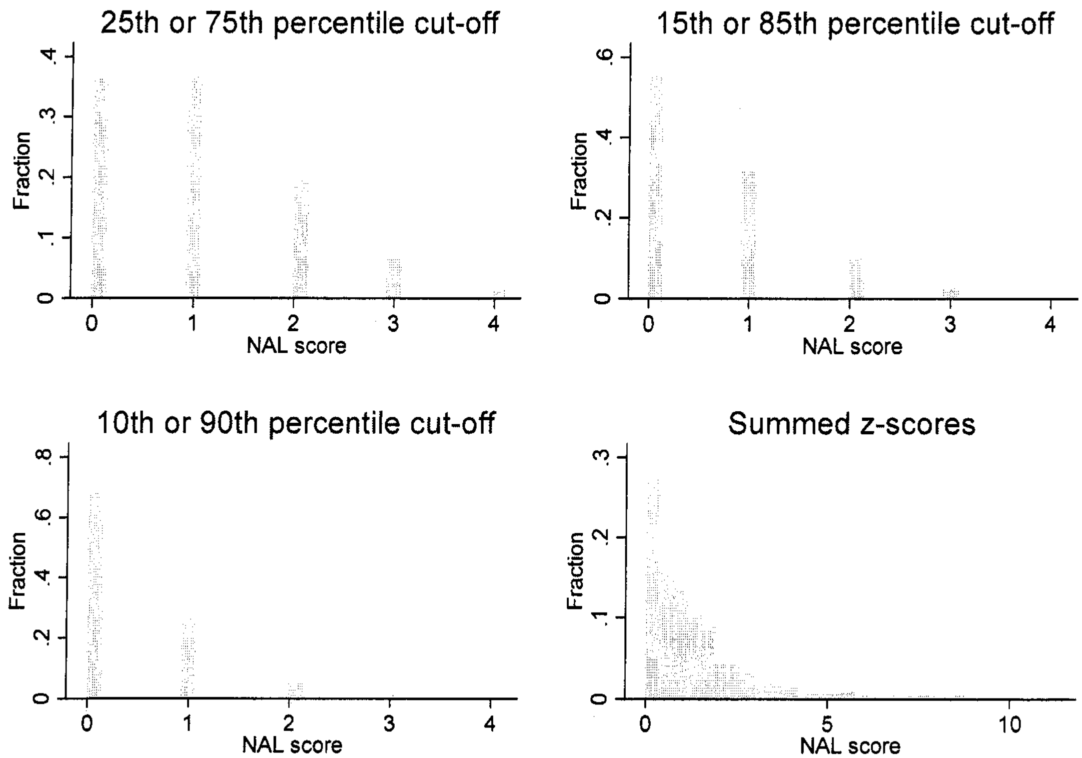
Table 7.3 Change in baseline levels of neuroendocrine biomarkers over age – as derived from allostatic load theory and as found in the clinical literature and SEBAS

	Allostatic load theory*	Clinical literature**	SEBAS survey***
System			
HPA axis			
DHEAS	↓	↓	↓
Cortisol	↑	↑ / → / ↓	→ / ↑
SNS			
Epinephrine	↑	→ / ↓	→ / ↑
Norepinephrine	↑	↑	→ / ↑

Note: * The allostatic load literature posits that load cumulates over the life course, and thus with increasing age biomarker levels for each biomarker should head toward "higher risk."
** Findings from the clinical literature are mixed for both cortisol and epinephrine, with studies showing increasing, level, and decreasing trends with age for cortisol and either flat or decreasing trends with age for epinephrine.
*** In the SEBAS, the trend with increasing age could be interpreted as either level or increasing for cortisol, epinephrine, and norepinephrine.

Source: Created by this author.

Figure 7.4 Distributions of neuroendocrine allostatic load (NAL) scores using various scoring methods – sample population, Taiwan (ages 54 to 91, year 2000, both sexes combined)



Note: The distribution of the summed z-scores shown here excludes the two cortisol outliers, whose values are 9.9 and 15.8. Results based on unweighted survey data.

Source: Author's plots based on the 2000 SEBAS (Goldman and Weinstein 2003).

Table 7.4 Descriptive statistics for the demographic and social variables – sample population, Taiwan (ages 54 to 91, year 2000, both sexes combined)

Variables	Percent %	Mean (SD)	Range
Demographics			
Age			
Men	--	68.7 (8.4)	54–90
Women	--	67.8 (8.6)	54–91
Sex			
Male	58	--	--
Education			
Years of schooling	--	5.2 (4.7)	0–17+
Residence			
Urban (vs. rural)	55	--	--
Ethnicity			
Mainlander (vs. Hakka/Fukienese)	17	--	--
Social factors			
Marital status*			
Married	71	--	--
Widowed	24	--	--
Divorced/separated	3	--	--
Never married	2	--	--
Residence**			
Lives w/married son	42		--
Lives alone	7	--	--
Group participation***			
Neighborhood association	6	--	--
Religious association	14	--	--
Farming, professional, or civic org.	7	--	--
Political association	4	--	--
Social service group	6	--	--
Village or lineage association	9	--	--
Elderly club	21	--	--
Elderly education	3	--	--
Participant ≥ 1 group	44	--	--

Note: Tabulations based on unweighted survey data.
* Marital status refers to status at the time of the interview. The four categories (i.e. married, widowed, divorced/separated, never married) are mutually exclusive and sum to 100%.
** I decided to show residential status for the variables that will be used in analysis in the next chapter. The survey also collected information on whether the respondent lives with spouse/companion, unmarried children, daughter-in-law, husband's parents, wife's parents, married daughter and son-in-law, grandchildren, other relatives, and other non-relatives.
*** The entirety of options for which a respondent could report group participation has been listed. Respondents could report participating in none or all of the activities (i.e. the categories are not mutually exclusive).

Source: Author's tabulations based on the 2000 SEBAS (Goldman and Weinstein 2003).

Table 7.5 Descriptive statistics for the psycho-social and control variables – sample population, Taiwan (ages 54 to 91, year 2000, both sexes combined)

Variables	Percent %
Psychosocial factors	
Current familial stressors	
Family's work situation	22
Family's financial situation	26
Family's health	21
Family's marital situation	22
Familial tension/conflict	6
Other familial stressor (volunteered)	1
Number of reported stressors*	
0	54
1	19
2	11
3	10
4	5
5	2
6	0
Controls	
Takes medication	57
Chews betel nut daily	2
Smokes daily	22
Consumes alcohol daily	5
Exercises six times a week or daily	41
Diet of at least two fruits and three vegetables daily	53

Note: * The total percent exceeds 100 because of rounding. No respondents reported six stressors. Tabulations based on unweighted survey data.

Source: Author's tabulations based on the 2000 SEBAS (Goldman and Weinstein 2003).

Table 7.6 Descriptive characteristics of the married and widowed – sample population, Taiwan (ages 54 to 91, year 2000, both sexes combined)

Variables	Married	Widowed
Demographics		
Percent female	35%	68%
Average age	67 years	73 years
Average education	5.8 years	3.5 years
Urban residence	54%	60%
Social factors		
Living situation		
Average number in household	4.7	4.9
Alone	1%	15%
With married son	38%	56%
Group participation		
Participant in 0 groups	53%	60%
Psychosocial factors		
Current familial stressors		
Family's work situation	22	25
Family's financial situation	25	29
Family's health	22	20
Family's marital situation	22	26
Familial tension/conflict	6	7
Other familial stressor (volunteered)	0	1
Average number of reported stressors	1.0	1.1

Note: Tabulations based on unweighted survey data.
Source: Author's tabulations based on the 2000 SEBAS (Goldman and Weinstein 2003).

Chapter 8

Neuroendocrine biomarkers, social relations, and the costs of cumulative stress in Taiwan

Summary: Allostatic load (AL) theory posits that load builds up over the life course as a consequence of the body's response to stress. An important aim of this chapter is to test this widely held – but hardly investigated – understanding of what AL represents. More specifically, using a nationally representative survey of Taiwan (2000 SEBAS), this chapter scrutinizes the connection between stressful life histories and neuroendocrine allostatic load (NAL). Stressful life histories are operationalized through the use of a variety of social and other stressors. Some of the stressors are respondents' subjective interpretations of their condition, and others are indicators of life states that are expected to be stressful based on readings of the relevant literatures. NAL, the dependent variable in the analysis, is scored using a variety of approaches.

The major finding of this chapter is twofold. First, there is little evidence to support the hypothesis that baseline levels of the neuroendocrine markers stem from stressful life histories. Second, report of current stress (amongst women only) is positively correlated with higher NAL levels. Taken together, these findings question whether the neuroendocrine markers of the allostatic load construct reflect long-term processes over the life course. Indeed, it seems that the neuroendocrine markers may reflect the exact opposite – an ephemeral state at the time of the survey.

Allostatic load (AL) theory posits that load builds up over the life course as a consequence of the body's response to stress. An important aim of this chapter is to test this widely held – but hardly investigated – understanding of what AL represents. More specifically, using a nationally representative survey of Taiwan (2000 SEBAS), this chapter scrutinizes the connection between stressful life histories and a measure of current neuroendocrine allostatic load (NAL). Stressful life histories are operationalized through the use of a variety of social and other stressors. Some of the stressors are respondents' subjective interpretations of their condition, and others are indicators of life states that are expected to be stressful based on findings in relevant literatures. An elaboration of the variables used in this analysis and their expected influence on NAL follows.

8.1 Research hypotheses

In regard to the social integration variables, it is expected that indicators of a lack of social connection represent more stressful states. Thus, it is hypothesized that all of the following should lead to higher NAL: widowhood, not living with a married son, living alone, and not participating in groups. These hypotheses are derived from the literature on social relations and health (see Chapter 4) and knowledge of the Taiwanese context (see Chapter 5). Widowhood is the state that is predicted to be by far the greatest stress or challenge (and thus contributes most strongly to the buildup of load), and living alone (which by definition excludes the possibility of living with a married son) is hypothesized to be more stressful than not living with a married son.

In regard to other demographic characteristics, low education and increasing age are expected to be associated with higher NAL. Without an income variable in the model, low education is an indicator of low socioeconomic status which, compared to its opposite, likely results in more stressors and less resources to deal with them once they occur. Since AL can supposedly only accumulate with time (see Chapter 3), greater age should be correlated with greater NAL. The direction of the effect of ethnicity on NAL is unclear. On the one hand, Mainlanders have traditionally held positions of power, are more educated, and are overwhelmingly male (an advantaged position). On the other hand, Mainlanders left behind family in their migration to Taiwan and are more likely to live alone (see Chapter 5; Beckett et al. 2002). The hypothesized impact of urban or rural residence on the buildup of load is also uncertain, but area of residence is potentially important, and is thus controlled for in the model.

I also analyze subjective reports of stress. From the perspective of AL theory, when *only* the number of currently reported stressors is in the model, its expected correlation with NAL is uncertain. On the one hand, reports of current stress should not affect NAL because a whole life history of stress should dwarf the impact of any current condition. On the other hand, a report of current stress may be indicative of having also experienced stress in earlier periods. In the case where *both* number of currently reported stressors and the duration of those stressors are in the model, the expectation is clear: duration of stress should be positively and strongly correlated with higher NAL levels, while the number of reported stressors should not be correlated with NAL levels.

8.2 Caveat about causal directionality

As alluded to above, causality is thought to run in the direction from stressful events to AL. Regarding this directionality, it is important to keep in mind the findings from the MacArthur studies that have shown that higher levels of baseline AL are associated with poorer health outcomes (i.e. physical and cognitive declines, and mortality) downstream (see Chapter 3). Because of the established correlation of AL with poor health, it is important to beware of the possibility that in the study here, poor health, and not AL, is responsible for an association between AL and an independent variable of interest. For example, suppose that this dissertation hypothesized that stress over one's own health led to high AL, and the final results showed such an association. An alternative hypothesis could be that AL contributed to poor health (which the respondent was stressed about). Thus, while stress over health and AL would be correlated, causality could run from AL to poor health and then to stress, not from stress to AL. In this hypothetical example, both hypotheses are probably partially correct. AL might have led in some way to poor health over which the respondent is stressed, but once the respondent is stressed a feedback loop to AL emerges.

In this dissertation, the variable most prone to the issue raised in the preceding example is group participation. That is, if high NAL is associated with poor health, poor health may limit the ability to participate in groups. I have nevertheless retained group participation in the model because the potential social disconnection resulting from no group participation (no matter the cause) might, like the example of worrying about one's own health, raise NAL. Other variables in the model seem far less prone to the pitfall described. For instance, poor health does not cause one to chronologically age or have Mainlander ethnicity. It also seems hard to construct a plausible scenario in which the respondent's poor health would increase her likelihood to be widowed, live alone, or not live with a married son. Indeed, in the case of the widowhood variable, it seems almost ideal, since the loss of a spouse is both highly stressful and an "exogenous" shock. The subjective psycho-social stressors also seem largely exogenous. In part to avoid (or mitigate) the aforementioned problems of (potential) reverse causality, I have included in the analysis those stressors that the respondent experiences, but that relate to others, such as direct familial conflict or stress over his family's marital situation. I have excluded from the analysis those stressors that relate to the respondent's own situation (i.e. personal health, financial situation, and so on).

8.3 Results

8.3.1 Bivariate analysis

For a preliminary picture of the data, Table 8.1 presents comparisons of mean NALs for different demographic characteristics, states indicating social connectedness, and reports of psycho-social stressors. I present results that stem from what has been the most common scoring method of AL, whereby respondents earn one point toward their NAL score on each biomarker for which their biomarker level ranks within the "riskiest" quartile (as based on the entire SEBAS sample). This approach is the "single-tailed elevated risk zone" approach, and since the NAL construct contains four biomarkers, individual NAL scores can range from 0 to 4[18].

As can be gleaned from the table, relative to men, women's mean NAL is nearly two times greater, and the largest ratio of the table. This differential must be explained by some phenomenon other than age, since men are actually older in this sample (see Chapters 5 and 7). Increasing age is associated with higher NAL, which is reassuring in light of the hypothesis stated above that advancing age can only yield greater loads. As expected, lower education is associated with higher mean NALs and, perhaps not surprisingly, there appear to be no ethnic differences in loads. Those widowed, in accordance with predictions, have some 30% higher NAL than their married counterparts. Contrary to predictions, the other social connectedness variables reveal no association with NAL. For each psycho-social stressor examined, the average NAL is the same or higher for those who report the stressor compared to those who do not. However, only the difference in mean NAL associated with a report of stress over family's financial situation is large enough to be statistically significant.

8.3.2 Stressors and their lengths

Because of potentially important sex differences stemming from biological, psychological, and social factors that could in the end affect NAL levels, further analysis will be conducted separately by sex. Table 8.2 shows the percent reporting various stressors and their durations, for men and women separately. Thirty-four percent of the

[18] Please see Chapters 3, 6, and 7 for more details about issues surrounding the scoring of NAL.

women in the sample are widowed compared to twelve percent for men, and amongst the widowed of both sexes women have been in the state longer. For every familial stressor, a greater percentage of women report being stressed and over half of all women (compared to 44% of men) report one or more of the familial stressors, with the difference relative to men measurable. To note in the table is the relatively long time periods of stress reported by some respondents. For instance, at least one female respondent reported being stressed about her family's health for 50 years, and at least one male respondent reported being stressed about his family's financial situation for 42 years. Summing the duration stressed across each of the six psycho-social stressors for a given respondent yields the variable "total psycho-social years stressed." Women's mean total psycho-social years stressed is about 2 1/2 years longer than that for men.

8.3.3 Multivariate analysis

Results from the bivariate analysis presented in Table 8.1 show that the following characteristics are correlated with higher NAL levels: female sex, older age, lower education, widowhood status, and (perhaps) greater number of reported current stressors. The multivariate analysis that follows here attempts to isolate the impact of these[19] and other factors on levels of NAL by holding constant observable characteristics that are included in the models and that are known to be (or may be) correlated with one another. Examples of known and relatively strong correlations in the study here include those between: widowhood status and older age (see Chapter 7), widowhood status and female

[19] Separate regressions by sex control for the potential influence of sex on other variables in the models, but

sex (see Table 8.2), number of stressors reported and female sex (see Table 8.2), total psycho-social years stressed and female sex (see Table 8.2), low educational levels and older age (data not shown), and low educational levels and female sex (data not shown).

Tables 8.3 and 8.4 present the results of multivariate analysis with NAL, scored using different methods, as the dependent variable. As mentioned elsewhere (see Chapters 2 and 3), there is no consensus for what constitutes "at risk" values for the neuroendocrine biomarkers, or even a best practice for scoring them. Thus, what is reported here are the results from various approaches, both in terms of the statistical methods used (i.e. linear regression and ordered logistic regression) and way of scoring NAL (i.e. cutpoint method and summed z-score method)[20].

Despite the different techniques used, results within each sex are quite consistent. For men, increasing age is positively and strongly correlated with greater NAL across all models and lack of group participation also is associated with higher NAL (at either the .05 or .10 level of significance). As with men, for women, age is significant in all models. Importantly, for women only, report of current stressors is also significant in all models. To take an example from the model using linear regression and top 25% risk cut points, for each additional current stressor reported, women's expected NAL increased by .12 points.

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do not allow for a comparison of the impact of sex on NAL levels.

[20] As briefly described in the bivariate analysis section, the cutpoint method of scoring assigns one point toward a respondent's NAL score for each of the four biomarkers on which the respondent has "risky" biomarker levels. Thus, a respondent's load score can range from zero to four. The summed z-score method of scoring has no predetermined upper limit, because it simply sums for each respondent the number of standard deviations from the mean in the direction of high risk for each biomarker. So, for example, if a respondent has cortisol levels that are five standard deviations from the mean and values on the other biomarkers that are exactly the mean, this respondent would have a z-score of five. Unlike the cutpoint method of scoring, the z-score method allows for unequal weighting of the biomarkers. Because of the sensitivity of the z-score method to outliers, two regressions will be performed, one that includes and

The primary purpose of Tables 8.5 and 8.6 is to examine whether length of widowhood correlates with higher NAL, and thus only includes the widowed. It is also of interest, though, to ascertain whether the relationships between NAL and other independent variables differ from those in which the widowed and married are combined in the regressions, since the widowed and married can differ on a number of key parameters (see Chapter 7). To address the possibility that the relationship between NAL and time widowed may take on a quadratic form (more in the Discussion Section), the models in Tables 8.5 and 8.6 include both a "years widowed" and a "years widowed squared" term.

As can be seen from the tables, for both sexes, widowhood length appears to have no impact on the various NAL measures, although this absence of measurable differences could be due to small sample sizes (n = 71 for men and n = 146 for women). In terms of the other independent variables, only one appears to have a different trend compared to the regressions containing all men and all women. It seems that for widowed women, not living with a married son is associated with higher NAL, whereas there is no association when the widowed and currently married are grouped together in the model presented in Table 8.4.

8.4 Discussion

This chapter investigated an index of neuroendocrine markers, or neuroendocrine allostatic load (NAL), in relation to various life stressors. The general hypothesis was that

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another that excludes two outlying cortisol values (see Chapter 7).

stressful life histories would positively correlate with higher NAL. By and large, the findings here have not supported this hypothesis (see Table 8.7). In contrast, an unexpected and important finding was discovered: report of a currently stressful state was positively and strongly correlated with higher NAL (amongst women). A broader discussion of these findings follows.

8.4.1 Life condition and years stressed variables

None of the variables capturing life conditions that one would assume a priori are stressful were significant. For example, for both sexes, low education, living alone, widowhood status, and years widowed among those without a spouse were not correlated with NAL. Even though the literature suggests that the indicators of social isolation used in this survey, by and large, are capturing more stressful states, one might still reasonably ask if the respondents actually experienced those conditions to be stressful. To address, to some degree, this potential limitation, questions were used that probed respondents' subjective interpretation of their psychological state. The resulting measure from this series of questions, total psycho-social years stressed, also was not correlated with levels of NAL. It must be noted that a respondent reflecting on his life history and reporting, say, 20 years of stress over his family's financial situation, is not the same as a survey over a period of 20 years periodically asking him the same question. Nevertheless, it seems hard to argue that a different social reality is not being captured when comparing those who report few stressors for short periods of time, to those reporting many stressors for long periods of time.

8.4.2 Current stress matters

As mentioned in the research hypotheses section, it follows from AL theory that a currently experienced stress (holding a history of stress constant) should have a negligible impact on current levels of AL. Here, however, amongst women only, the number of current stressors reported was positively correlated with higher NAL. If the operationalization of AL better matched theory, the results presented in this dissertation would be reversed. That is, reports of current stress would not be significant, whereas length of stress would be.

It is important to keep in mind that a nuanced formulation of what the neuroendocrine components capture emphasizes that the markers measure two phenomena simultaneously. One component of NAL supposedly captures readjusted baseline levels that become dysregulated through the life course. The second component can capture effects of more immediate events of the day and even weeks before biomarker collection (McEwen and Seeman 1999). I suggest here that, according to the literature on AL theory, the first component should predominate and can be thought of as the "signal," whereas the second part can be considered "noise" and should be reduced to the extent possible. However conceived, the interplay between more proximate and distal influences on AL biomarker values has probably been underemphasized in the literature.

Given the above discussion, assuming a linear relationship between NAL and a major life stressor like widowhood may be a mistake. For example, the NAL of those recently widowed may be similar to those widowed for a long time, but for different reasons. There is the initial shock of losing a spouse from which one slowly recovers on one end of the spectrum (a peak in NAL). At the other end there is the widow or widower who, after many years, has coped with the loss, but whose NAL has incrementally increased (another peak in NAL) because the unmarried state is presumably more stressful than the married one. Put differently, the former case may capture more of the noise, and the latter, the signal. Testing for a quadratic relation over time, rather than a linear one in which the differing phenomena could potentially be obscured, seems prudent, but this strategy appears rarely to have been adopted.

Figure 8.1 (created by this author) depicts in schematic form some of the issues just described. The top panels present a hypothesized, non-zero stress level stemming from everyday activity, and then levels after exposure to a stressful shock that remains a permanent stressor (i.e. stress levels do not return to baseline). One could imagine a number of potential stressors fitting this scenario, including chronic disease or widowhood. The panels on the right incorporate the idea that stressors have an acute phase and recovery period, and that corresponding NAL trends are influenced by current events. The panels on the left ignore the psychological coping involved in dealing with stress, as well as the observation here that one's current state may affect the NAL construct. This work posits that the panels on the right may be more accurate than their counterparts on the left.

8.4.3 Age and allostatic load theory

As mentioned in Chapter 3, the theory of AL is to some extent a theory of aging. AL, in some measure, should represent "biological age" in contrast to "chronological age." Also, a fundamental tenet of AL theory is that the load is cumulative; it supposedly builds up inexorably over time, with age, since the passing of time only brings slings and arrows of misfortune. In this chapter, increasing age was positively and strongly correlated with higher NAL for both men and women. This finding, on the surface, is reassuring. However, as was shown in the previous chapter (and in separate analyses by sex not shown), DHEAS is a primary driver of the NAL index. What is more, from the perspective of the clinical literature, only DHEAS values convincingly head toward "high-risk" ranges with increasing age. The directionality of any change with age (at rest) for the remaining three neuroendocrine biomarkers (cortisol, epinephrine, and norepinephrine) is ambiguous. This lack of discernible trend is an especially troubling finding since changes toward high-risk values are a necessary but not sufficient condition for AL theory to hold. Once it is established that biomarker values head toward high-risk ranges with increasing age, the (greater) challenge then becomes demonstrating that a more stressful life history accelerates these changes.

8.4.4 Reconciliation with previous work

How do the findings in this chapter compare and reconcile with other published work? Two articles closely related to this work are by Seeman et al. (2004) and Goldman et al. (2005), which have both examined the same data set. Seeman and colleagues investigated the impact of a number of variables related to the social environment, including marital status, on a specific operationalization of AL. They separated the analysis by two age categories, the elderly and near elderly. The authors did not investigate years widowed as in the chapter here, but a change in state (e.g. married to widowed) from the beginning to the end of the period. For the elderly, the period ranged from 1989 to 2000, and for the near elderly, from 1996 to 2000. Only in one case (near elderly men) did the authors find that the presence of a spouse was associated with lower levels of AL. That is, for most study participants (i.e. elderly men, elderly women, and near elderly women) the expected association between spousal presence and lower AL levels was not found. Seeman and co-authors also find that high levels on other measures tapping social support and social connection are only weakly linked to levels of their AL measure.

A comparative advantage of the analysis here is its use of the actual years widowed ranging over a long span (from less than a month to 49 years) and an analysis of a possible quadratic functional form of NAL levels. Additionally, the analysis here scores NAL with a variety of statistical and methodological approaches. This chapter found no evidence that in Taiwan marital status and duration of widowhood (amongst both men and women) correlate with levels that stem from a measure attempting to capture the costs of cumulative stress. Unlike the Seeman et al. study, the analysis here focuses on one physiologic system[21], does not perform separate analyses by elderly and near elderly age categories, does perform separate analyses by sex, and uses different measures of social connection and support. Despite these differences in study design, I found similarly weak relationships between levels of social connection and levels of load. The findings here, then, both in reference to widowhood status and its duration, and other measures of

[21] One advantage to focusing on a single physiologic system is the greater ease with which one can interpret results. If many biomarkers representing many different biological systems are used in one measure, it may be difficult to derive the meaning of results using this measure. For an expanded discussion of these issues,

social connection, generally strengthen and extend the earlier findings of Seeman and co-authors.

The paper by Goldman et al. focuses on perceived stress and an expanded construct of AL that contains a total of 16 biomarkers[22]. The perceived stressors used in their article need not stem from more direct interpersonal sources (e.g. personal financial problems could be included). Goldman and co-authors examine reported stressors between 1996 and 2000 of those aged 54 and older in the SEBAS and linked surveys, with only the demographic variables age and sex used as controls. They find that among female (but not male) Taiwanese, a greater number of reported stressors in 2000 is positively associated with higher levels on their AL construct. These results are congruent with the findings here, which use an abbreviated AL construction (NAL) and a somewhat differently constituted index of number of current stressors. Goldman and others also find that when a measure of stress during the period from 1996 to 2000 is included in the model, it has explanatory power over and above that of the 2000 measure alone. They suggest that the length of time one experiences perceived stress may increase the pace of biological dysregulation. While this suggested link may be further supported by future studies, the findings in the chapter here seem to suggest something different, at least in regard to baseline levels of the neuroendocrine biomarkers.

There are numerous possible reasons for the discrepancy. One is that the Goldman et al. design allowed for the possibility that respondents report stress in 1996, 1999, and 2000. Use of longitudinal data to capture chronic levels of stress is ideal, but the years of longitudinal data available to Goldman et al. are quite restricted, especially since AL

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please consult Chapter 3.

attempts to capture the consequences of stress experienced over the entire life course in respondents of advanced age. In the study here, respondents were first asked whether they currently experience a stressor and, if so, for how long. One of the shortcomings of this retrospective measure is that it suffers from respondent recall bias. The advantage, however, of such a measure is that respondents have the opportunity to report stress experienced over very long periods of their life (and some survey respondents reported having experienced stressors for many decades). The second possible reason for the discrepancy in suggestions about the strength of the link between perceived stress and load is that Goldman et al. use a much expanded construct of AL, whereas the analysis here uses an abbreviated one. A third possibility is that the authors used a different scoring scheme to classify high-risk. Like this study, they used an "elevated risk zone" approach, but for three of the four biomarkers they considered not just relatively high values, but relatively low ones as well, as signifying elevated risk. I had also considered scoring NAL using a two-tailed, instead of one-tailed approach, but opted instead to begin analysis by thoroughly investigating (with a wide range of methodological and statistical strategies) the single-tailed approach. This decision was made in large part because the single-tailed approach has to date been the most commonly used and has been shown to be predictive of worse health outcomes using longitudinal data (see Chapter 3). Further analysis of the results here could investigate whether the main findings are altered by using one of a number of alternate approaches to the scoring of AL, including one based on a two-tailed elevated risk zone.

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[22] The MacArthur studies used 10 biomarkers.

8.4.5 Survey limitations and future directions

Decades of social science research have been able to establish that certain social conditions such as social isolation and low socioeconomic status are positively correlated with, and perhaps result in, poor health. The recent integration of biomarkers into social surveys, such as in the SEBAS, promises a deeper understanding of potential pathways that lie between these social realities and poor health. In this respect, the SEBAS is a pathbreaking study. Nevertheless, like any survey, it can be improved, and some suggested advancements are articulated below[23].

Since a key element of AL theory is that it purportedly captures lifetime cumulative adversity, a simple question could be posed in the mold of the global self-assessed health question that we know to be highly predictive of future morbidity and mortality. For example, "Over your entire life course (from birth until the present), would you say the stress that you have experienced is very high…moderate…very low?" A variant of this question could ask the respondent to compare lifetime adversity to that of age peers. One would expect that the answers would highly correlate with AL levels. The respondent could also be asked about overall levels of stress currently experienced, which would allow a more direct comparison of the contributions of current and past stress to NAL or AL measures.

Other methodological considerations include collection of the biomarkers as soon as possible after respondents give their survey answers to whether they are currently

[23] It is my understanding that the SEBAS has been funded for at least another wave of data collection and many of the following issues are well-known to those involved with the survey and are being addressed as fully as possible.

stressed. In the SEBAS, biomarkers were collected weeks after the interview. It is likely that the strength of the correlation between report of current stressors and NAL would be greater if this lapse were reduced. A further improvement in studies like the SEBAS would be a tighter correspondence between the life condition and subjective stress measures. "Stress" is an elusive concept, but we can be more assured one is stressed if physiological measurements correspond to both life conditions and subjective interpretations of those very same conditions. In the case of widowhood, for instance, this study assumed that it was stressful, based on a prior understanding of the world and readings of the literature. Combining this widowhood variable with questions probing respondents' subjective stress related to the loss would be more ideal. As well, it would be helpful to have more variables that tapped stress over the life course (e.g. early death of a parent, death of a child or other loved one, early and severe health problem or disability).

AL was originally presented as a general theory, and it has since been operationalized by various biomarkers and various methodological approaches. The neuroendocrine markers used here have generally been thought to be "core" to any reasonably complete AL construct. However, it may turn out to be the case that resting, baseline levels of these markers are an inappropriate measure. In addition to examining resting levels, the clinical literature has commonly examined levels before, during, and after exposure to a stressor (see Chapter 2). A healthy bodily response to stress shows elevated levels after a stressor, and then a return to baseline shortly after the threat has passed. At the very least for the biomarker cortisol, persons of different ages show similar increases in cortisol levels after exposure to a stress (see Chapter 2). The difference between older and younger subjects is revealed in the time it takes to return to baseline levels after the threat has passed, where older subjects have a "sluggish" recovery relative to younger ones (see Chapter 2). It may turn out to be the case that AL is caused by, or revealed in, this recovery differential, and not in baseline levels. At least two authors quite familiar with AL and its measurement in surveys have suggested, financial and other considerations permitting, the collection of such "reactivity" data as a way to improve AL's measurement (McEwen and Seeman 1999).

As discussed or alluded to in sections above, there are a number of potential reasons for why values stemming from measures attempting to capture stressful life histories would not be correlated with levels of an AL construct. I summarize three main reasons below. First, the survey questions posed to respondents may not be adequately representing the various types of stress, and their intensity and duration, experienced over the life course. Second, the theory of AL might be accurate, but its operationalization (concerning both the biological markers and methodological and/or statistical approaches to scoring load) could be flawed. Third, AL theory itself may be flawed.

The first two reasons have already been discussed at some length in this chapter. In regard to the third, I think that one of the key issues that AL theory has yet to fully address is the possibility that the body has considerable potential to recuperate and rejuvenate from stressful insults (Selye 1950; Timiras 2003). Is it not at all possible that the summation of load across different physiologic systems remains level, or perhaps declines, over shorter and longer periods? If the summation of load across different physiologic systems does build up in the body, could it still be that load in *particular* physiologic systems declines or remains level? How does AL theory incorporate the increasing body of research indicating that various types of mild stress (e.g. dietary restriction, physical and mental exercise, social stimulation) is beneficial at the cellular, molecular, and perhaps other levels (Kyriazis 2005; Rozman and Doull 2003; Le Bourg 2003) into newer formulations of the theory? In trying to better answer these questions, I think that a fruitful direction for future research involving the allostatic framework would be to focus on both the ways in which stress may harm or damage the body and the ways in which the body is capable of resisting, ameliorating, or even benefiting from the impact of such insults.

8.4.6 Stress as an explanatory mechanism between social disconnection and poor health

Lastly, in returning to the motivation of the dissertation, to what extent has this work made progress in the larger project of uncovering the causal mechanisms of social connectedness and health? Given the apparent limitations of the NAL measure and the survey it is hard to say. More than anything, it seems that the results here highlight the need for future research to consider the negative side of social relations. Many respondents reported social stressors in their lives, and for women the reports were linked to higher NALs, a risk factor for poor health. It is also important to distinguish between types of social stressors. For instance, in this survey, some involved direct conflict with others, arguably more deleterious than those involving "worrying" about others, which seems to presume a certain amount of positive social connection.

Table 8.1 Relative levels of mean neuroendocrine allostatic load (NAL) as a function of demographic, social connectedness, and psycho-social stressor variables – estimated total Taiwanese population (ages 54 to 91, year 2000)

Variables	Ratio of NAL means	% (N)
Demographics		
Sex		
Male	1	58 (585)
Female	1.9***	42 (431)
Age		
54–64	1	37 (380)
65–79	1.2**	54 (546)
80+	1.6**	9 (90)
Education		
High (> primary)	1	59 (596)
Low (≤ primary)	1.3**	41 (420)
Ethnicity		
Mainlander	1	17 (173)
Hakka/Fukienese	0.97	83 (842)
Social connectedness		
Marital status		
Married	1	75 (721)
Widowed	1.3**	25 (245)
Lives w/married son		
Yes	1	42 (423)
No	0.95	58 (593)
Lives alone		
No	1	93 (942)
Yes	1.1	7 (74)
Group participation		
Yes	1	44 (449)
No	1.1	56 (567)
Psycho-social factors		
Current familial stressors		
Family's work situation		
No	1	78 (743)
Yes	1.1	22 (211)
Family's financial situation		
No	1	75 (714)
Yes	1.2*	25 (243)
Family's health		
No	1	79 (754)
Yes	1.0	21 (206)
Family's marital situation		
No	1	78 (736)
Yes	1.2	22 (209)
Familial tension/conflict		
No	1	94 (895)
Yes	1.0	6 (60)
Other familial stressor (volunteered)		
No	1	99 (989)
Yes	1.2	1 (6)

Note: * Significant at 5%; ** Significant at 1%; *** Significant at .1%. NAL is scored using one-tailed cut-off points either at the 25th or 75th percentile (see Chapters 6 and 7). Significance levels arerelative to the baseline category. Bivariate analysis based on weighted survey data.

Source: Author's calculations based on the 2000 SEBAS (Goldman and Weinstein 2003).

Table 8.2 Percent reporting various stressors and stressor duration in years, estimated Taiwanese population (ages 54 to 91, year 2000), by sex

	% Reporting stressor		Duration of stressor in years[+]			
Stressor	Men	Women	Men Mean[++]	Range	Women Mean[++]	Range
Life event (social)						
Widowhood	12	34***	10.3	0–40	14.6	0–49
Psycho-social						
Family's work situation	22	27	1.1	0–30	1.7*	0–50
Family's financial situation	24	33*	1.5	0–42	2.4*	0–50
Family's health	20	25	1.9	0–89	2.1	0–50
Family's marital situation	20	29**	1.2	0–28	1.8**	0–50
Familial tension/conflict	6	7	0.5	0–31	0.8	0–30
Other familial stressor (volunteered)	0.003	0.01	0.09	0–40	0.04	0–8
≥ 1 psycho-social stressor	44	53*	--	--	--	--
Total psycho-social years stressed	--	--	6.2	0–146	8.8**	0–150

Note: *, **, and *** represent statistical significance at the .05, .01, and .001 levels, respectively. Tabulations based on weighted survey data.

[+] For determining the statistical significance of sex in regards to stressor length, length of stressor was the dependent variable in a linear regression with only sex and age included as covariates. For determining the statistical significance of sex in regards to total psycho-social years stressed, total psycho-social years stressed was the dependent variable in a linear regression with sex, age, and number of stressors reported included as covariates.

[++] For tabulations of the widowhood mean, only those widowed are included since the analysis of stressor length confines itself to those who have lost a spouse. In contrast, calculations of the mean for the psychosocial stressors do include zero values (i.e. those who do not report the stressor).

Source: Author's tabulations based on the 2000 SEBAS (Goldman and Weinstein 2003).

Table 8.3 Estimated regression results with neuroendocrine allostatic load (NAL), scored using different methods, as the dependent variable – Taiwanese men (ages 54 to 90, year 2000)

	Cut-point method of scoring						**Summed z-score method of scoring**	
	Linear regression Percent cut-off points			Ordered logistic regression Percent cut-off points			Linear regression No. outliers removed	
	10%	15%	25%	10%	15%	25%	2	0
Widowed	-.03	-.06	-.03	-.08	-.34	-.24	.09	.19
	(.655)	(.568)	(.857)	(.815)	(.356)	(.465)	(.675)	(.437)
Lives alone	-.09	-.18	-.16	-.58	-.66	-.27	-.16	-.22
	(.291)	(.065)	(.413)	(.391)	(.255)	(.636)	(.455)	(.348)
Does not live with married son	-.01	-.02	-.04	-.03	-.10	-.12	-.10	-.13
	(.772)	(.639)	(.472)	(.912)	(.529)	(.356)	(.467)	(.259)
Participates in no group activity	.07	.11	**.12**	.44	.36	.29	.14	**.17**
	(.079)	(.059)	**(.041)***	(.051)	(.079)	(.057)	(.078)	**(.048)***
Reported family stressors (0-6)	.01	-.01	-.02	.08	-.04	-.05	-.04	-.05
	(.813)	(.673)	(.637)	(.611)	(.717)	(.555)	(.412)	(.361)
Total psycho-social years stressed	-.00	.00	.00	-.01	.00	.00	-.00	-.00
	(.472)	(.473)	(.437)	(.242)	(.656)	(.656)	(.535)	(.751)
Education (years)	.01	.01	.00	.04	.02	.01	.01	.00
	(.298)	(.339)	(.757)	(.167)	(.499)	(.829)	(.767)	(.960)
Age (years)	**.01**	**.02**	**.02**	**-32**	**.06**	**.05**	**.03**	**.03**
	(.031)*	**(.001)****	**(.000)*****	**(.000)*****	**(.001)*****	**(.000)*****	**(.017)****	**(.010)****
Mainlander	-.06	-.12	-.08	-.35	-.36	-.08	.01	.00
	(.433)	(.149)	(.341)	(.333)	(.218)	(.699)	(.969)	(.998)
Urban residence	-.06	-.05	-.03	-.36	-.09	-.08	-.14	-.07
	(.223)	(.467)	(.683)	(.182)	(.703)	(.695)	(.201)	(.567)
N	505	505	505	505	505	505	505	505

Note: *, **, and *** represent statistical significance at the .05, .01, and .001 levels, respectively. Precise levels of statistical significance are inside the parentheses. All regressions control for medication use, diet, exercise, drinking, betel quid chewing, and smoking. Analysis based on weighted survey data.

Source: Author's calculations based on the 2000 SEBAS (Goldman and Weinstein 2003).

Table 8.4 Estimated regression results with neuroendocrine allostatic load (NAL), scored using different methods, as the dependent variable – Taiwanese women (ages 54 to 91, year 2000)

	Cut-point method of scoring						Summed z-score method of scoring	
	Linear regression Percent cut-off points			Ordered logistic regression Percent cut-off points			Linear regression No. outliers removed	
	10%	15%	25%	10%	15%	25%	2	0
Widowed	-.09	-.14	-.16	-.14	-.17	-.24	-.20	-.17
	(.333)	(.179)	(.162)	(.597)	(.498)	(.230)	(.359)	(.406)
Lives alone	-.15	-.01	**.52**	-.15	.12	**.90**	.27	.28
	(.398)	(.922)	**(.006)****	(.728)	(.600)	**(.012)***	(.315)	(.326)
Does not live with married son	.05	.04	-.01	.13	.09	.05	.00	.03
	(.549)	(.524)	(.939)	(.596)	(.578)	(.811)	(.993)	(.855)
Participates in no group activity	.02	-.01	-.01	-.03	-.02	-.08	-.12	-.12
	(.791)	(.903)	(.873)	(.856)	(.867)	(.584)	(.406)	(.398)
Reported family stressors (0-6)	**.10**	**.11**	**.12**	**.26**	**.19**	**.20**	**.26**	**.26**
	(.026)*	**(.040)***	**(.015)***	**(.023)***	**(.050)***	**(.025)***	**(.005)****	**(.004)****
Total psycho-social years stressed	.00	-.00	-.00	.00	-.00	-.00	-.01	-.01
	(.895)	(.644)	(.749)	(.870)	(.892)	(.937)	(.186)	(.180)
Education (years)	-.01	.00	.01	.02	.02	.04	.00	.01
	(.731)	(.991)	(.314)	(.659)	(.453)	(.212)	(.958)	(.844)
Age (years)	**.02**	**.02**	**.02**	**.06**	**.05**	**.04**	**.04**	**.04**
	(.001)***	**(.004)****	**(.047)***	**(.001)****	**(.006)****	**(.033)***	**(.031)**	**(.043)***
Mainlander	.09	.15	.15	-.00	.26	.22	.33	.33
	(.767)	(.625)	(.603)	(.995)	(.667)	(.693)	(.448)	(.417)
Urban residence	.09	.11	.11	.17	.17	.20	.20	.18
	(.394)	(.352)	(.485)	(.577)	(.523)	(.503)	(.477)	(.524)
N	375	375	375	375	375	375	375	375

Note: *, **, and *** represent statistical significance at the .05, .01, and .001 levels, respectively. Precise levels of statistical significance are inside the parentheses. All regressions control for medication use, diet, exercise, drinking, betel quid chewing, and smoking. Analysis based on weighted survey data.

Source: Author's calculations based on the 2000 SEBAS (Goldman and Weinstein 2003).

Table 8.5 Estimated regression results with neuroendocrine allostatic load (NAL), scored using different methods, as the dependent variable – widowed Taiwanese men (ages 54 to 90, year 2000)

	Cut-point method of scoring						Summed z-score method of scoring	
	Linear regression Percent cut-off points			Ordered logistic regression Percent cut-off points			Linear regression No. outliers removed	
	10%	15%	25%	10%	15%	25%	2	0
Years widowed	.02	.03	.07	.38	.12	.13	.06	.00
	(.118)	(.141)	(.027)	(.112)	(.335)	(.151)	(.103)	(.995)
Years widowed squared	-.00	-.00	-.00	-.01	-.00	-.00	-.00	-.00
	(.080)	(.295)	(.061)	(.098)	(.486)	(.179)	(.267)	(.963)
Lives alone	-.09	-.11	.30	-1.06	-1.37	.69	-.04	.061
	(.492)	(.506)	(.275)	(.238)	(.177)	(.398)	(.938)	(.897)
Does not live with married son	-.11	-.33	**-.60**	-1.37	-1.91	**-1.64**	-.49	-.73
	(.386)	(.075)	**(.043)***	(.258)	(.117)	**(.045)***	(.244)	(.178)
Participates in no group activity	.09	.10	.48	1.47	.65	1.03	.46	.59
	(.464)	(.620)	(.087)	(.221)	(.579)	(.178)	(.328)	(.237)
Reported family stressors (0-6)	.08	.14	-.06	**93**	.70	-.13	.14	-.05
	(.138)	(.097)	(.667)	**(.002)****	(.077)	(.710)	(.485)	(.811)
Total psycho-social years stressed	**-.02**	**-.04**	.00	**-.26**	**-.17**	.01	**-.06**	-.01
	(.038)*	**(.010)****	(.839)	**(.005)****	**(.016)***	(.855)	**(.038)***	(.855)
Education (years)	.00	.02	.03	-.07	.06	.04	.06	.05
	(.939)	(.347)	(.402)	(.494)	(.597)	(.624)	(.144)	(.277)
Age (years)	.26	.01	**.43**	**.24**	.07	**.09**	.02	.08
	(.160)	(.445)	**(.048)***	**(.007)****	(.257)	**(.031)***	(.338)	(.166)
Mainlander	.36	.26	.03	**3.9**	2.05	.77	.77	.48
	(.067)	(.211)	(.993)	**(.041)***	(.159)	(.357)	(.317)	(.513)
Urban residence	-.06	-.13	-.09	.39	-.01	-.04	-.82	-.18
	(.618)	(.507)	(.739)	(.689)	(.990)	(.946)	(.063)	(.780)
Joint F-test (widowhood and widowhood squared terms)	(.220)	(.286)	(.094)	(.266)	(.582)	(.364)	(.202)	(.989)
N	71	71	71	71	71	71	71	71

Note: *, **, and *** represent statistical significance at the .05, .01, and .001 levels, respectively. Precise levels of statistical significance are inside the parentheses. All regressions control for medication use, diet, exercise, drinking, betel quid chewing, and smoking. Analysis based on weighted data.
Source: Author's calculations based on the 2000 SEBAS (Goldman and Weinstein 2003).

Table 8.6 Estimated regression results with neuroendocrine allostatic load (NAL), scored using different methods, as the dependent variable – widowed Taiwanese women (ages 54 to 91, year 2000)

	Cut-point method of scoring						Summed z-score method of scoring	
	Linear regression Percent cut-off points			Ordered logistic regression Percent cut-off points			Linear regression No. outliers removed	
	10%	15%	25%	10%	15%	25%	2	0
Years widowed	.01	.03	.03	.03	.07	.06	.02	.02
	(.691)	(.177)	(.338)	(.705)	(.267)	(.279)	(.708)	(.725)
Years widowed squared	-.00	-.00	-.00	-.00	-.00	-.00	-.00	-.00
	(.631)	(.186)	(.336)	(.685)	(.268)	(.266)	(.571)	(.591)
Lives alone	-.15	-.10	**.61**	-.27	-.19	**1.35**	.42	.41
	(.394)	(.463)	**(.005)***	(.663)	(.640)	**(.004)****	(.317)	(.380)
Does not live with married son	**.22**	**.36**	.10	**.59**	**.96**	.25	.27	.30
	(.014)*	**(.003)****	(.551)	**(.045)***	**(.019)***	(.508)	(.267)	(.209)
Participates in no group activity	-.08	-.07	-.02	-.24	-.24	-.03	-.16	-.20
	(.580)	(.615)	(.892)	(.589)	(.567)	(.938)	(.686)	(.608)
Reported family stressors (0-6)	.09	**.13**	**.17**	.31	**.35**	.36	**.26**	.24
	(.081)	**(.030)***	**(.035)***	(.071)	**(.039)***	(.076)	**(.050)***	(.065)
Total psycho-social years stressed	.00	-.00	.00	.01	.00	.00	-.01	-.00
	(.504)	(.953)	(.685)	(.582)	(.917)	(.661)	(.315)	(.462)
Education (years)	.01	.03	.04	.02	.08	.10	.04	.05
	(.748)	(.122)	(.092)	(.801)	(.129)	(.060)	(.376)	(.288)
Age (years)	.02	**.03**	.03	.06	**.08**	.06	.05	.05
	(.102)	**(.016)***	(.054)	(.109)	**(.015)***	(.055)	(.084)	(.098)
Mainlander	-.28	-.25	-.44	-.80	-.72	-1.03	-.49	-.52
	(.304)	(.479)	(.160)	(.370)	(.495)	(.161)	(.330)	(.316)
Urban residence	.20	.28	.20	.54	.67	.51	.42	.44
	(.140)	(.052)	(.277)	(.156)	(.087)	(.216)	(.367)	(.317)
Joint F-test (widowhood and widowhood squared terms)	(.878)	(.409)	(.632)	(.922)	(.543)	(.547)	(.611)	(.642)
N	146	146	146	146	146	146	146	146

Note: *, **, and *** represent statistical significance at the .05, .01, and .001 levels, respectively. Precise levels of statistical significance are inside the parentheses. All regressions control for medication use, diet, exercise, drinking, betel quid chewing, and smoking. Analysis based on weighted data.

Source: Author's calculations based on the 2000 SEBAS (Goldman and Weinstein 2003).

Table 8.7 Extent to which indicators of a stressful life history and social disconnection investigated in this study support the hypothesis that neuroendocrine allostatic load (NAL) reflects the costs of cumulative stress

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Correlations between levels on indicators of a stressful life history/greater social disconnection and levels of NAL*

Correlated (positively)

Social connectedness variables

- Does not live with married son (amongst widowed Taiwanese women only)
- No group participation (support amongst all Taiwanese men only, but susceptible to reverse causality critique)

Not correlated

Demographic, social connectedness, and stress duration variables

- Low education
- Widowhood
- Lives alone
- Does not live with married son (amongst all Taiwanese men, all Taiwanese women, and widowed Taiwanese men)
- No group participation (amongst all women, widowed women, and widowed men)
- Length, psycho-social stress
- Length, widowhood

Unclear/problematic

Demographic variables

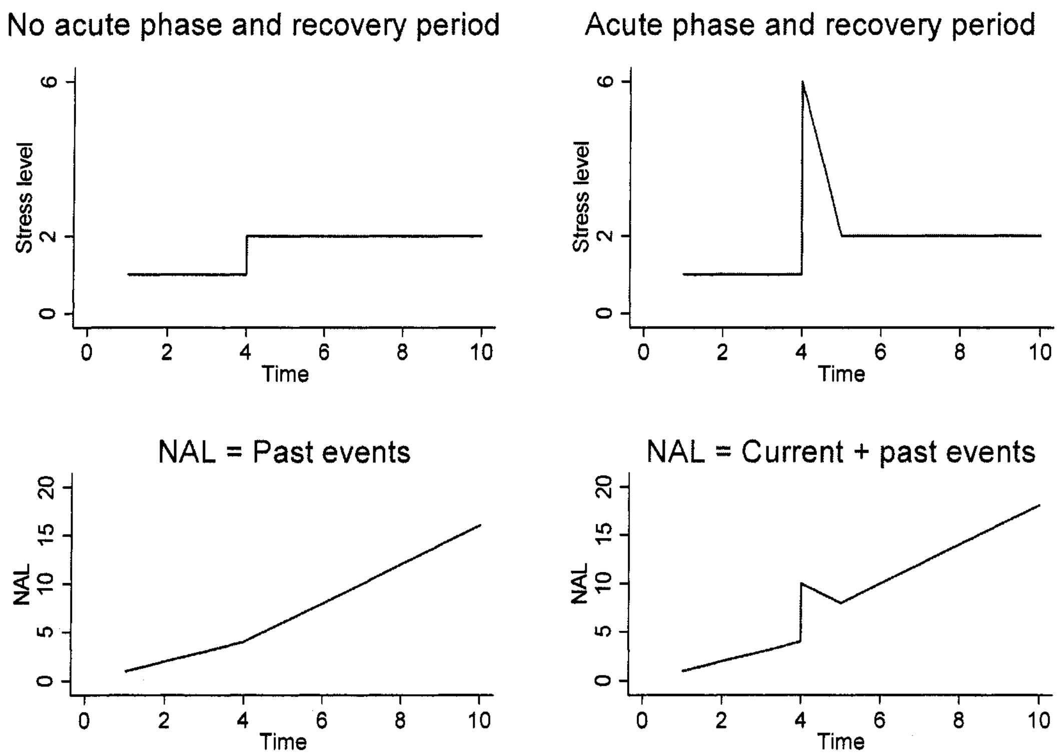
- Age. For the theory of allostatic load to hold, it is a necessary but not sufficient condition that NAL increases with age. However, other analysis conducted in this dissertation reveals that only DHEAS values convincingly head toward "higher risk" with age**.

Note: This table summarizes results from four separate regressions: all Taiwanese men, all Taiwanese women, widowed Taiwanese men, and widowed Taiwanese women. For more details see Tables 8.3 – 8.6.

* Unless otherwise indicated with a note in parenthesis, the variables in Table 8.7 refer to regression results generated for the four groups of respondents (i.e. all Taiwanese men, all Taiwanese women, widowed Taiwanese men, and widowed Taiwanese women).

** Please consult Chapter 7 for more details.

Figure 8.1 Permanent stressors with and without an acute phase and recovery period, and corresponding neuroendocrine allostatic load (NAL) trends with and without the influence of current events



Source: Created by this author.

Chapter 9

Conclusion

This dissertation was motivated by the hypothesis that increased stress levels amongst the socially disconnected might partly explain findings linking those who are socially impoverished to poor health outcomes downstream. The primary research question investigated in this work was the following: do those with stressful and socially disconnected life histories have riskier levels on a physiological measure that purportedly captures the body's costs in coping with such insults?

The physiological measure investigated here is called neuroendocrine allostatic load (NAL) and is comprised of four neuroendocrine biomarkers (cortisol, DHEAS, epinephrine, norepinephrine) measured at resting levels. Stressful and socially disconnected life histories were operationalized using variables including low education, widowhood, living alone, and subjective reports of personal stress histories. I analyzed data from the Social Environment and Biomarkers of Aging Study (SEBAS), a nationally representative survey of the Taiwanese elderly and near elderly conducted in 2000. In reference to the above question, the answer of this dissertation, in its limited scope, has been no. That is, no association was found between enduring stressors and the NAL measure. In contrast, report of current stress (amongst women) was positively correlated with NAL levels. Thus, baseline neuroendocrine levels may not be capturing the costs of coping with stress that (according to allostatic load theory) accumulates throughout the life course. In fact, the NAL measure might merely represent a fleeting state at the time of interview.

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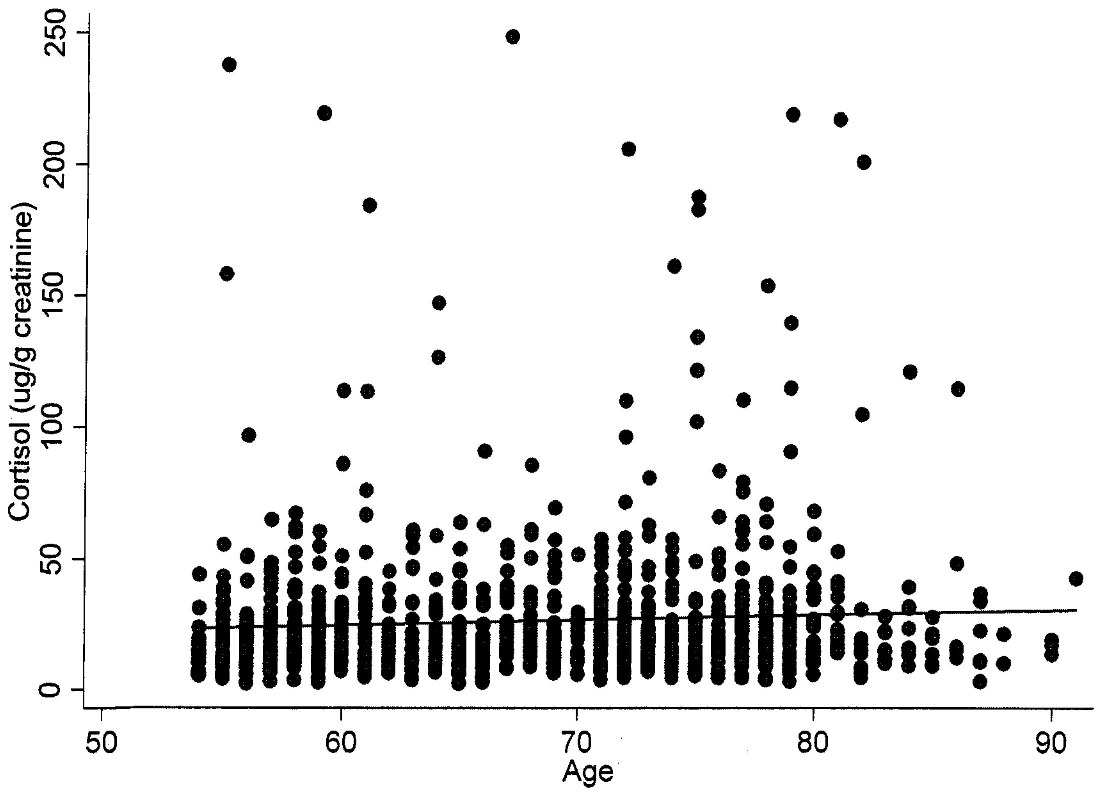
Appendix

Figures A.1 – A.4 are plots of survey respondents' absolute biomarker levels over age, for cortisol, DHEAS, epinephrine, and norepinephrine. The plots are overlaid with fitted values from OLS regressions, with the regression lines intended to suggest any population-level changes in biomarker values with increasing age. The regression lines in these figures form the basis of Figure 7.3, which presents not absolute values, but values relative to those at age 54.

Perhaps the most striking feature in the figures is the sharp decline in DHEAS levels, as well as an apparent narrowing of value range, over age (see Figure A.2). In regard to Figure A.1, note that it excludes two extreme, high cortisol values occurring at older ages, and with their inclusion the fitted regression line would be far more positively sloped. Also note the disproportionate amount of null epinephrine values in Figure A.3. Original values that read below assay sensitivity were assigned null values, and do not represent true zeros. Of the neuroendocrine biomarkers, for only epinephrine and DHEAS did some respondents have values that read below assay sensitivity (see Goldman and Weinstein 2003 for a more thorough discussion). It is unclear what the impact of the assigned null values has on the fitted regression lines.

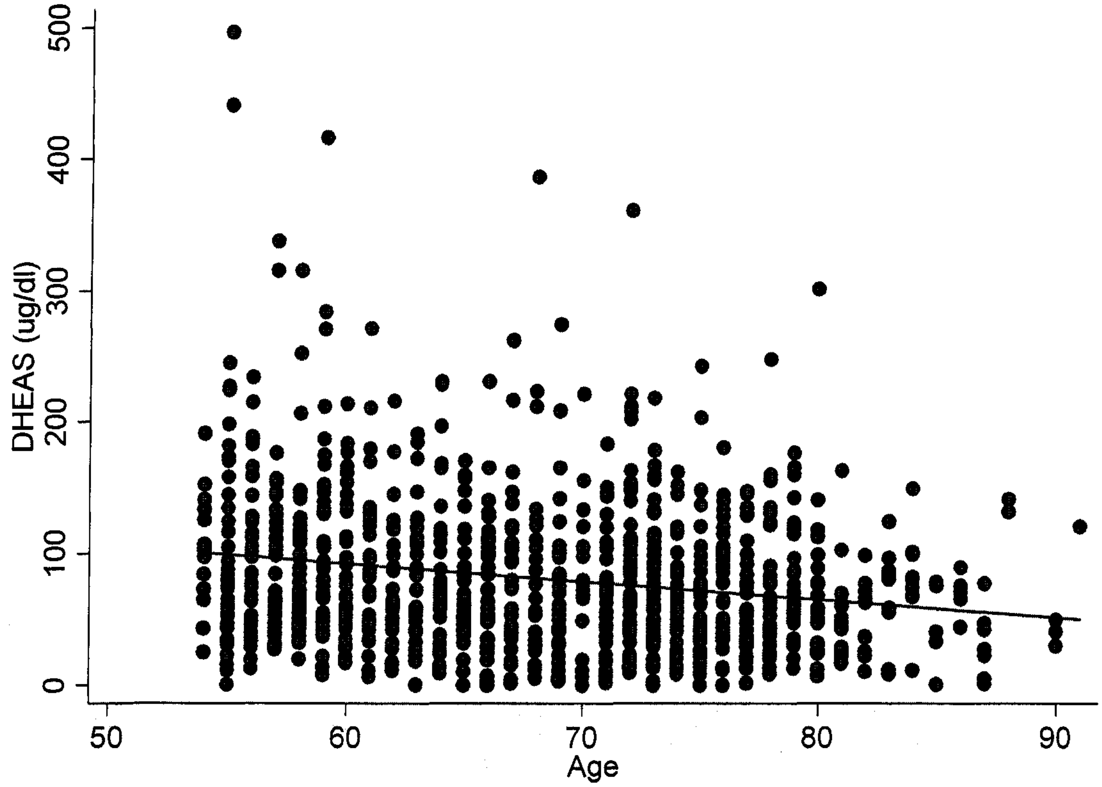
Figure A.1 Plot of cortisol over age with fitted regression line – sample population, Taiwan (ages 54 to 91, year 2000, both sexes combined)



Note: Plot and regression based on unweighted survey data. The plot and regression exclude the two outlying values.

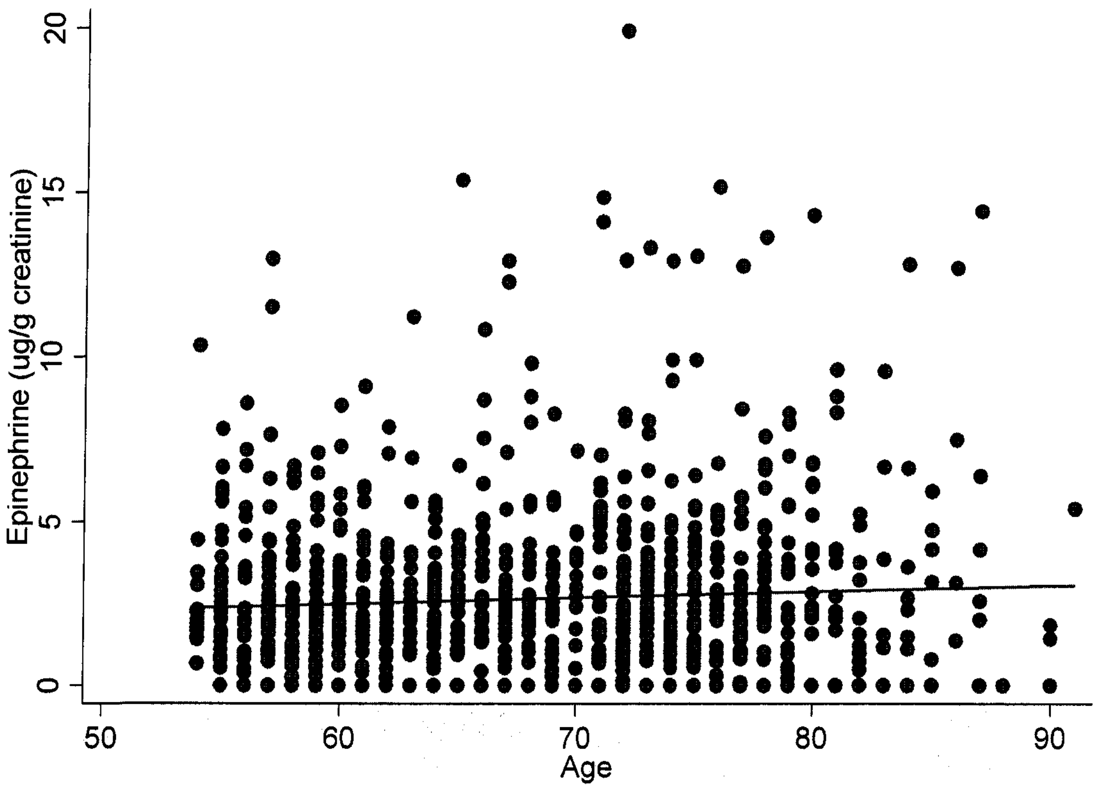
Source: Author's plot and regression based on the 2000 SEBAS (Goldman and Weinstein 2003).

Figure A.2 Plot of DHEAS over age with fitted regression line – sample population, Taiwan (ages 54 to 91, year 2000, both sexes combined)



Note: Plot and regression based on unweighted survey data.
Source: Author's plot and regression based on the 2000 SEBAS (Goldman and Weinstein 2003).

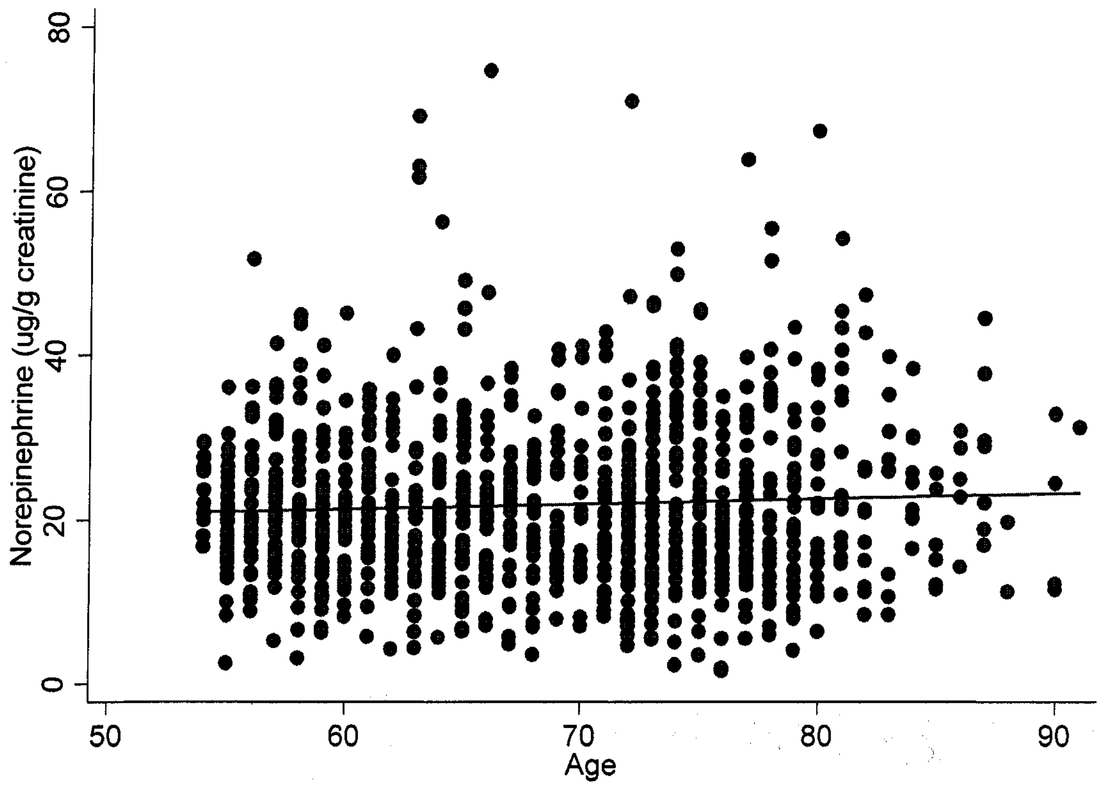
Figure A.3 Plot of epinephrine over age with fitted regression line – sample population, Taiwan (ages 54 to 91, year 2000, both sexes combined)



Note: Plot and regression based on unweighted survey data.

Source: Author's plot and regression based on the 2000 SEBAS (Goldman and Weinstein 2003).

Figure A.4 Plot of norepinephrine over age with fitted regression line – sample population, Taiwan (ages 54 to 91, year 2000, both sexes combined)



Note: Plot and regression based on unweighted survey data.
Source: Author's plot and regression based on the 2000 SEBAS (Goldman and Weinstein 2003).