Life course stressors and physiological dysregulation in Taiwan and Costa Rica

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Outline

1. Motivation (precise physiological mechanisms ---> poor health)
2. Background (stress concepts & terms)
3. 1st Taiwanese project (SEBAS)
4. Costa Rican project (CRELES)
5. SEBAS II/Future directions

Uncovering mechanisms of the "black box"

↑Social connection --> ■ --> ↑Health

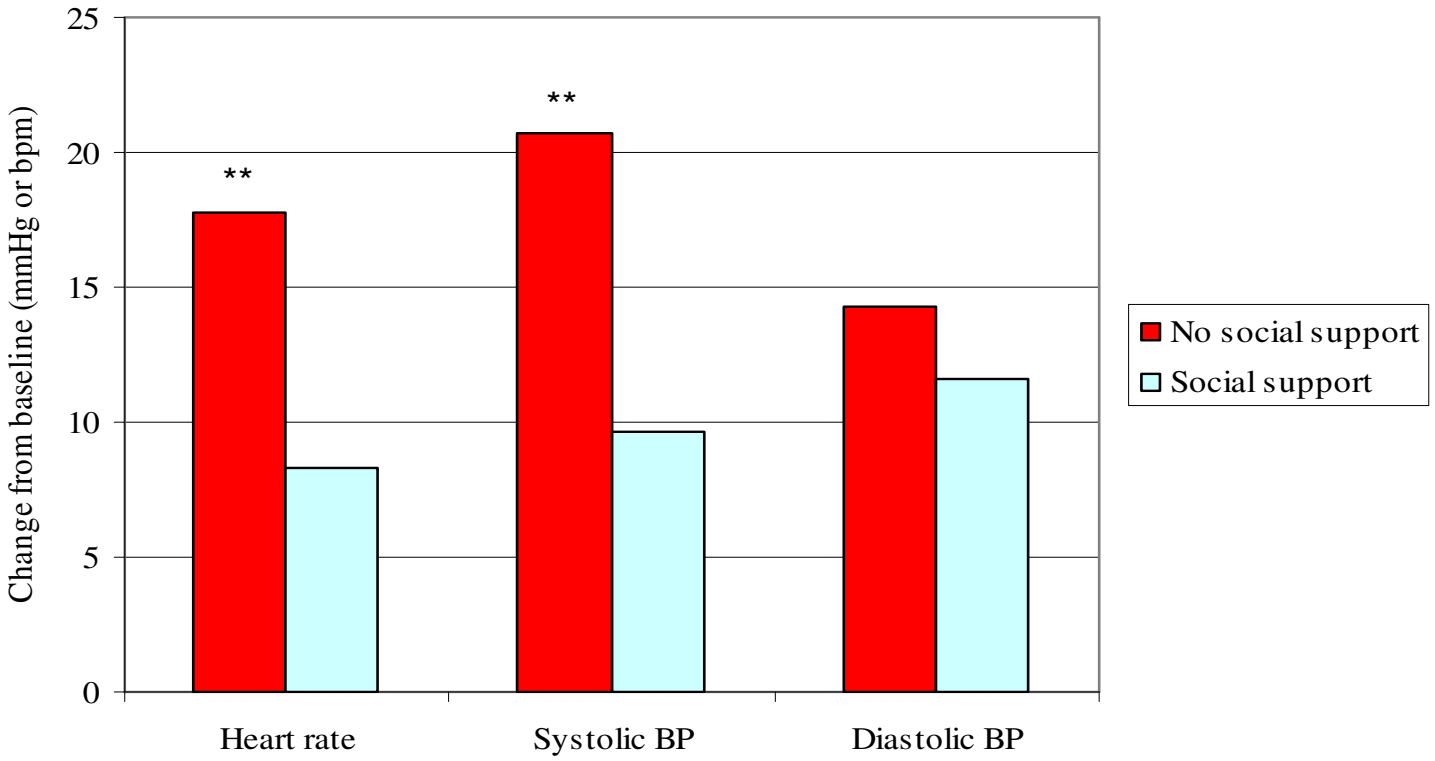
Marriage
Religious attendance
Other community participation
Number of friends

Mortality
Cardiovascular disease
Depression

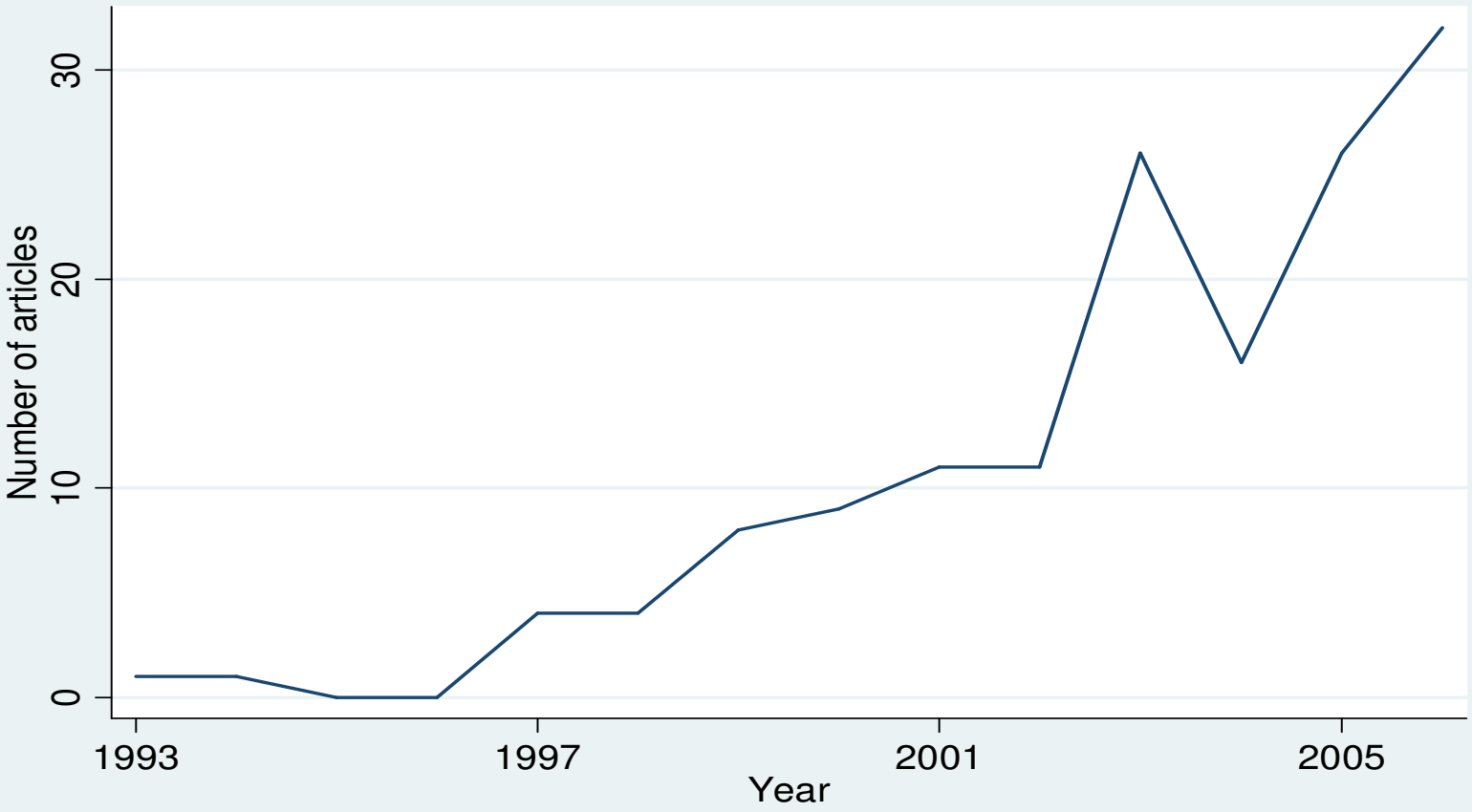
- Health consequences of similar magnitude as: low physical activity, obesity, and smoking
- Longitudinal studies have accounted for: health status and personality characteristics

↑ Social connection --> ↓ Stress --> ↑ Health

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



Articles on “allostasis” and “allostatic load”



1. Literature search conducted on Feb. 7, 2007
2. Number of retrieved articles in MEDLINE/PubMed for 'allostasis' and 'allostatic load' (1993-2006)

Allostatic theory: defining homeostasis and allostasis

- Homeostasis is the body's equilibrium or "ideal" steady-state
- Allostasis refers to all the physiological mechanisms that attempt to bring the body into homeostasis
- Allostatic mechanisms respond to all types of challenges (i.e., physical, psychological, acute, "day to day")

Allostatic theory: how “allostatic mechanisms” extend the idea of “homeostatic mechanisms”

- Allostasis emphasizes normal operating ranges of physiological parameters (e.g. different, flexible setpoints in contrast to fixed setpoints)
- Allostasis emphasizes the role of the brain/psyche in recognizing threats and orchestrating holistic responses
- Allostatic responses can learn from experience and can anticipate and respond (in advance) to challenges

Allostatic theory: defining allostatic load (AL)

- AL represents cumulative “wear and tear” on the body caused by activation of the allostatic systems

- AL accumulates over the life course and affects multiple biological systems

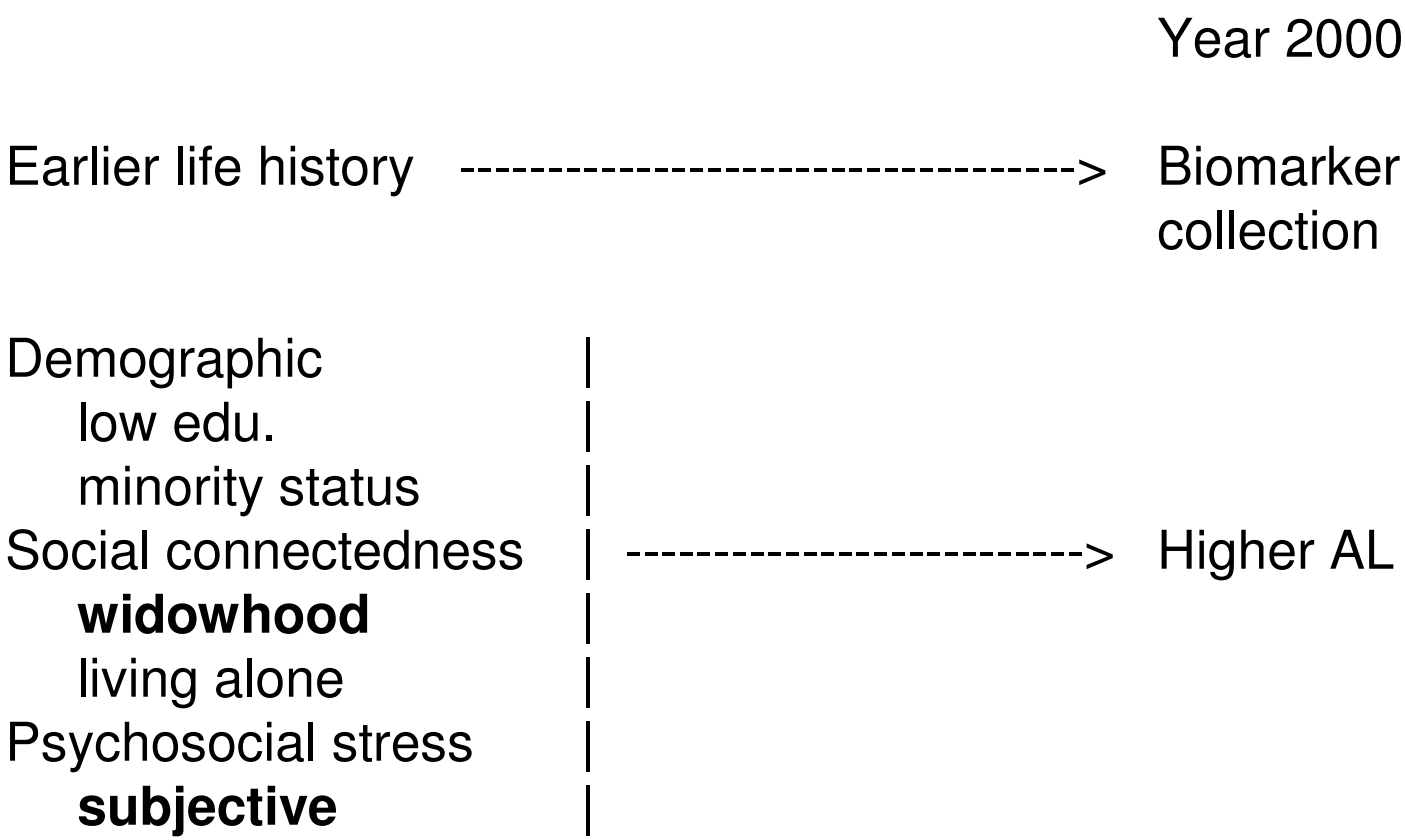
Allostatic load (AL)

- Predisease indicator -----> morbidity -----> mortality

(System dysregulation)

Research question & hypothesis

- Are various indicators of life stress linked to riskier neuroendocrine biomarker profiles?



Data: “Social Environment and Biomarkers of Aging Study” (SEBAS)

Strengths:

- Nationally representative survey
  (Taiwan, year 2000)
- Large (>1000 respondents)
- Wide age range (54-91)
- High response rate (>90% interview portion)

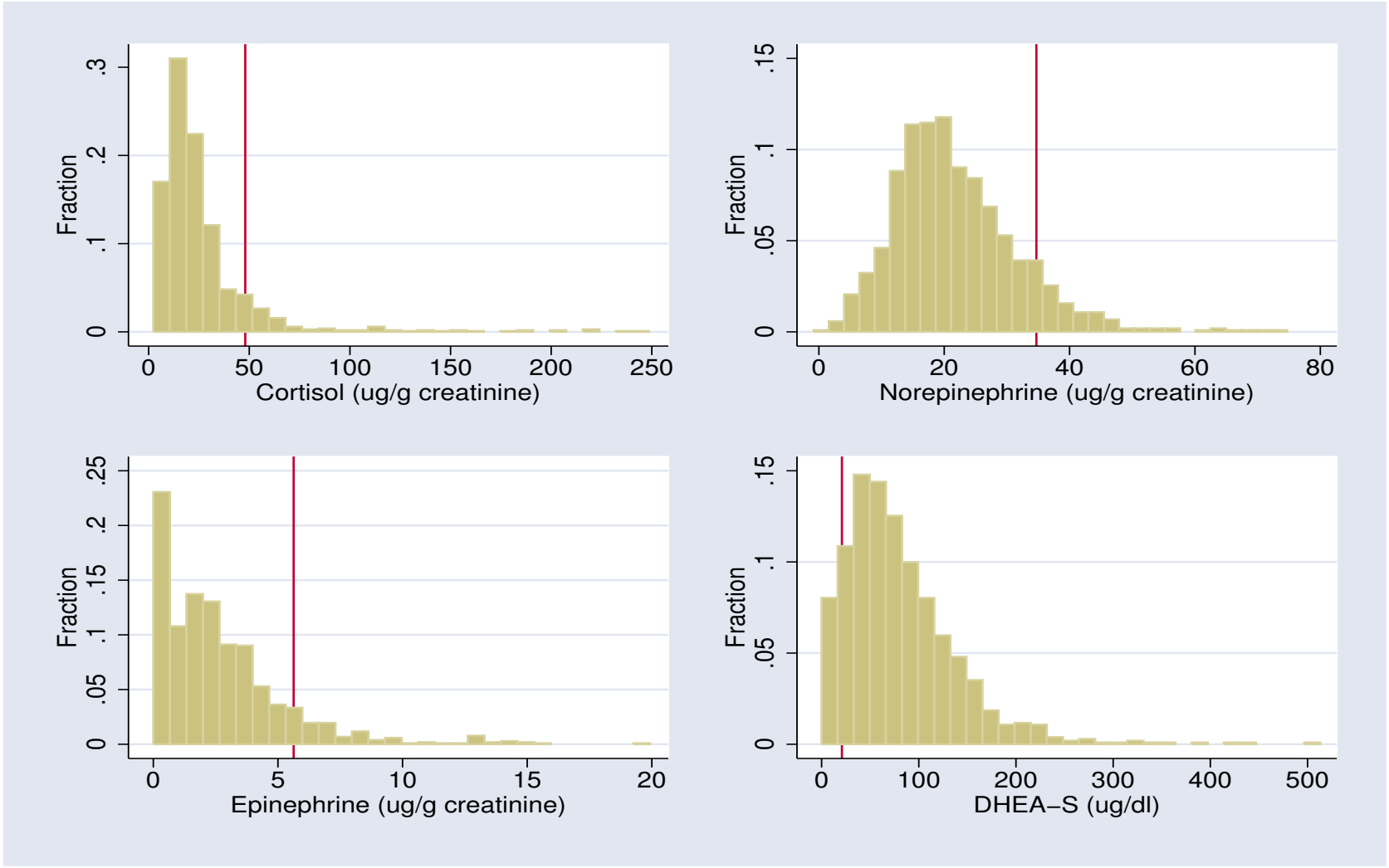
Data: dependent variable

"Neuroendocrine allostatic load" (NAL)

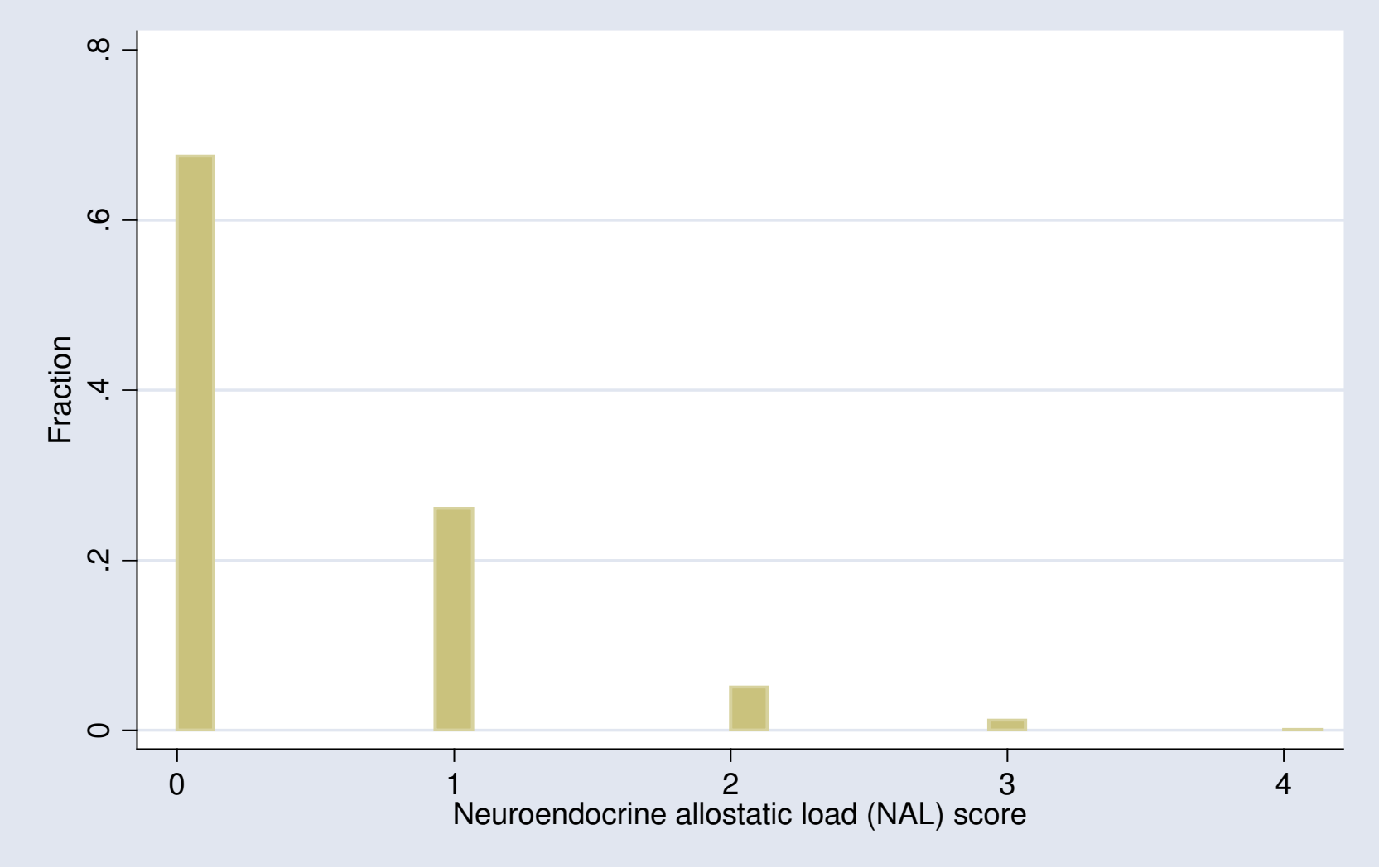
- Neuroendocrine markers represent the body's most immediate stress response
- Survey measures resting, nonstressed levels

Biomarkers	Physiologic systems
Epinephrine ----------> Norepinephrine	Sympathetic nervous system (SNS)
Cortisol ----------> DHEAS	Hypothalamic-pituitary-adrenal (HPA) axis

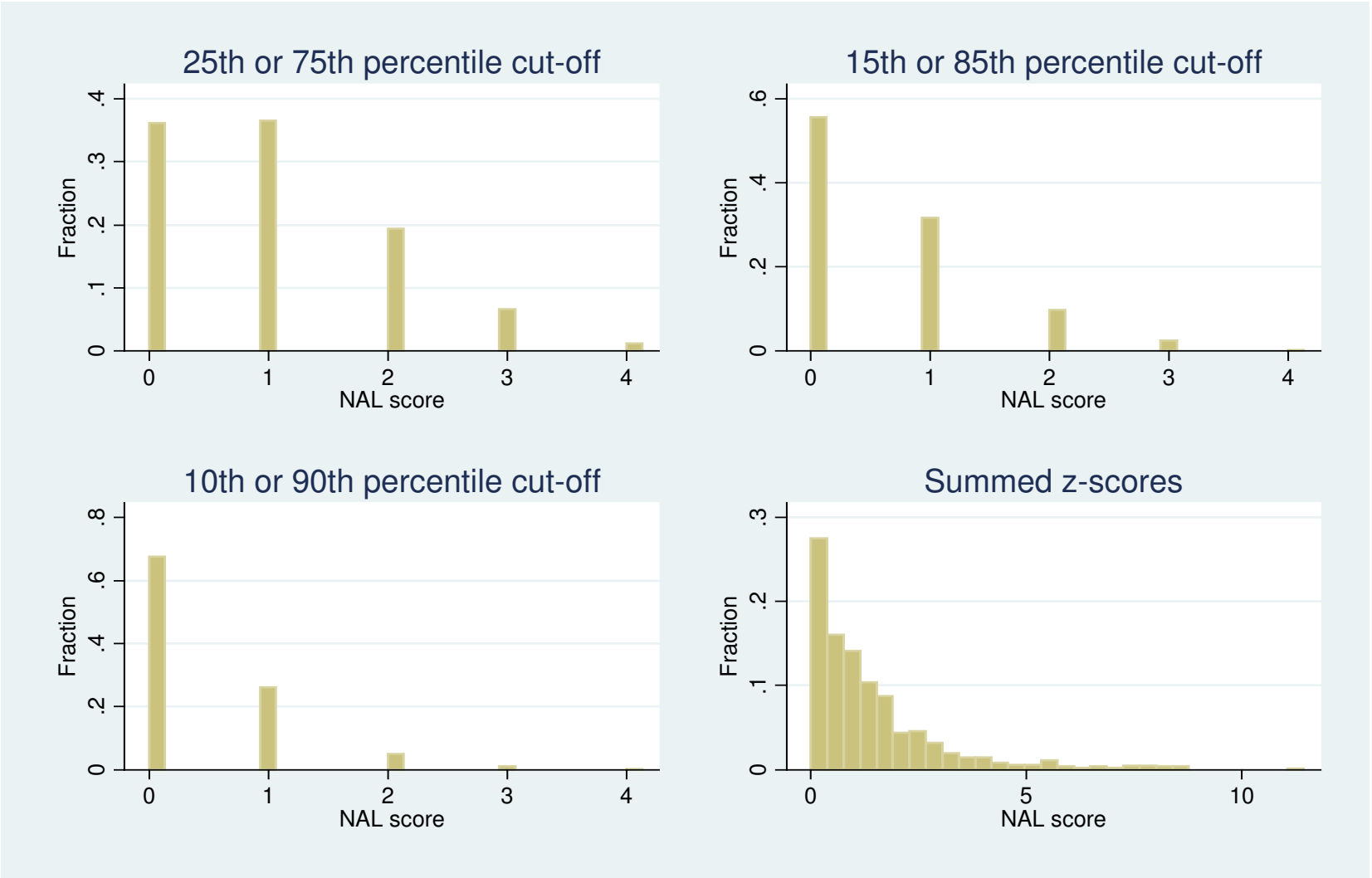
Distributions and cutpoints (10th or 90th percentile)



Distribution of NAL scores (10th or 90th percentile)



Distribution of NAL scores



Descriptive statistics (N = 880)

Variables	% or Mean (SD)	Range
Demographic		
Age (years)	68.3 (8.4)	54-90
Male sex	57%	--
Education (years)	5.3 (4.7)	0-17+
Urban residence (v. rural)	56%	--
Mainlander ethnicity (v. Taiwanese)	15%	--
Social connectedness		
Current marital status		
Married (v. widowed)	75%	--
Residence		
Lives with married son	44%	--
Lives alone	4%	--
Other	52%	--
Group participation		
Participant in 0 groups (v. ≥ 1 group)	53%	--
Psycho-social		
Current familial stressors	.93 (1.3)	0-5
Stressor length		
Widowhood	13.3 (11.0)	0-49
Total psycho-social years stressed	7.2 (16.2)	0-150

Duration of various stressors (in years)

	Men Mean	(Range)	Women Mean	(Range)
Life event (social)				
Widowhood	10.3	(0–40)	14.6	(0–49)
Psycho-social				
Family's work situation	1.1	(0–30)	1.7*	(0–50)
Family's financial situation	1.5	(0–42)	2.4*	(0–50)
Family's health	1.9	(0–89)	2.1	(0–50)
Family's marital situation	1.2	(0–28)	1.8**	(0–50)
Familial tension/conflict	0.5	(0–31)	0.8	(0–30)
Other familial stressor (volunteered)	0.09	(0–40)	0.04	(0–8)
Total psycho-social years stressed	6.2	(0–146)	8.8**	(0–150)

Regression results, women (NAL is the dependent variable)

	Cut-point scoring						**Summed z-score scoring**
	Linear regression Percent cut-off points			Ordered logistic regression Percent cut-off points			Linear Regression
	10%	15%	25%	10%	15%	25%	
Widowed	-.09	-.14	-.16	-.14	-.17	-.24	-.20
Lives alone	-.15	-.01	**.52****	-.15	.12	**.90***	.27
Does not live w/married son	.05	.04	-.01	.13	.09	.05	.001
Participates in no group activity	.02	-.01	-.01	-.03	-.02	-.08	-.12
Reported family stressors (0-5)	**.10***	**.11***	**.12***	**.26***	**.19***	**.20***	**.26****
Total psychosocial yrs. stressed	.00	-.00	-.00	.00	-.00	-.00	-.01
Education (years)	-.01	.00	.02	.02	.02	.04	.00
Age (years)	**.02****	**.02****	**.02***	**.06****	**.05****	**.04***	**.04***
Mainlander	.09	.15	.15	-.00	.26	.22	.33
Urban residence	.09	.11	.11	.17	.17	.20	.20

Regression results, men (NAL is the dependent variable)

	Cut-point scoring						**Summed z-score 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%	1	0
Widowed	-.03	-.06	-.03	-.08	-.34	-.24	.09	.24
Lives alone	-.09	-.18	-.16	-.58	-.66	-.27	-.16	-.21
Does not live w/married son	-.01	-.02	-.04	-.03	-.10	-.12	-.09	-.12
Participates in no group activity	.07	.11	**.12***	.44	.36	.29	.14	**.16***
Reported family stressors (0-5)	.01	-.01	-.02	.08	-.04	-.05	-.04	-.05
Total psychosocial yrs. stressed	-.00	.00	.00	-.01	.00	.00	-.00	-.00
Education (years)	.01	.01	.00	.04	.02	.01	.01	-.00
Age (years)	**.01***	**.02****	**.02*****	**.04***	**.06****	**.05*****	**.03***	**.027***
Mainlander	-.06	-.12	-.08	-.35	-.36	-.08	.01	-.02
Urban residence	-.06	-.05	-.03	-.36	-.09	-.08	-.14	-.06

Additional analyses

- NAL = a + b_1(**years widowed**) + … + …
- Including self-rated health in all regressions does not change main results
- Using cutpoints based on entire sample (i.e. men & women combined) or sex-specific cutpoints does not change main results

“Costa Rican Study on Longevity and Healthy Aging” (CRELES)

<u>Early life events</u>
- early death of mother
- low edu. of mother
- live w/out biological father
- econ. problems (index) <15 yrs. old
- health problems (index) <15 yrs. old

<u>Loss</u>
- death of children
- widowhood/years widowed

----------> 2004-2006 High NAL

<u>Social deprivation</u>
- low/no church attendance
- lives alone

<u>Spousal characteristics</u>
- low edu.
- poor health

<u>Demographic</u>
- low edu.
- poorer
- rural residence

Conclusions

Q: Are various indicators of life stress linked to riskier neuroendocrine biomarker profiles?

A: On the whole, no.

But, we need to better measure respondents' stress over the life course and neuroendocrine biomarkers

SEBAS II (2006)

Added stress related questions:

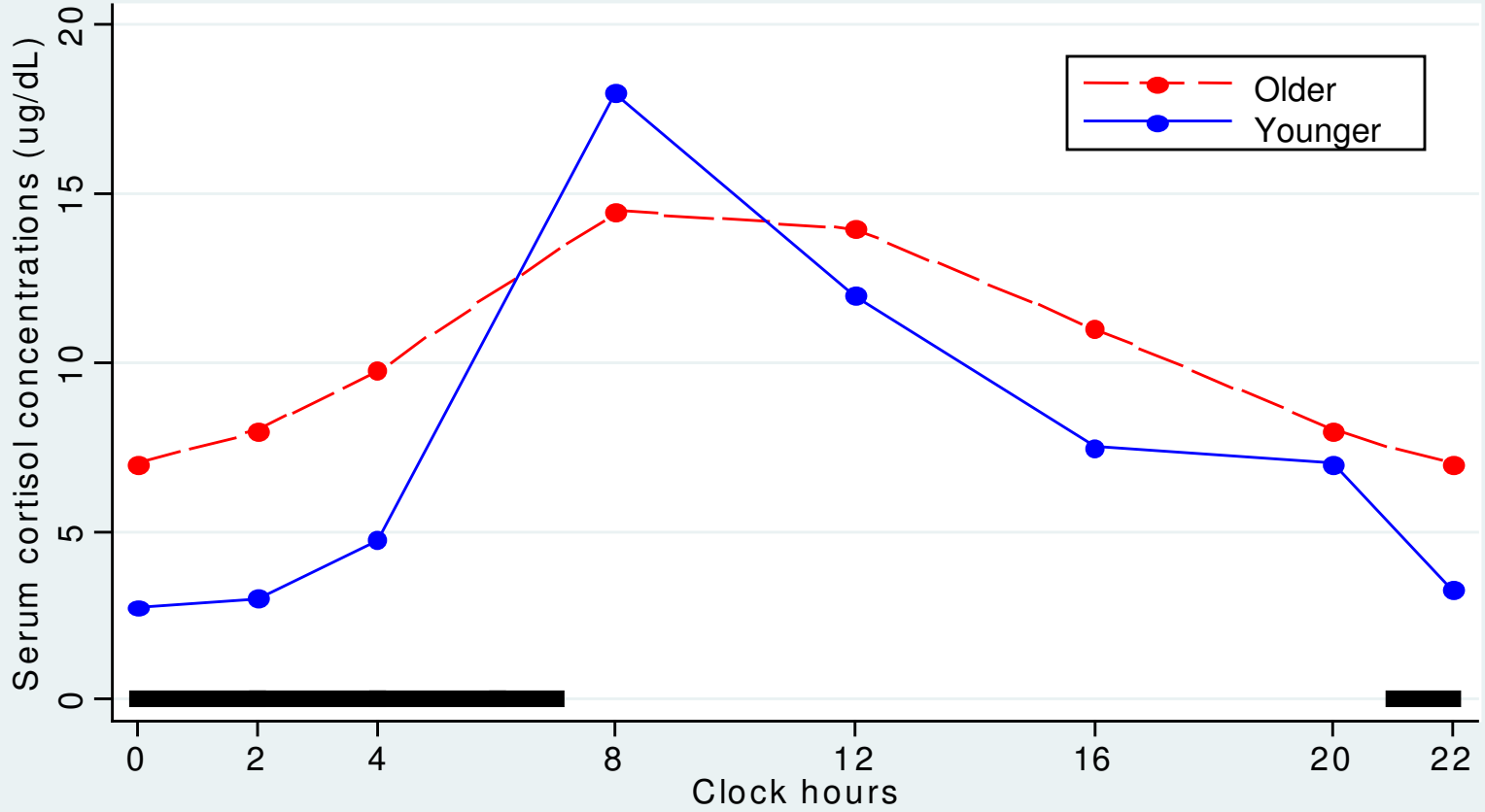
- Daily hassles (e.g. argument w/anyone since yesterday)
- Major life events (e.g. job change, major illness, death of family member) in past year
- Traumas (e.g. being beaten, homicide or suicide of family member) at any time in one's life
- Perceived stress (e.g. difficulty coping with events, feelings of loss of control) in past month
- Security-related (e.g. feeling safe in neighborhood) and caregiving stress

Future possible improvements in the SEBAS

- Multiple measures of urinary samples (e.g. 3 overnight urinary samples over 2 weeks and/or daily and nightly urinary samples)

- A measure of cortisol's diurnal rhythm (e.g. 5 salivary cortisol samples over the day)

Cortisol's diurnal rhythm – younger & older persons



1. Adapted from 'Age-related changes of the adrenal secretory pattern: possible role in pathological brain aging' (Ferrari et al., 2001)

Future possible improvements in the SEBAS

- Multiple measures of urinary samples (e.g. 3 overnight urinary samples over 2 weeks and/or daily and nightly urinary samples)

- A measure of cortisol's diurnal rhythm (e.g. 5 salivary cortisol samples over the day)

- A measure of reactivity (e.g. stress test w/attention to speedy return to baseline levels)

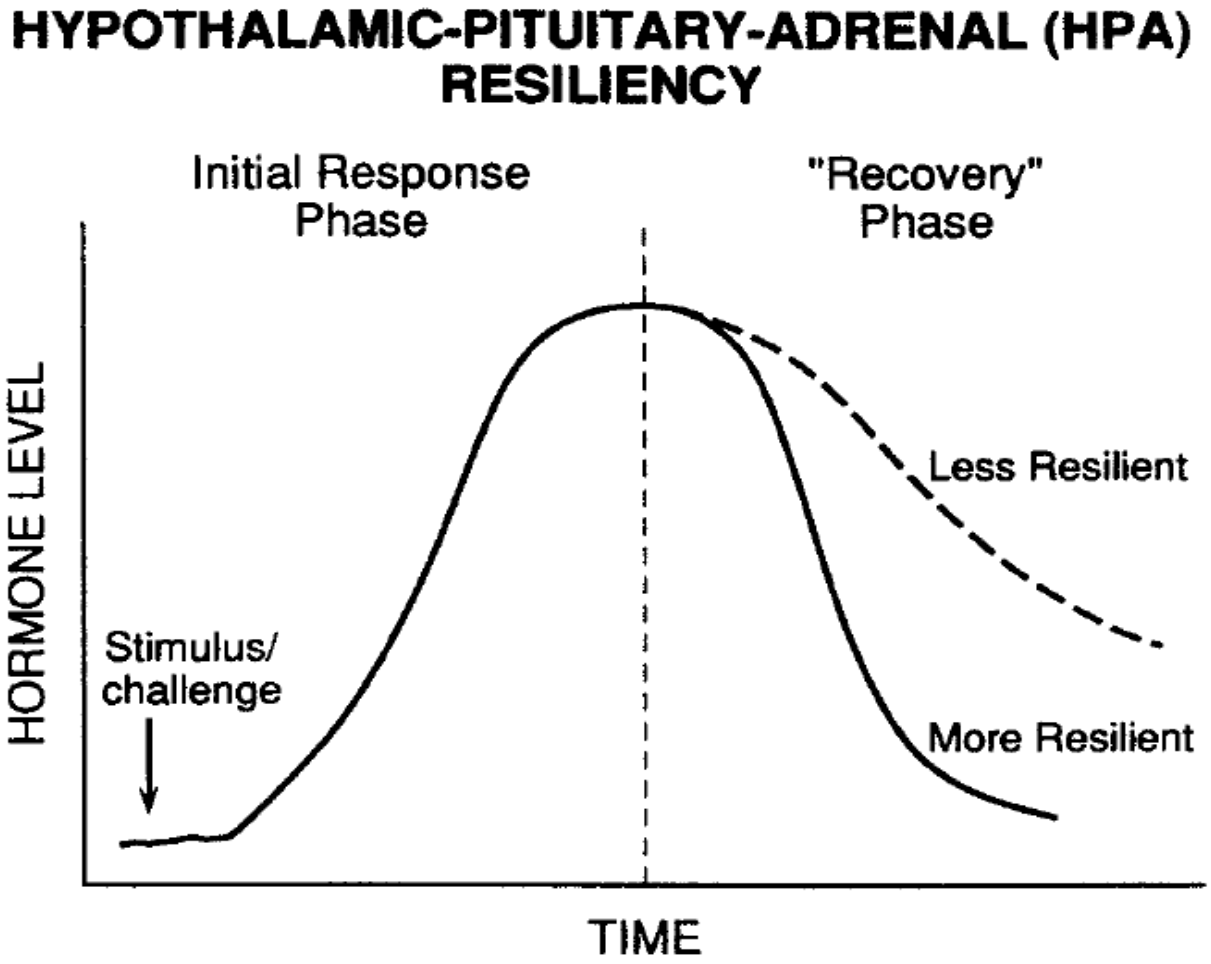


FIG. 1. HPA axis resiliency in response to challenge.

Fin

Muchas gracias!

Recommended biomarkers across different physiological systems to test AL

Cardiovascular system
- Systolic blood pressure**
- Diastolic blood pressure**

Antioxidant profiles

Metabolic system
- BMI/waist-hip ratio**
- Total cholesterol**
- HDL/LDL cholesterol**
- Homocysteine
- Glycosylated hemoglobin**

Inflamation and coagulation factors
- IL-6, CRP, low cholesterol
- Albumin
- Fibrinogen

Hypothalmic-pituitary-adrenal (HPA) axis
- Cortisol**
- DHEAS**

Sympathetic nervous system
- Norepinephrine**
- Epinephrine**

Renal function
- Creatinine clearance

Lung function
- Peak flow rate

** First used to operationalize AL (in the MacArthur studies)