PAA 2008 Abstract

Do biomarkers mediate the relationship between socioeconomic status and health in two older populations?

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Introduction

Throughout life, individuals, particularly those in the lower strata of socioeconomic status, confront numerous demands. In the face of repeated challenges, cumulative biological burden may arise from disruption in a process known as allostasis, defined as the ability of the body to adapt and maintain stability in its physiological systems (Korte et al. 2005; Sterling and Eyer 1988). While beneficial in the short-term, adaptation may eventually result in physiological dysregulation if biological mediators (i.e. neurotransmitters, hormones, and proteins from the immune system) are released too often or are not efficiently terminated (Korte et al. 2005; McEwen 2002). The consequences of such physiological dysregulation, or allostatic load (McEwen and Stellar 1993), include wear-and-tear on diverse organs and tissues and ultimately a range of chronic conditions and diseases (McEwen 2002). While many studies have linked low socioeconomic status, measured primarily through education, income and occupation, to poor health, there is still much to be learned about the underlying mechanisms that explain these strong associations. Thus, it is not surprising that allostatic load has emerged as an appealing framework for relating environmental stressors over the life-course to changes in health status later in life.

Studies in the U.S. have provided evidence that physiological measures mediate the relation between socioeconomic status and health outcomes. For example, analyses based on the data from the MacArthur Studies of Successful Aging have estimated that about one third of socioeconomic differences in mortality among the elderly can be explained by differences in the allostatic load, primarily in the cardiovascular risk components (Seeman et al. 2004). Strong associations between socioeconomic status and biomarkers of chronic disease have been found in other studies in the U.S., as well as in Great Britain, and several other Western countries (e.g. Germany, Canada and Sweden) (Brunner et al. 1997, Hemingway et al 2003, Winkleby et al. 1998). However, these relationships may not be ubiquitous. For example, a recent study based on data from Taiwan found that relatively few biomarkers associated with the cardiovascular, neuroendocrine, and immune systems were significantly associated with education and income (Dowd and Goldman 2006).

These contradictory findings underscore the need to examine the consequences of life challenges on health status in different cultural and socioeconomic settings. The purpose of this paper is to start to fill this gap in knowledge by examining whether biomarkers associated with

the stress response mediate the relationship between socioeconomic status and health in two different populations: Taiwan and Costa Rica. Our analysis benefits from two recent nationally-representative surveys that contain a comprehensive set of biological markers. We test for the relationship between ten individual biomarkers and three health outcomes, including self-rated health and measures of chronic conditions and functional limitations. The findings provide an opportunity to identify the mechanisms linking social and physical dimensions in socioeconomic settings outside the U.S and Europe.

Materials and Methods

Data

Data for this analysis come from two sources: the 2000 Social Environment and Biomarkers of Aging Study (SEBAS) and the Costa Rican Study on Longevity and Healthy Aging (CRELES). The SEBAS is based on a follow-up of the Survey of Health and Living Status of the Near Elderly and Elderly in Taiwan, a nationally representative longitudinal survey (including the institutionalized population) that was administered four times between 1989 and 1999. The initial survey consisted of 4,049 eligible respondents who were aged 60 years and older in 1989. In 1996, the study added a new cohort of 2,462 near-elderly respondents who were aged 50 to 66 years in 1996. The two cohorts were interviewed again in 1999. In 2000, a subsample of respondents for SEBAS were drawn randomly from the combined near-elderly and elderly cohorts who were surviving in 1999. Persons aged 70 years and older in 1999 and persons in urban areas were oversampled. SEBAS consists of two parts: a face-to-face in-home interview and a medical exam. Among the 1,713 respondents selected for this study, a total of 1,497 answered face-to-face in-home interviews (a response rate of 92 percent among survivors). The interviews comprise information regarding demographic and socioeconomic characteristics, physical health, health-related behaviors, psychological well-being and health service utilization. Respondents were interviewed in their homes between July and December 2000.

Among the 1,497 participants who completed in-home interviews, 1,023 participated in the medical examinations (68% of those interviewed). Disproportionately high non-participation rates were found among the healthiest respondents as well as the least healthy, with persons who received the medical exam reporting the same average health status as those who did not. Results

presented elsewhere suggest that, in the presence of controls for age, estimates from the medical exam portion of SEBAS are unlikely to be seriously biased.

SEBAS respondents collected a 12-hour urine specimen overnight and accompanied a member of the Bureau of Health Promotion in Taiwan to a hospital visit the following morning. During the hospital visit, respondents provided a spot urine sample and a fasting blood sample, and staff members measured the respondents' waist and hip circumference, height, weight, and blood pressure. The clinical data provided biological markers that are comparable to those collected in recent surveys in the U.S (Seeman et al. 1997; Singer and Ryff 1999).

The CRELES is an on-going longitudinal study of a nationally representative sample of 3,000 adults born in 1945 or before (ages 60 and over at the first interview) and residing in Costa Rica in the year 2000, with over-sampling of the older old. For this analysis we use the data for the first wave of interviews, conducted in 2004. A sample of 9,600 individuals was randomly selected from the 2000 census database after stratification by 5-year age groups. Sampling fractions ranged from 1.1% among those born in 1941-45 to 100% for the born before 1905. This sub-sample included near 5,300 individuals and covers 59% of Costa Rican territory, yielding the following non-response rates: 19% of the individuals deceased by the contact date, 18% were not found in the field, 2% moved to other addresses, 2% rejected the interview, and 2% remained as pendant interviews after several visits (likely rejections). Among those interviewed, 95% of the participants provided blood sample, 92% collected urine, 91% had anthropometric measures, and 24% required a proxy to answer the questionnaire.

The data and specimens in the CRELES study were collected at the participants' homes, usually in two visits. In the first visit, participants provided informed consent and answered a 90-minute long questionnaire (including some mobility tests and two blood-pressure measures) as well as a 10-minute frequency of tracer food consumption questionnaire. In a second visit early the next day, fasting blood samples were collected by venipuncture: 1 EDTA purple top tube (for 3-4 ml. of whole blood) and 2 serum separating tubes (SST), with a clot activator (for 10-12 ml. of blood, to obtain 4-6 ml. of serum). In this visit, the field team also picked up a cooler containing 12-hour overnight urine and took the anthropometric measures. All field data were collected using Personal Digital Assistants (PDAs), also known as palm computers, with software applications developed by CCP for this study.

Variables

Population-based studies on the biology of stress have used physiological markers pertaining to the cardiovascular, metabolic, immune, and neuroendocrine systems. In order to preserve comparability across populations, we limit the analysis in this paper to ten biomarkers that were ascertained in both surveys. Eight of these markers are measures of the metabolic syndrome. Two are measures of the neuroendocrine system: urinary cortisol and DHEAS. Whenever clinical cutoff values for biomarkers are available, we use these cutoff points to construct dichotomous variables for the given marker, coded as 1 when the respondent has a high risk value and 0 otherwise.

We include two indicators of body fatness: BMI and waist circumference. BMI, calculated as weight divided by height squared (Kg/m^2), is recoded into a dichotomous variable that takes the value of one for respondents who have values larger than 30 and lower than 18.5. To look at the effects of waist circumference, we code values larger than 88 centimeters for women and 102 for men as high risk. Two markers for hypertension – systolic and diastolic blood pressure – derived from readings using a mercury sphygmomanometer, are coded as dichotomous variables that take the value of one for respondents who have values larger than 120 and 80 mmHg respectively. We include measures of total serum cholesterol (risk values larger than or equal to 250 mg/dL) and triglycerides (risk values larger than 200 mg/dL), taken from blood specimens. Two biomarkers relate to glucose metabolism – fasting glucose and glycosylated hemoglobin (HbA_{1c}) . Cutoff values for these measures are 100 mg/dl and 6.5 mmol/L, respectively.

In the absence of guidelines for normal ranges of nonclinical markers, we use cut points for cortisol and DHEAS that are based on the distribution of these biomarkers in the surveys. These biomarkers take the value 1 for respondents who have values in the lowest quartile (DHEAS) and in the lowest or highest quartiles (cortisol), with the cutoff points calculated separately for men and women.

Health outcomes comprise three measures. We use self-rated health, reported according to the conventional 5-point ordinal scale: excellent, very good, good, fair and poor. We also include self-reports of chronic conditions and functional limitations that are comparable in both surveys and that have been shown to reflect health deterioration at older ages. Chronic conditions are recorded as a count of seven common serious conditions in Costa Rica and Taiwan: high

blood pressure, diabetes, cancer or malignant tumor, chronic respiratory diseases, heart problems, stroke, and cataracts in the eye. Functional limitations are based on self-reports of four mobility limitations (lifting or carrying weight, raising arms above shoulders, walking many blocks and climbing stairs), two measures of instrumental activities of daily living (buying personal items and managing money), and three measures of activities of daily living (bathing, eating, and toileting).

The preliminary analysis presented here includes only education as a measure of socioeconomic status. Education is coded in three-categories: no formal education, primary education (literate or 1 to 6 years of education), or secondary education (7+ years of education). All models include a linear control for age.

Analytic Strategy

To examine the associations between education and the physiological measures, we estimate, for each population, separate logistic regression models for each biomarker, controlling for age and educational attainment. We fit separate models for men and women because of sex differences in the biological mechanisms linking socioeconomic status and health (Dowd and Goldman 2006).

To test for the mediating effects of biomarkers in the relation between education and health, we estimate sex-specific models separately for Costa Rica and Taiwan. Ordered logistic regression models are used for self-rated health, and Poisson regression models for the counts of functional limitations and of chronic conditions. We compare two models for each health outcome. The first one controls only for age and education. In the second model, we add the ten individual biomarkers to the first model. In both populations, the multivariate models are based on unweighted data. Because of the multi-stage sampling design of SEBAS, we use a robust estimator of variance and adjust for clustering by primary sampling units (PSUs) to produce correct standard errors for all models based on these data. We limit our analysis to individuals 60 to 91 years old to make the age distributions consistent in both surveys. We use Stata 8.2 to estimate the models (StataCorp 2003).

Preliminary Results

Except for DHEAS and BMI, we find no statistically significant associations between education and the physiological measures in Taiwan (Table 1). These results are consistent with previous

analyses based on the Taiwan data but with a somewhat different set of biomarkers and cutoff points (Dowd and Goldman 2006). The number of significant associations between education and the probability of having high risk values of the biomarkers is also modest in Costa Rica, although we find statistically significant associations with BMI, waist circumference and glucose values among men, and significant associations with blood pressure and glucose levels among women (Table 2).

Education is related to self-rated and functional limitations health outcomes (Tables 3 and 4), but not surprisingly, we find no evidence that physiological measures of stress mediate the relationship between education and health in either country. That is, the coefficients on the education variables change relatively little with the inclusion of the biomarkers in the second model.

Future work will adjust for outliers in the biological data and include at least one additional measure of socioeconomic status (e.g. wealth). Given the large number of respondents with zero mobility limitations and zero chronic conditions we will consider using zero-inflated Poisson models for these health outcomes. We will also explore using a quadratic term for age and the inclusion of low values of diastolic and systolic blood pressure in the high risk range.

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Table 1 - Estimated Coefficients from logistic models of having high risk values of each biomarker, by education and sex. SEBAS, 2000

	BMI	Waist Circumference	Systolic BP	Diastolic BP	Glucose	HbA1c	Cholesterol	Triglycerides	DHEAS	Cortisol
Men										
No Education (omitted)										
1-6 years of Education	-0.7206	0.1225	0.6386	-0.0015	0.1512	-0.2135	-0.0492	0.7835	-0.3383	0.1631
	[0.3886]	[0.7333]	[0.3380]	[0.2673]	[0.3748]	[0.4409]	[0.3873]	[0.6270]	[0.2717]	[0.2932]
7+ years of Education	-0.766	-0.2973	0.4111	-0.1349	0.5521	-0.1646	-0.5298	0.3234	-1.4403**	-0.0849
	[0.5356]	[0.9360]	[0.3328]	[0.2822]	[0.3781]	[0.4590]	[0.5177]	[0.7697]	[0.2801]	[0.3114]
Number of observations	474	475	475	475	460	474	474	474	473	474
Women										
No Education (omitted)										
1-6 years of Education	-0.0334	-0.1542	0.278	-0.0562	0.158	-0.2316	-0.2827	0.2261	-0.3519	0.0993
	[0.2634]	[0.2428]	[0.2705]	[0.2674]	[0.1990]	[0.3216]	[0.3448]	[0.3687]	[0.2511]	[0.2553]
7+ years of Education	-1.9911*	-0.3856	0.067	-0.5344	-0.346	-0.3456	-0.4004	0.7989	-1.8728*	0.1301
	[0.9115]	[0.3377]	[0.4965]	[0.3700]	[0.3706]	[0.5272]	[0.6479]	[0.6151]	[0.8787]	[0.3051]
Number of observations	339	339	339	339	332	338	339	339	339	337

All models control for age
Standard errors in brackets
* significant at 5%; ** significant at 1%

Table 2 - Estimated Coefficients from logistic models of of having high risk values of each biomarker, by education and sex. CRELES, 2004-2006

	BMI	Waist Circumference	Systolic BP	Diastolic BP	Glucose	HbA1c	Cholesterol	Triglycerides	DHEAS	Cortisol
Men										
No Education (omitted)										
1-6 years of Education	0.2064	0.1821	0.0195	-0.046	0.2648	0.5279	0.1601	0.4456*	0.2802	-0.2402
	[0.2377]	[0.2073]	[0.2148]	[0.1540]	[0.1631]	[0.3376]	[0.2279]	[0.2121]	[0.1949]	[0.1695]
7+ years of Education	0.8075**	0.5355*	0.3938	-0.003	0.6361**	0.4402	0.4347	0.4844	0.2718	0.1651
	[0.2868]	[0.2631]	[0.3169]	[0.2102]	[0.2197]	[0.4243]	[0.2923]	[0.2721]	[0.2754]	[0.2293]
Number of observations	1131	1120	1172	1172	1107	1087	1111	1111	1094	971
Women										
No Education (omitted)										
1-6 years of Education	-0.1222	-0.2216	-0.0614	0.0235	0.2927*	-0.2849	0.2551	-0.0151	-0.0703	0.0762
	[0.1607]	[0.1562]	[0.2274]	[0.1476]	[0.1478]	[0.1974]	[0.1698]	[0.1751]	[0.1736]	[0.1592]
7+ years of Education	-0.3073	-0.3603	-0.5723*	-0.5548**	0.2412	-0.6788*	0.2508	0.0453	0.2317	0.025
	[0.2284]	[0.2120]	[0.2806]	[0.2002]	[0.2025]	[0.3011]	[0.2274]	[0.2378]	[0.2356]	[0.2201]
Number of observations	1351	1330	1400	1400	1331	1323	1340	1339	1319	1144

All models control for age
Standard errors in brackets
* significant at 5%; ** significant at 1%

Table 3 - Estimated regression coefficients for three health outcomes, by education and sex. SEBAS, 2000

	Men			Women		
	Self Rated Health	Functional Limitations	Chronic Conditions	Self Rated Health	Functional Limitations	Chronic Conditions
Model 1						
No Education (omitted)						
1-6 years of Education	-0.2501	-0.2900	0.0251	-0.5490*	-0.3324*	-0.0901
	[0.2108]	[0.1758]	[0.1363]	[0.2598]	[0.1656]	[0.1046]
7+ years of Education	-0.7636**	-0.7116*	0.0641	-1.1984*	-0.4909**	0.0265
	[0.2563]	[0.3211]	[0.1691]	[0.4738]	[0.1787]	[0.1384]
Model 2						
No Education (omitted)						
1-6 years of Education	-0.2456	-0.1662	-0.0048	-0.5729*	-0.2952	-0.0933
	[0.2135]	[0.1527]	[0.1316]	[0.2813]	[0.1603]	[0.1006]
7+ years of Education	-0.6715**	-0.4887	0.0141	-1.2074*	-0.3481	0.0228
	[0.2600]	[0.2548]	[0.1511]	[0.5493]	[0.1874]	[0.1271]
Number of observations	452	457	454	320	327	326

Model 1 controls for age. Model 2 controls for age and ten biomarkers: BMI, waist circumference, systolic blood pressure, diastolic blood pressure, fasting glucose, HbA1c, total cholesterol, triglycerides, DHEAS and cortisol

Standard errors in brackets

* significant at 5%; ** significant at 1%

Table 4 - Estimated regression coefficients for three health outcomes, by education and sex. CRELES, 2004-2006

	Men			Women		
	Self Rated Health	Functional Limitations	Chronic Conditions	Self Rated Health	Functional Limitations	Chronic Conditions
Model 1						
No Education (omitted)						
1-6 years of Education	-0.5527**	-0.2222**	0.0369	-0.3460*	-0.2423**	-0.0898
	[0.1658]	[0.0664]	[0.0755]	[0.1580]	[0.0527]	[0.0620]
7+ years of Education	-1.7620**	-0.5837**	-0.047	-1.5161**	-0.5620**	-0.0732
	[0.2237]	[0.1198]	[0.1073]	[0.2157]	[0.0892]	[0.0879]
Model 2						
No Education (omitted)						
1-6 years of Education	-0.5752**	-0.2335**	-0.0231	-0.3324*	-0.2141**	-0.0751
	[0.1675]	[0.0671]	[0.0764]	[0.1591]	[0.0531]	[0.0623]
7+ years of Education	-1.7798**	-0.5741**	-0.1251	-1.5343**	-0.5386**	-0.051
	[0.2262]	[0.1216]	[0.1089]	[0.2182]	[0.0899]	[0.0884]
Number of observations	885	794	851	1054	894	1024

Model 1 controls for age. Model 2 controls for age and ten biomarkers: BMI, waist circumference, systolic blood pressure, diastolic blood pressure, fasting glucose, HbA1c, total cholesterol, triglycerides, DHEAS and cortisol

Standard errors in brackets

* significant at 5%; ** significant at 1%