



Assessing the biological stress system: considerations for family research

Darlene A. Kertes, Ph.D.
University of Florida

Genes

Specific genes
Genetically-influenced traits

Environment

Distal: Rearing
Proximal: Life stressors

Biological Processes

Biological Stress Response Neurotransmitter Activity
Neural Circuits

Poor Outcomes

Emotional Problems Behavior Problems
Health Problems

Overview

- Relevance of the HPA system
- Early care effects on stress system activity
- Methodological issues in biological stress research
- The case for multi-level research

Relevance

- Why should you care about the biological stress response system?
 - Affects nearly every organ system, impacts on cognition, memory, emotion, behavior, health
 - Mechanism by which prior experiences impact response to future life events

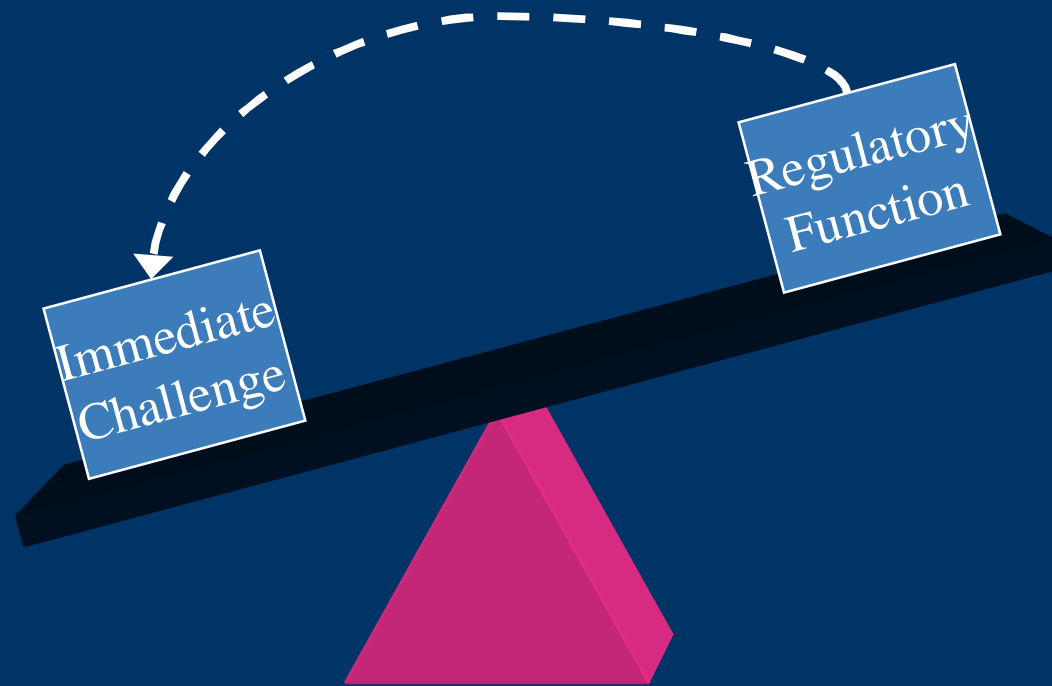
Functions of Stress Physiology



Functions of Stress Physiology



Functions of Stress Physiology



Allostasis

Stress system activity essential for life & to meet challenges...

- Circadian rhythms
- Neurons responsive to NTs
- Liberate glucose
- Enhance amino acid production

Repeated/chronic elevations:

- Growth
- Immune function
- Memory and attentional processes
- “Fear” circuits

HPA axis alterations observed in disorders

- b Addiction
- b Depression & anxiety disorders
- b Cardiovascular disease
- b Alzheimer's
- b Asthma
- b Immunogenic cancers
- b Infectious diseases
- b Obesity
- b Diabetes
- b Gastric disorders
- b Wound healing & general immune function
- b And more...

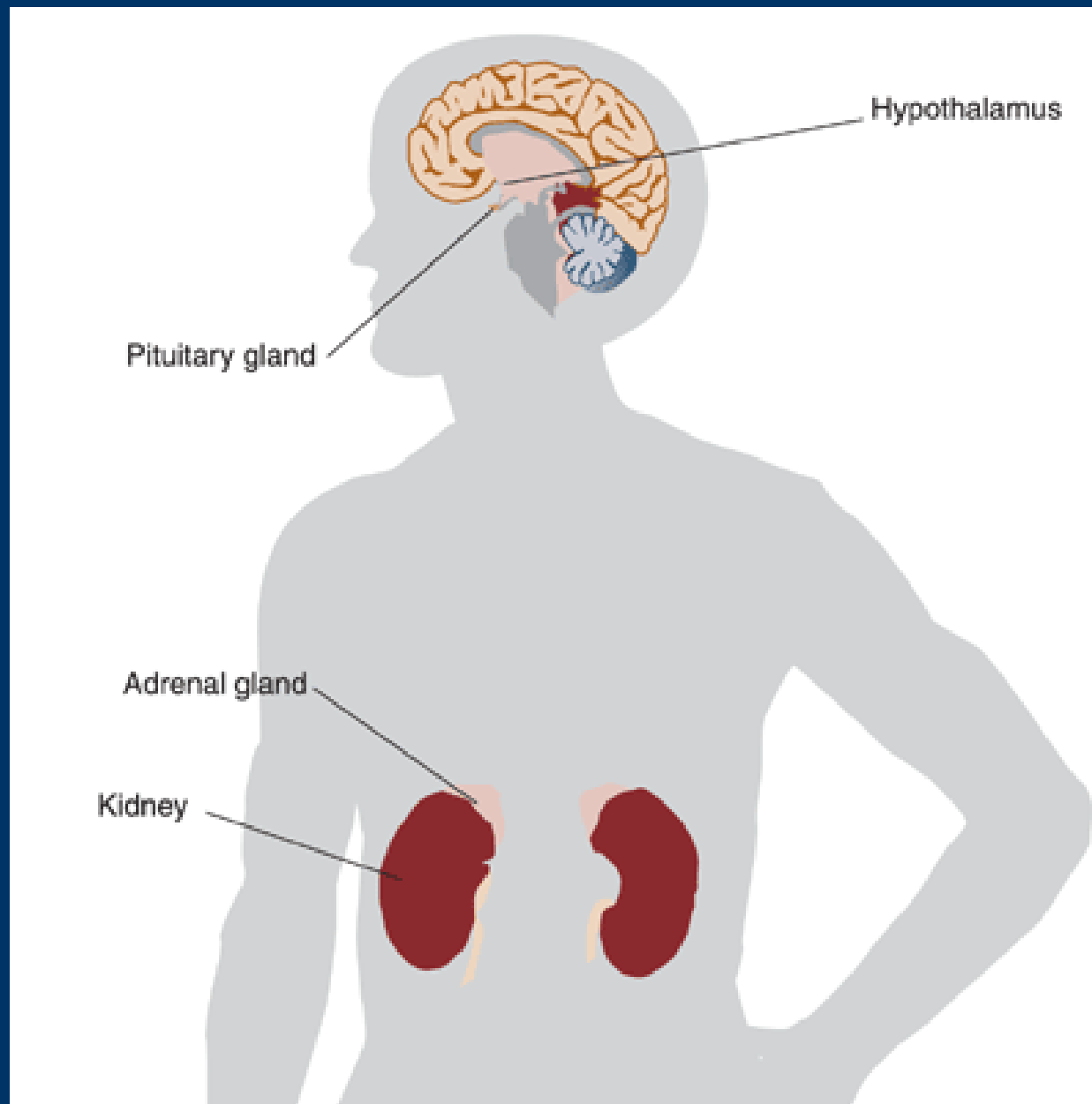
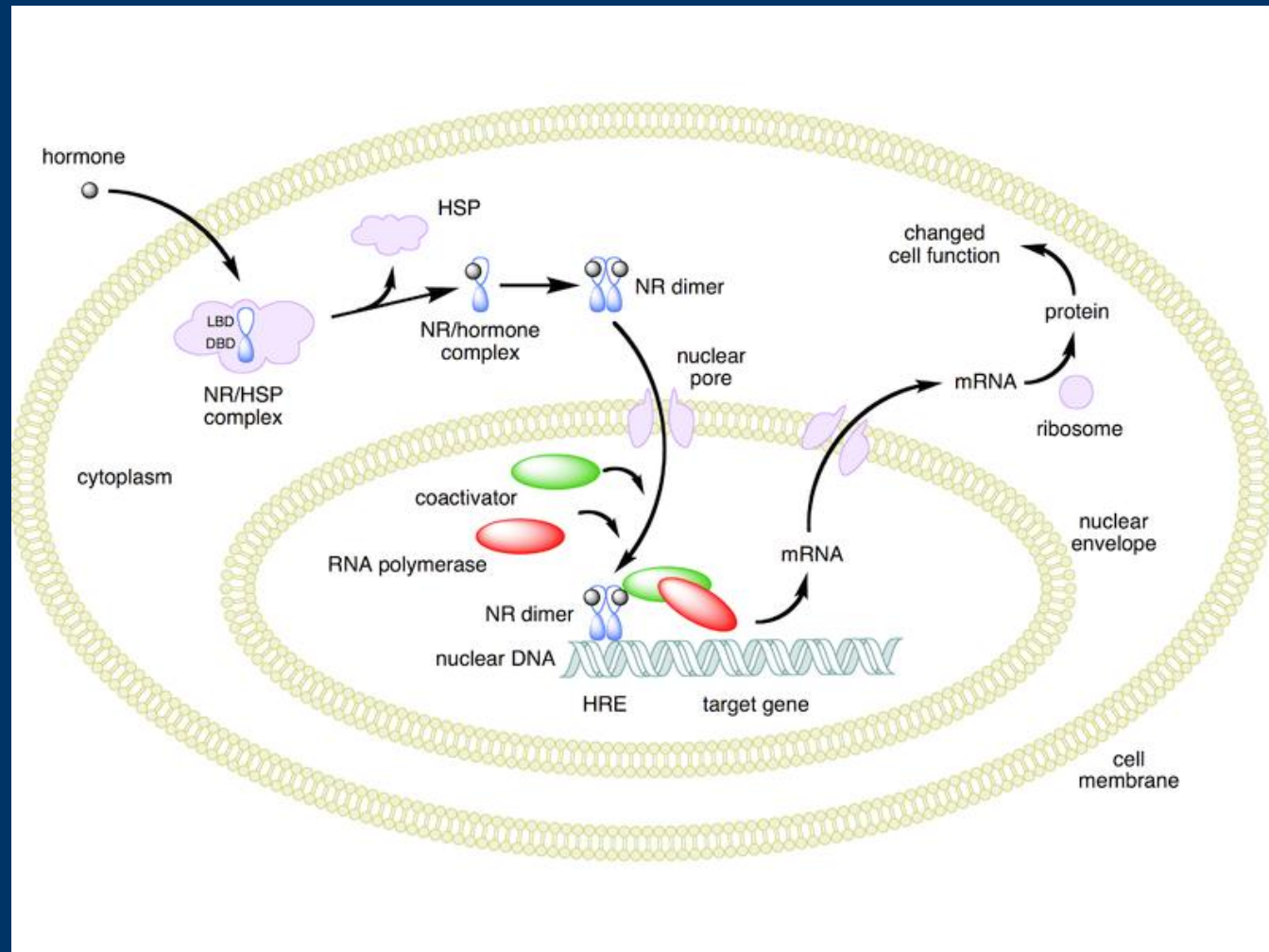


Image: Adinoff et al. (1998)

Life experience affects gene expression via cortisol



Family effects on cortisol

- **Relationship quality**
 - Spouses/romantic partners
 - Parent-child conflict
 - Early attachment/ parenting quality
- **Life stress**
 - Parental depression
 - Family stress
 - Poverty
- **Child care and maltreatment**
 - Abuse
 - Neglect
 - Orphanage care
 - Day care quality
- **Familial risk**
 - Relatives of depressed or addicted individuals

Overview

- Overview of the HPA system
- **Early care effects on stress system activity**
 - Basal activity & stress reactivity
 - Early adversity & typically developing
- Methodological issues in biological stress research
- The case for multi-level research

Effects of early experience

- Do early experiences in close relationships with caregivers alter the development of the HPA axis?
 - Extreme adversity/ Deprivation of relationships with caregivers
 - Typical variation in parenting quality



Long-term effects of early adversity on basal cortisol levels

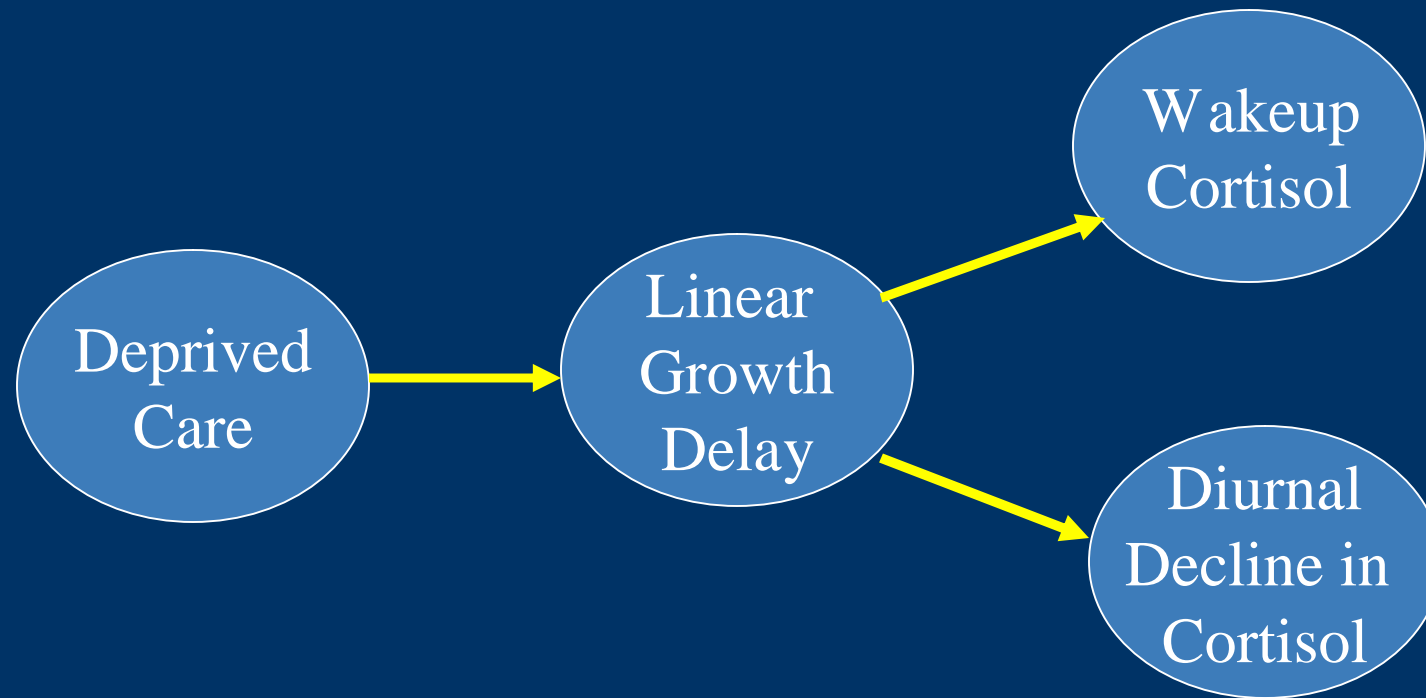
- Participants
 - Internationally adopted children aged 7-11.
 - Adopted birth- 8 yrs
 - With adoptive families >3yrs
- Key measures
 - Parent-reported pre-adoption conditions
 - Linear growth delay
 - Basal cortisol (wake-up & bedtime)

Linear growth delay as indicator of early adversity/relationship disruption

b Psychosocial Dwarfism / Short Stature

- Impact on growth of bone
(long bones, skull)
- Weight appropriate for height

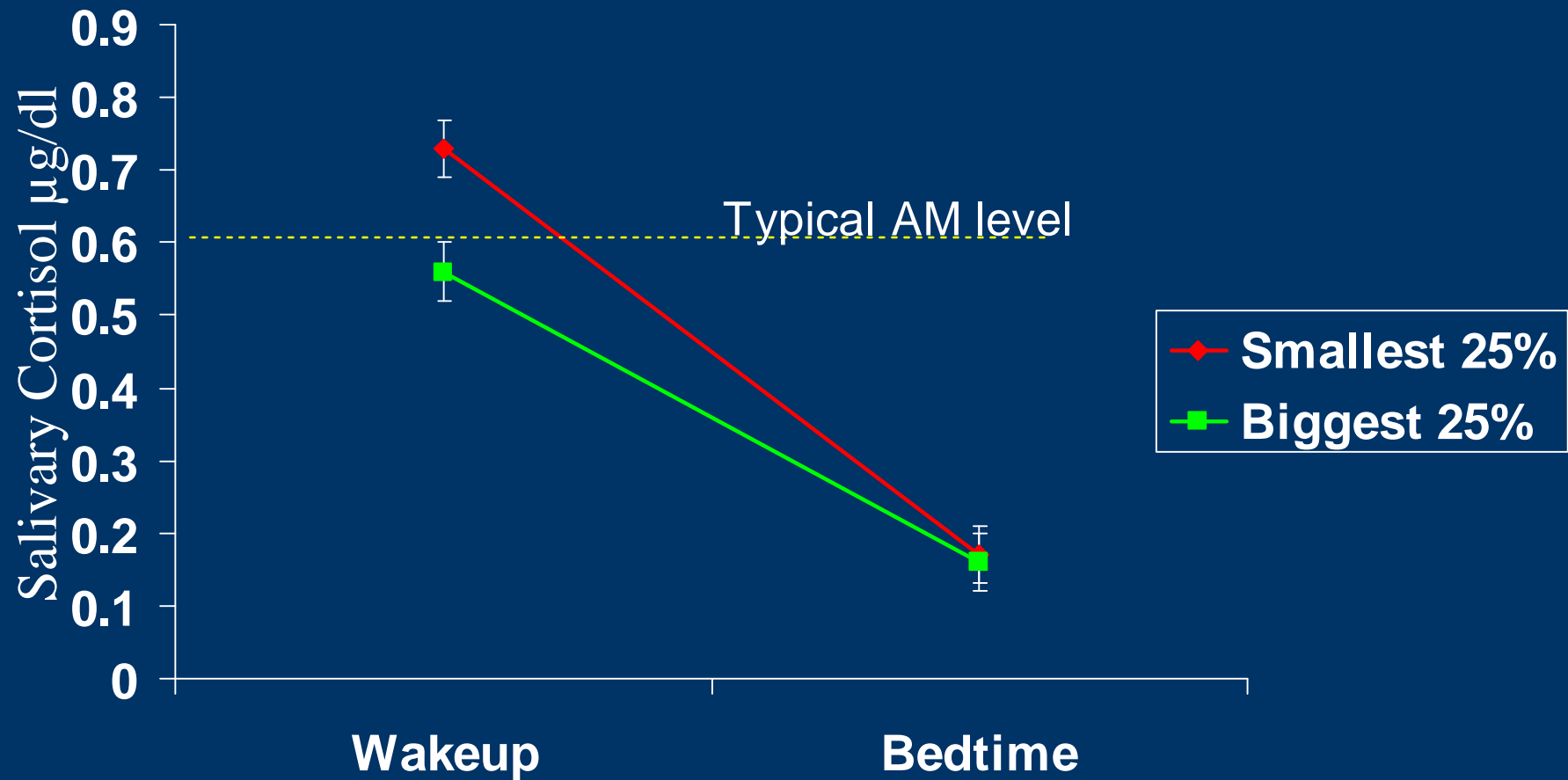




Deprived care (adoptive parent report):

- Age at adoption
- Institutionalization
- Pre-adoption neglect & abuse

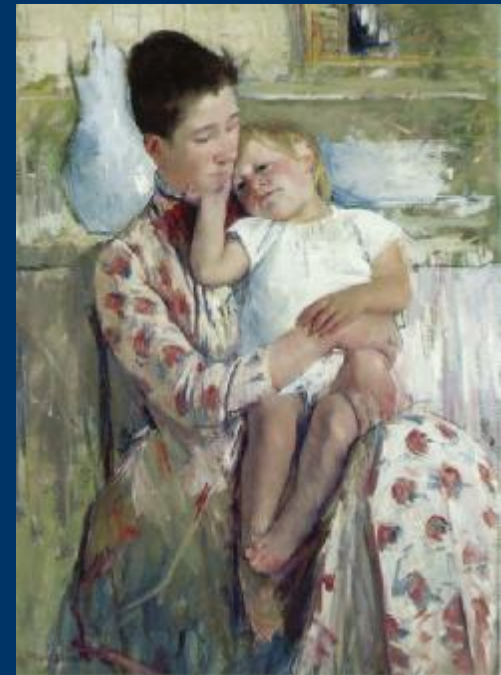
AM cortisol levels higher for growth delayed children



Kertes et al (2008) *Development and Psychopathology*

Effects of early experience

- Do early experiences in close relationships with caregivers alter the development of the HPA axis?
 - Deprivation of close, supportive relationships with caregivers
 - Typical variation in caregiver quality

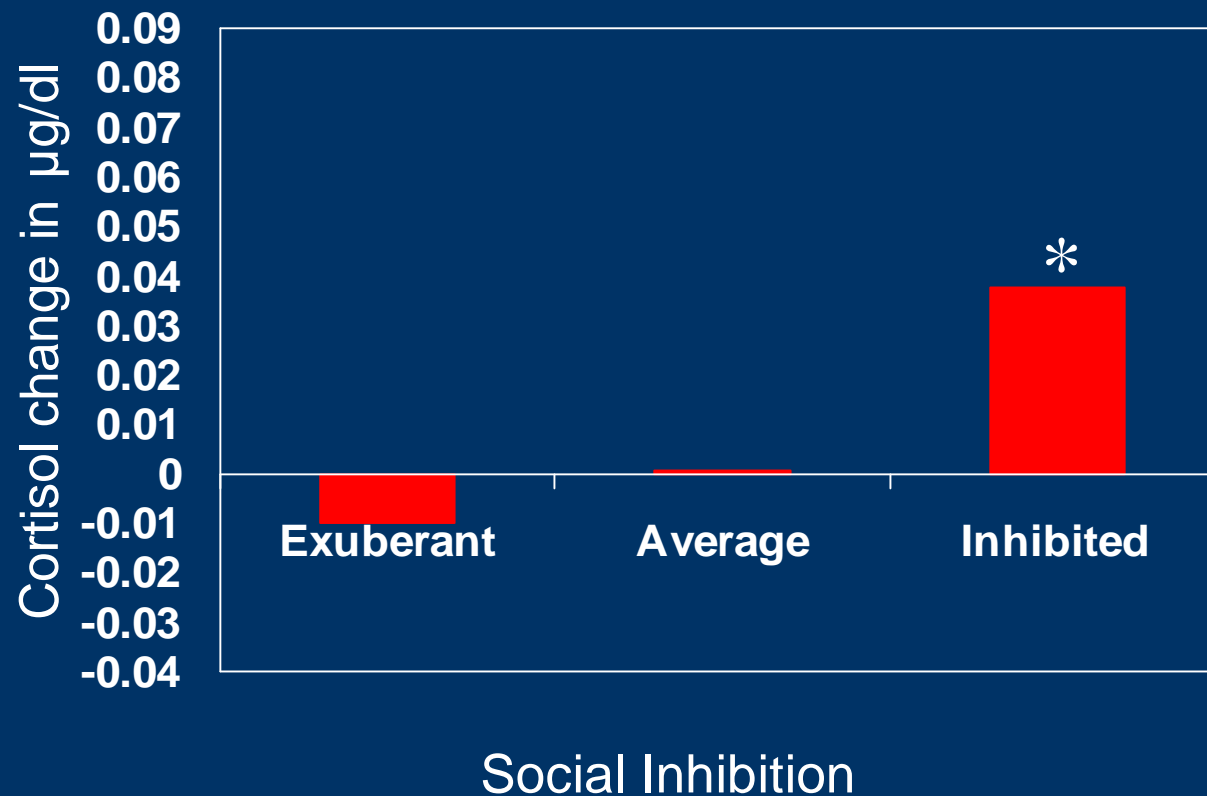


Parental buffering of temperamental vulnerability to stress response

- Assn of behavioral fear/inhibition - cortisol reactivity in early childhood (4 yrs)
 - General or stressor-specific?
- Parenting quality (behavioral observation):
 - Buffer/exacerbate temperamental vulnerability to stress at bio level?

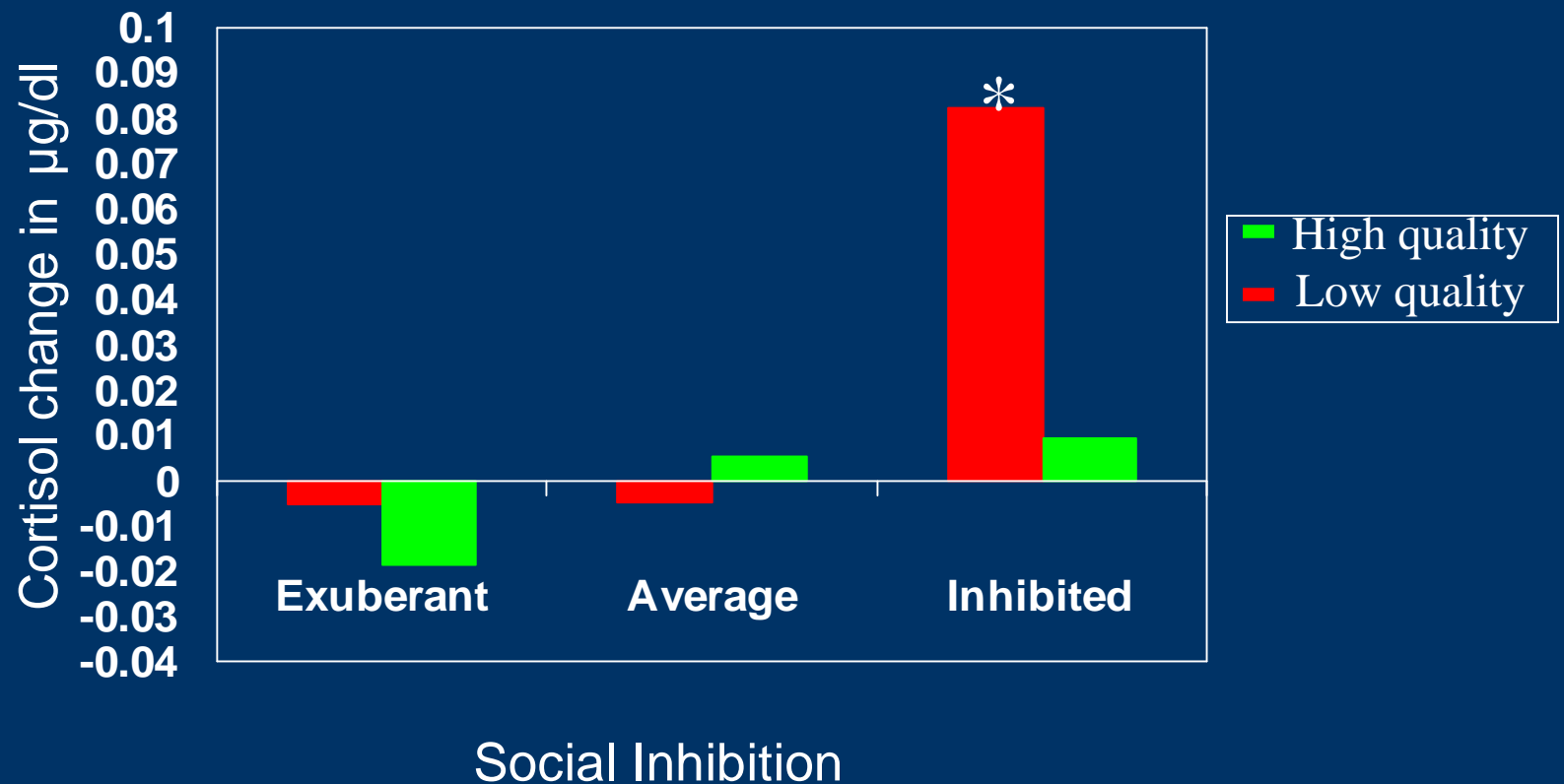


Socially inhibited children show cortisol response to social stressor



Kertes et al. (2009) *Developmental Psychobiology*

High parenting quality buffers cortisol responses for socially inhibited children



Kertes et al. (2009) *Developmental Psychobiology*

Overview

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Targeted paradigms & research questions (detecting effects)

§ Paradigms that provoke “stress” response*

- § Diverse methods used in children

- § Ethical limitations – mild stressors

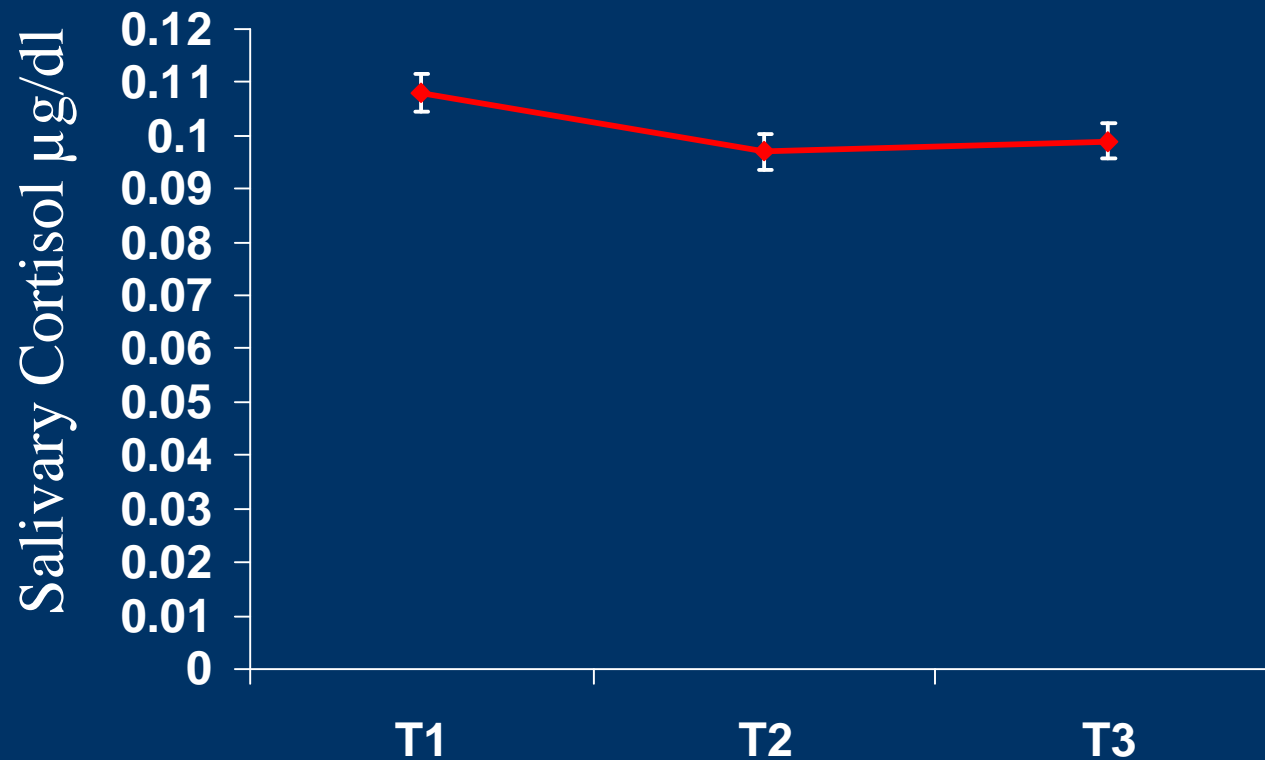
§ Strategies

- § Develop standard protocols for children

- § Focus on subgroups of responders in particular contexts

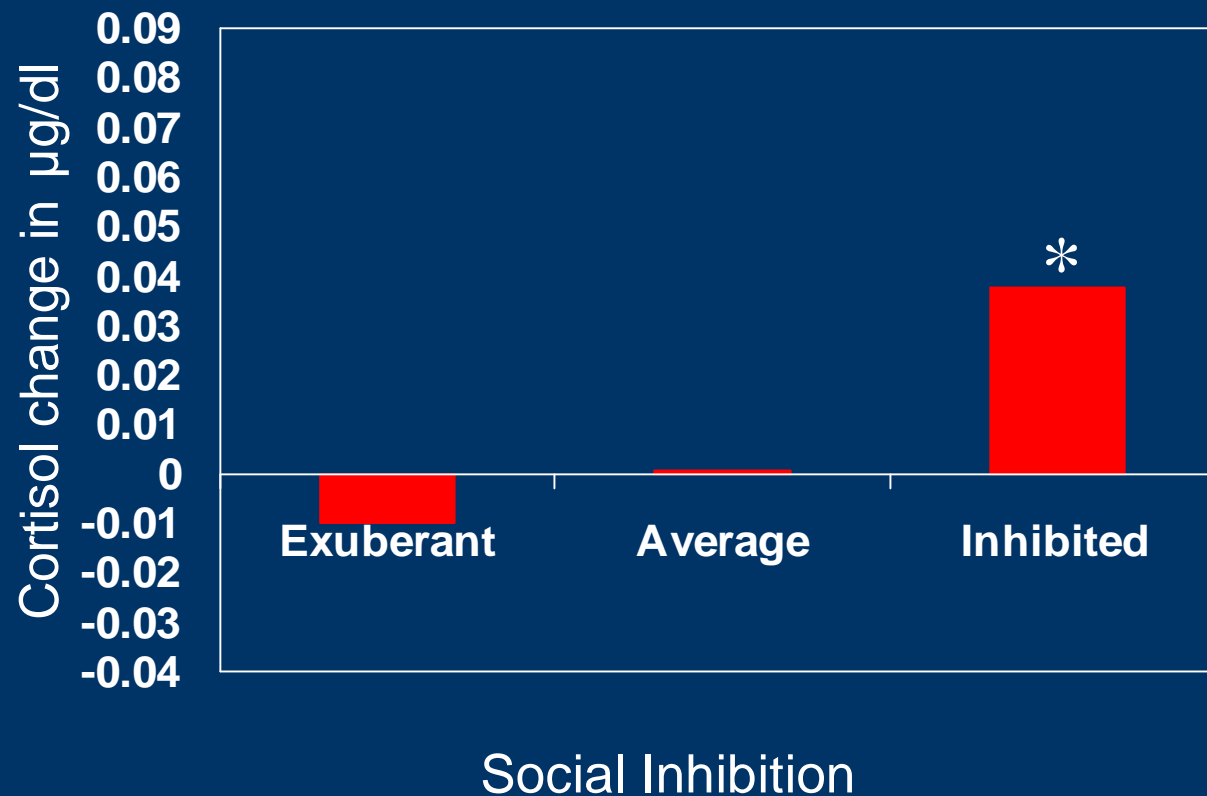
*Dickerson & Kemeny (2004); Gunnar et al., (2008)

No evidence for general biological stress response



Kertes et al. (2009) *Developmental Psychobiology*

Socially inhibited children show cortisol response to social stressor



Kertes et al. (2009) *Developmental Psychobiology*

Multiple factors influence stress system

§ *Target psychosocial variable*

&

§ Digestion, sleep, exercise

§ Systemic stressors (inflammation, pain)

§ Caffeine, alcohol, tobacco

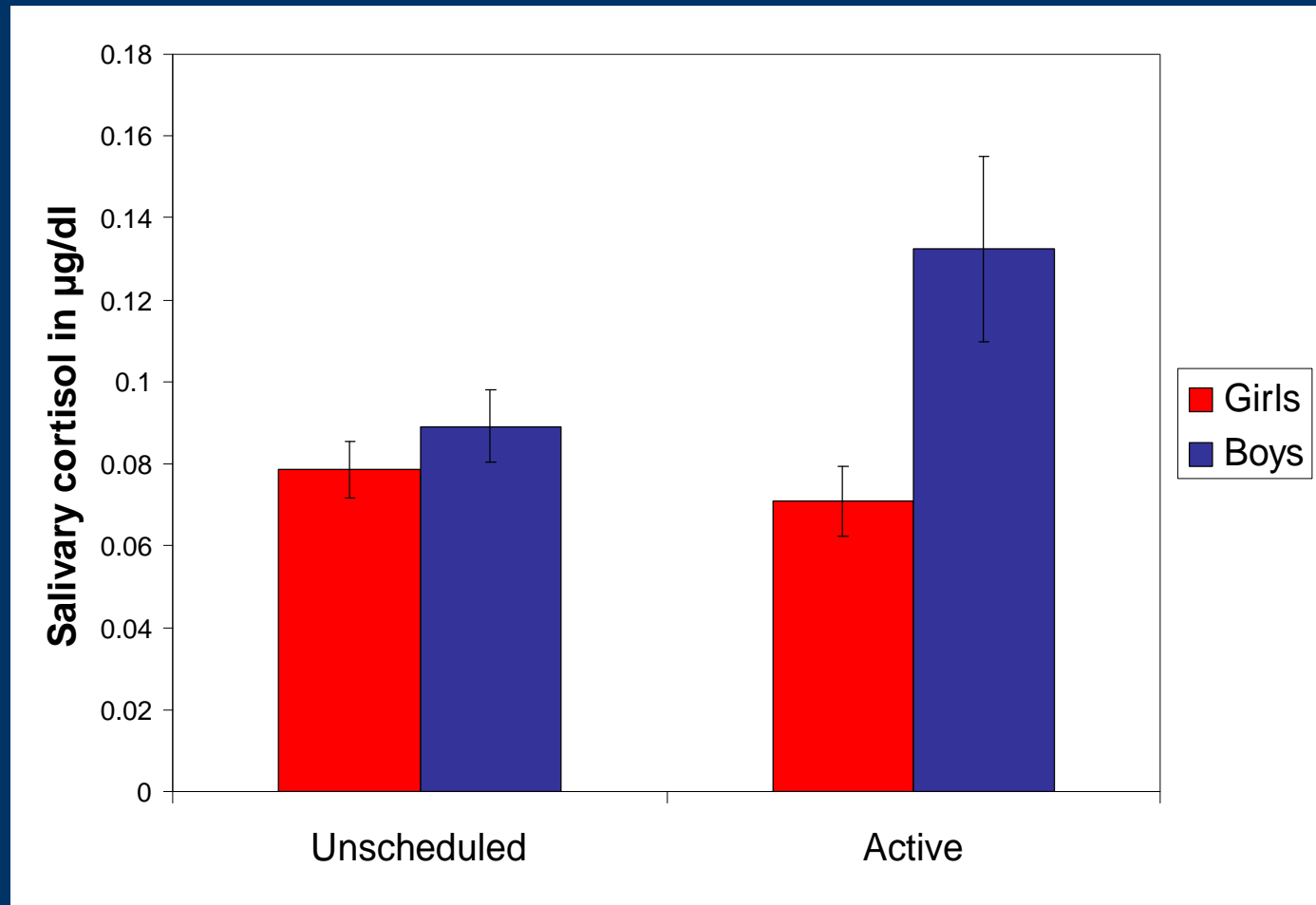
§ Endogenously regulated basal activity

§ Other perceived/actual psychosocial stressors

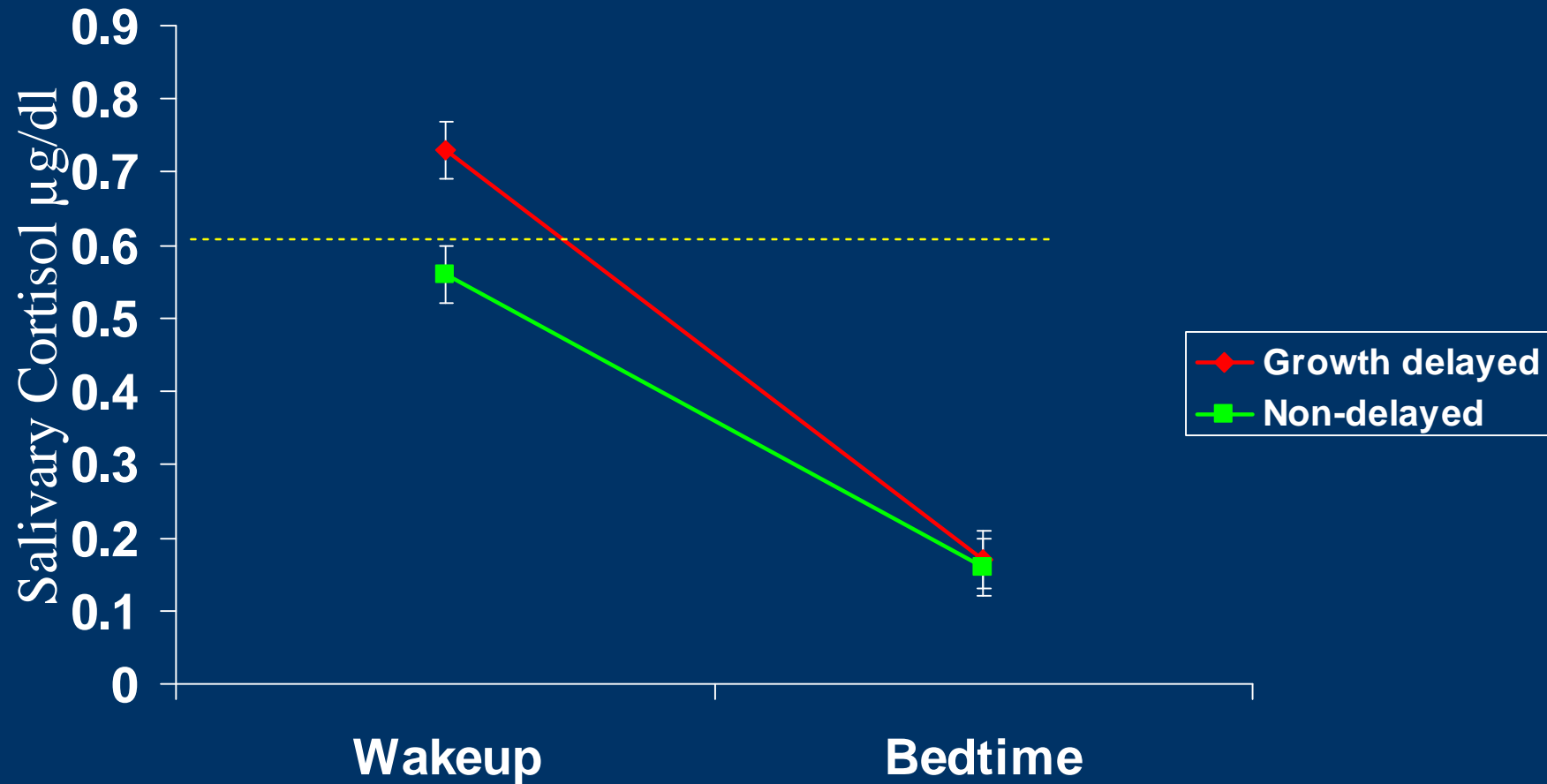
§ **Strategy 1: Data collection constraints**

§ **Strategy 2: Identify “trait” cortisol**

School-aged children: bedtime cortisol affected by after-school activities

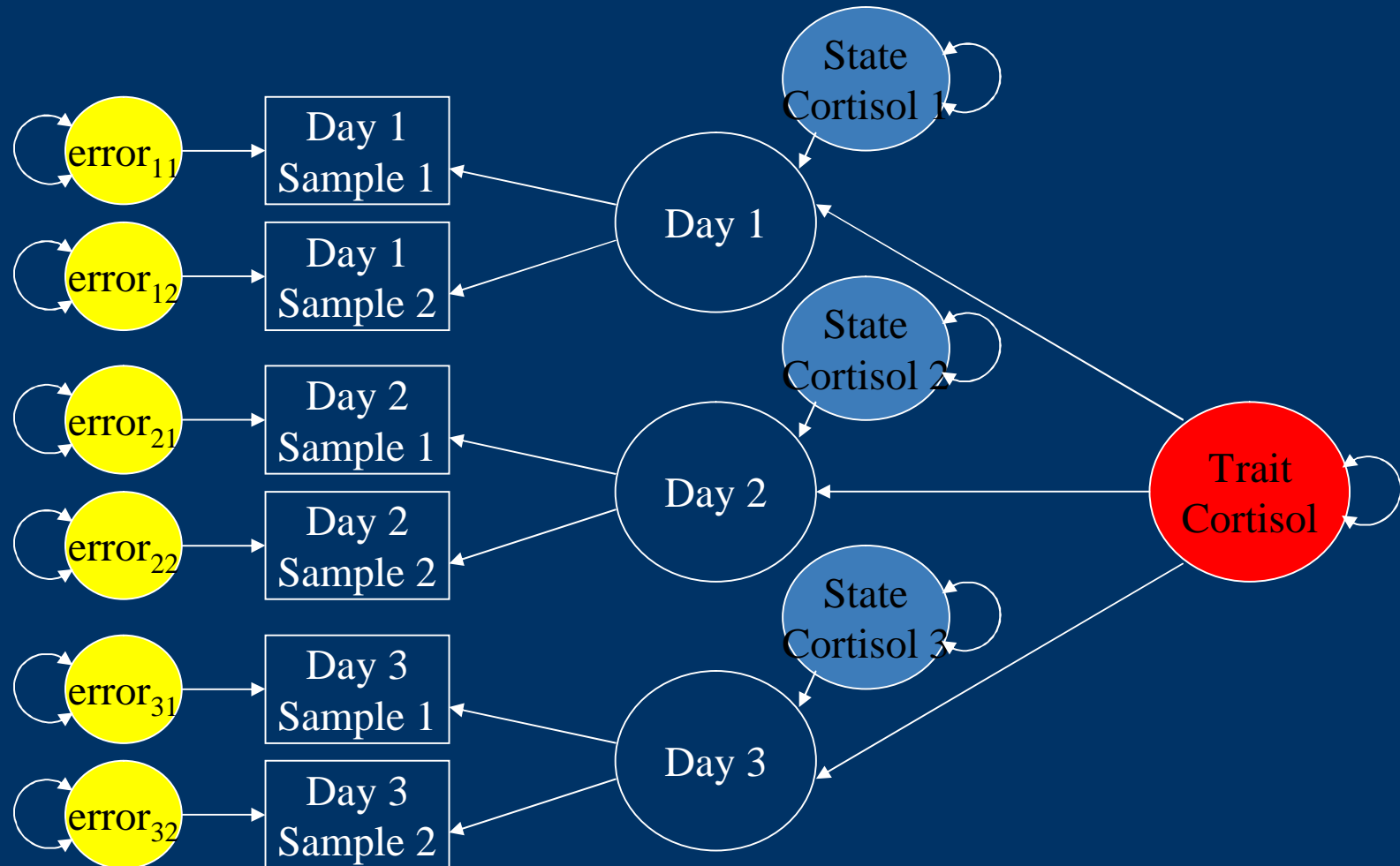


Basal cortisol among internationally-adopted children



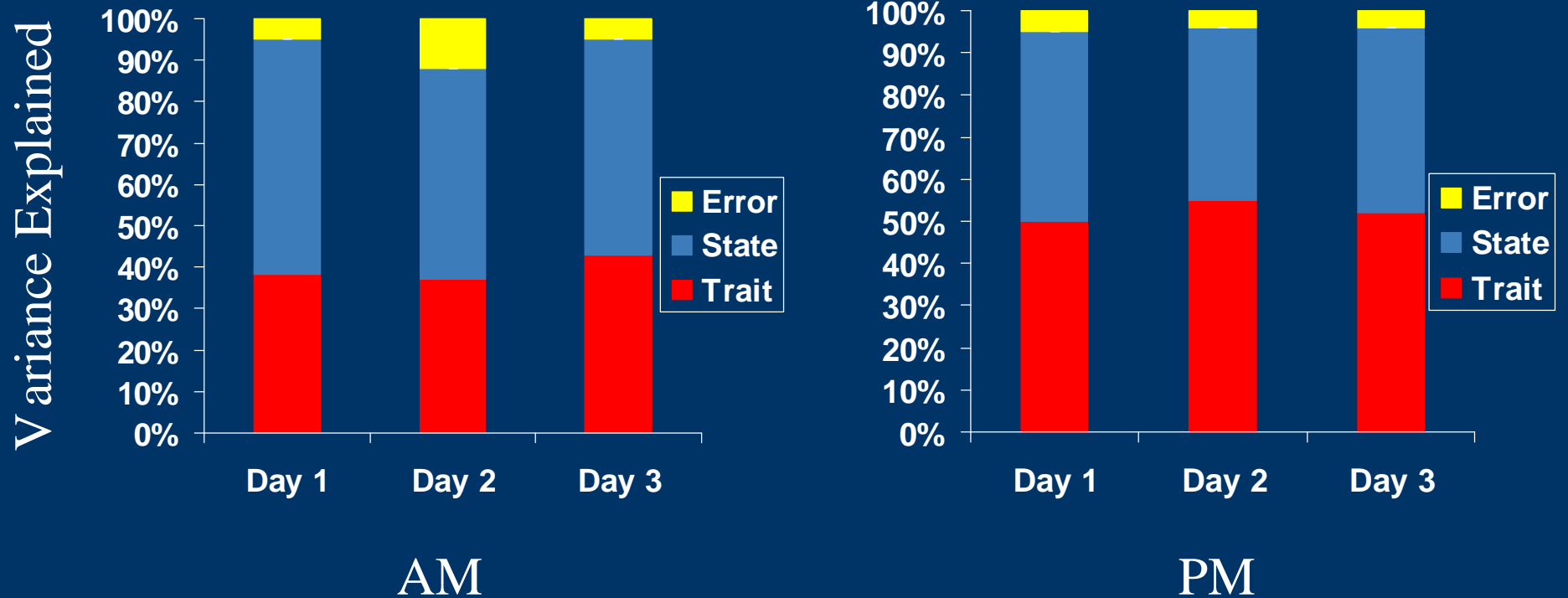
Kertes et al. (2008) *Development and Psychopathology*

Identifying trait cortisol



Kertes & van Dulmen (in preparation)

Cortisol due to trait, state, and error



Kertes & Van Dulmen (in preparation)

Methodological considerations: HPA axis acts/interacts with other systems

- HPA axis
- SAM system
- Immune function
- Sleep/circadian cycles
- Other steroid hormones
- Peptides
- Neural activity

(Other biomarkers of potential interest)

Assessing multiple levels of analysis

Behavioral & biological stress measures

- Often uncorrelated
- Update/standardize behavioral measures*
- Intervening factors†
- *Provide different information*
 - Exposure & response
 - Objective & subjective
 - Differentiate from systemic stressors

*Monroe (2008)

†Helhammer et al. (2009); Jessop & Turner-Cobb (2008)

Assessing multiple levels of analysis

Multiple modes of transmission



- § Routes of transmission for family effects
 - § Epigenetic
 - § Genetic (or G x E)
 - § Cultural (socialization)

- § Strategy: Interdisciplinary research via collaboration/
cross-training

Challenges to integration

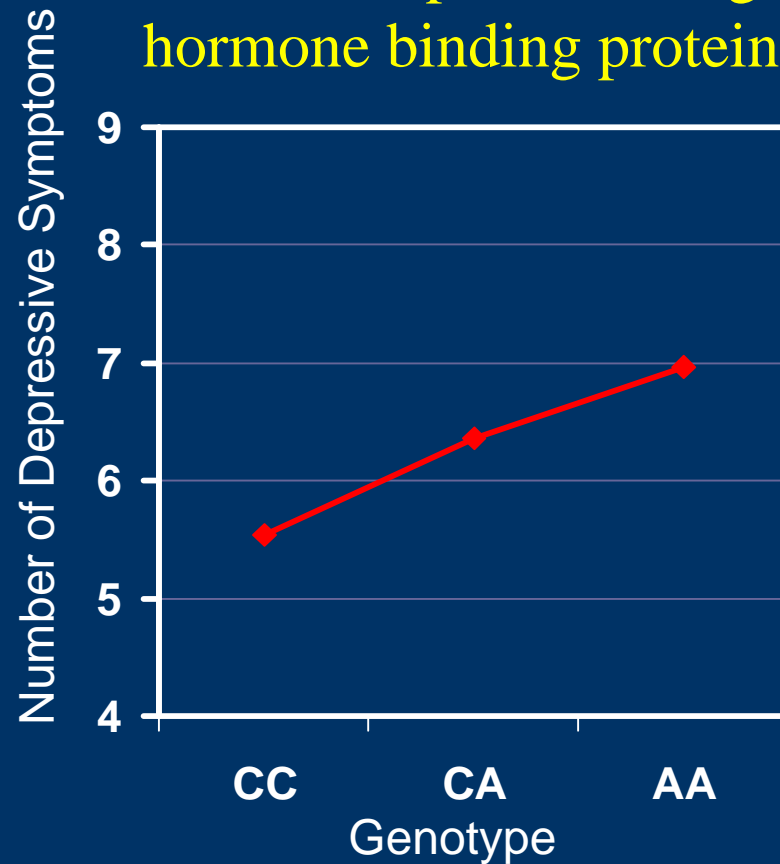
- Pragmatic
- Methodological
 - Investment in phenotyping vs. sample size
 - Analysis

Genetic research on familial stress-related disorders

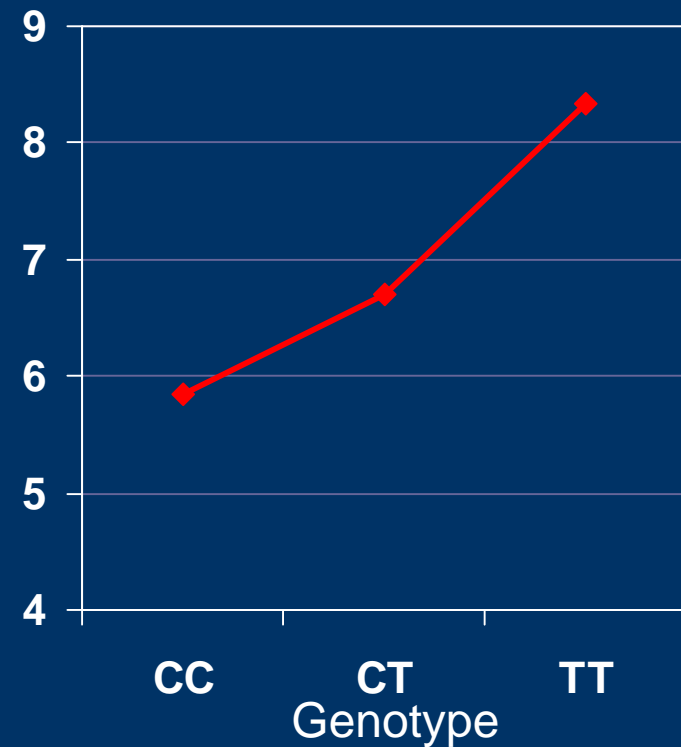
- Major Depression and Alcohol Dependence
 - Family risks & other life stress
 - Stress biology system implicated
 - Neurobiology-guided gene selection

Genetic studies can identify “best candidates”...

Corticotropin-releasing hormone binding protein



Mu-opioid receptor



Kertes et al. (submitted)

...to examine multiple modes of transmission
for familial stress-related disorders

- Gene-environment interplay in the Child Development Project
 - Early life family stress
 - Adolescence experiences
- Types of research questions
 - Basic science
 - Preventive intervention
- Multi-level research?

Biological stress system in family research: Take home points

- Mechanism by which family experiences impact response to future life events & emotional/physical health
- Family experiences impact stress system activity
- Implementation requires careful methodology to detect effects
- Behavioral & biological complementary, not redundant
- Family effects transmitted via social, biological, genetic paths