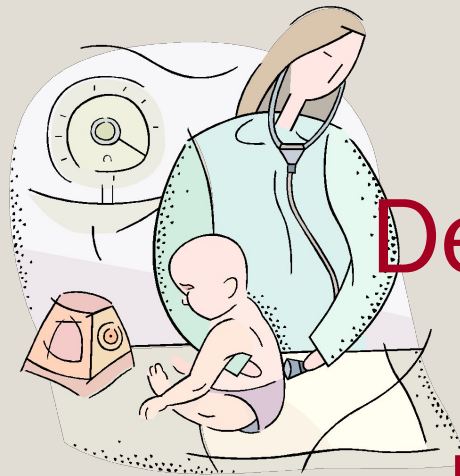


The First 1000 days: The Importance of Early Brain and Childhood Development



Translating Developmental Science into Healthy Lives

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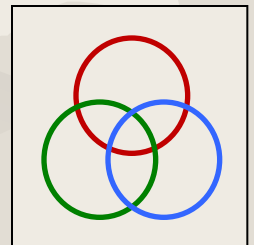
Disclosures

- Oxford University press



Learning Objectives

- Understand the role of **toxic stress** in the intergenerational transfer of health disparities;
- Present an organizing, integrated, **ecobiodevelopmental** framework;
- Discuss ways **early childhood professionals** might advocate in **translating** science into healthier life-courses

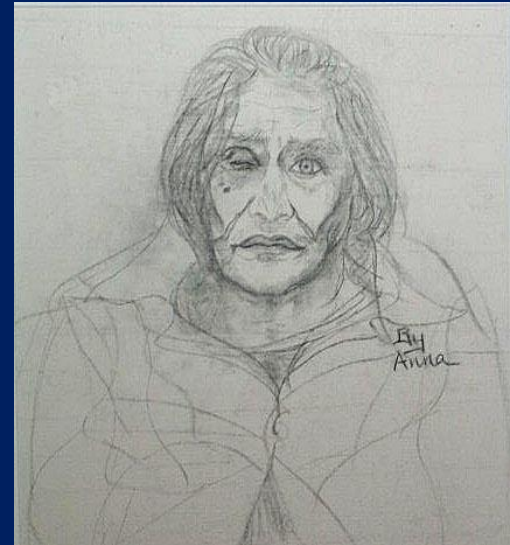


Critical Concept #1

Childhood Adversity has **Lifelong Consequences.**

Significant adversity in childhood is **strongly** associated with **unhealthy** lifestyles and poor health **decades** later.

ACE Study Findings



- Childhood experiences are **powerful** determinants of who we become as adults

ACE Categories



Abuse

- Emotional
- Physical
- Sexual
- Household Dysfunction
- Mother Treated Violently
- Household Substance Abuse
- Household Mental Illness
- Parental Separation or Divorce
- Incarcerated Household Member
- Neglect*
- Emotional
- Physical

) Data from www.cdc.gov/nccdphp/ace/demographics

The higher the ACE Score, the greater the likelihood of :

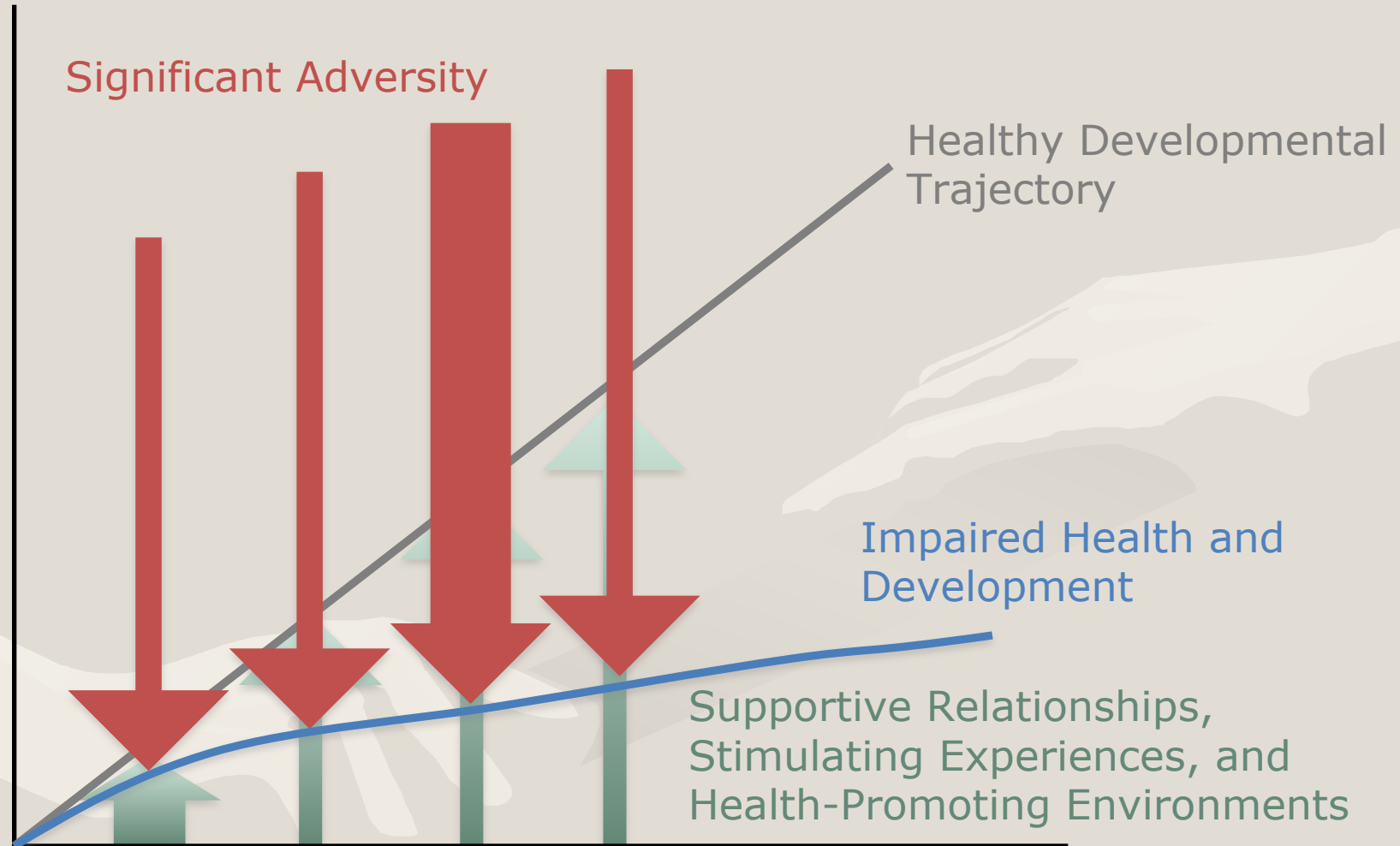
- Severe and persistent emotional problems
- Health risk behaviors
- Serious social problems
- Adult disease and disability
- High health, behavioral health, correctional and social service costs
- Poor life expectancy

Higher ACE Score = significant rise in chronic health conditions:

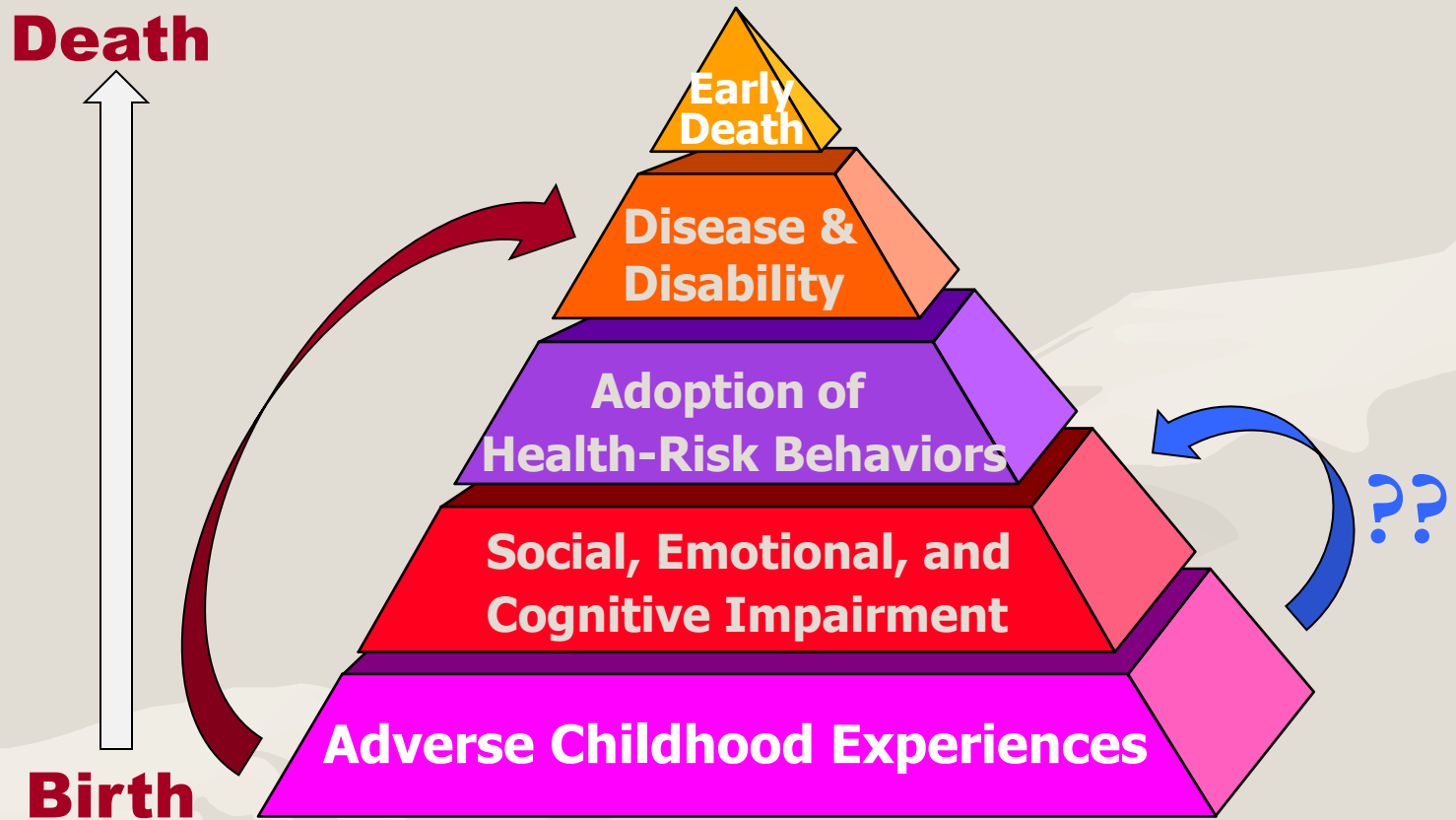
- Sexually Transmitted Disease
- Liver Disease
- COPD
- Ischemic Heart Disease
- Autoimmune Disease
- Lung Cancer
- *****BRING BACK TO LONG TERM CONSEQUENCES



Current Conceptual Framework Guiding Early Childhood Policy and Practice



The True Nature of Preventive Medicine



Mechanisms By Which Adverse Childhood Experiences Influence Adult Health Status

Slide modified from V. J. Felitti



Defining **Adversity** or **Stress**

- Hypothalamic-Pituitary Axis Reactivity
 - Levels of Cortisol
 - Epinephrine/Norepinephrine
 - Inflammatory markers
- National Scientific Council on the Developing Child (Dr. Jack Shonkoff and colleagues)
 - **Positive** Stress
 - **Tolerable** Stress
 - **Toxic** Stress

Based on the **REACTION**
(objective physiologic responses)

Defining Adversity or Stress



- **Positive** Stress
 - Brief, infrequent, mild to moderate intensity
 - Most normative childhood stress
 - Inability of the 15 month old to express their desires
 - The 2 year old who stumbles while running
 - Beginning school or daycare
 - The big project in middle school
 - **Social-emotional buffers** allow a return to baseline
(responding to non-verbal clues, consolation, reassurance, assistance in planning)
 - **Builds motivation and resiliency**
 - Positive Stress is **NOT** the **ABSENCE** of stress

Defining Adversity or Stress



- **Toxic Stress**
 - Long lasting, frequent, or strong intensity
 - More extreme precipitants of childhood stress (**ACEs**)
 - Physical, sexual, emotional abuse
 - Physical, emotional neglect
 - Household dysfunction
 - **Insufficient social-emotional buffering**
(Deficient levels of emotion coaching, re-processing, reassurance and support)
 - Potentially permanent changes and long-term effects
 - **Epigenetics** (there are life long / intergenerational changes in how the genetic program is turned **ON** or **OFF**)
 - **Brain architecture** (the mediators of stress impact upon the mechanisms of brain development / **connectivity**)

Critical Concept #2

Epigenetics:

- **Which** genes are turned on/off, **when**, and **where**
- **Ecology** (environment/experience) influences how the genetic blueprint is read and utilized
- Ecological effects at the **molecular level**
- **Stress-induced changes in epigenetic markers**

Critical Concept #3

Developmental Neuroscience:

- **Synapse** and **circuit** formation are experience and activity dependent
- **Ecology** (environment/experience) influences how brain architecture is formed and remodeled
- Early childhood adversity -> **vicious cycle of stress**
- **Diminishing cellular plasticity** limits remediation
- **Potentially permanent** alterations in brain architecture and functioning

Early Experiences are Crucial



- By age 3, 80% of synaptic connections are already made
- By the second decade of life growth levels off and pruning begins
- Increased experiences define the wiring of an infant's brain

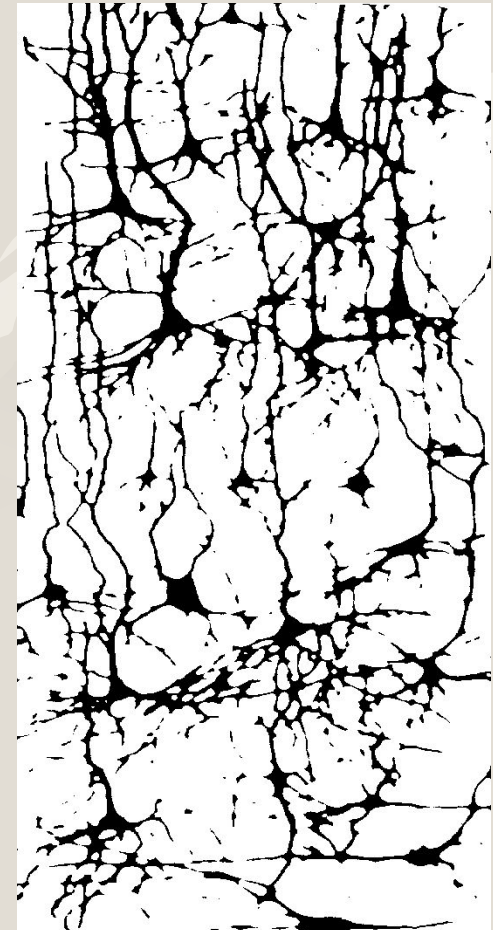
Human Brain at Birth



6 Years Old



14 Years Old



Impact of Early Stress

```
graph TD; A[CHILDHOOD STRESS] --> B[Hyper-responsive stress response; ↓ calm/coping]; A --> C[Chronic “fight or flight;” adrenaline / cortisol]; B --> D[Changes in Brain Architecture]; C --> D; D --> A;
```

CHILDHOOD STRESS

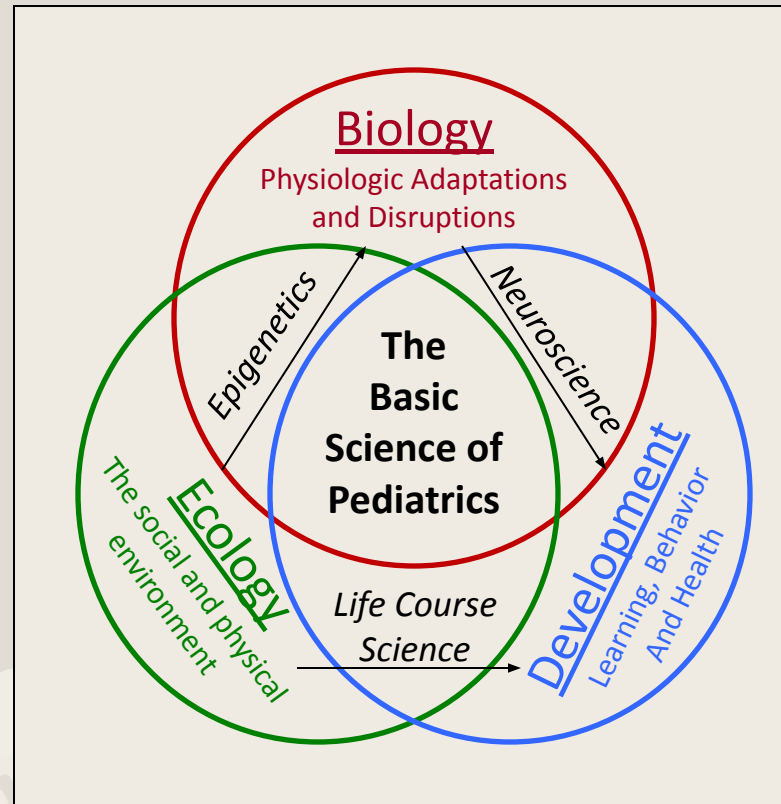
Hyper-responsive stress response; ↓ calm/coping

Chronic “fight or flight;”
adrenaline / cortisol

Changes in Brain
Architecture

Eco-Bio-Developmental

Model of Human Health and Disease

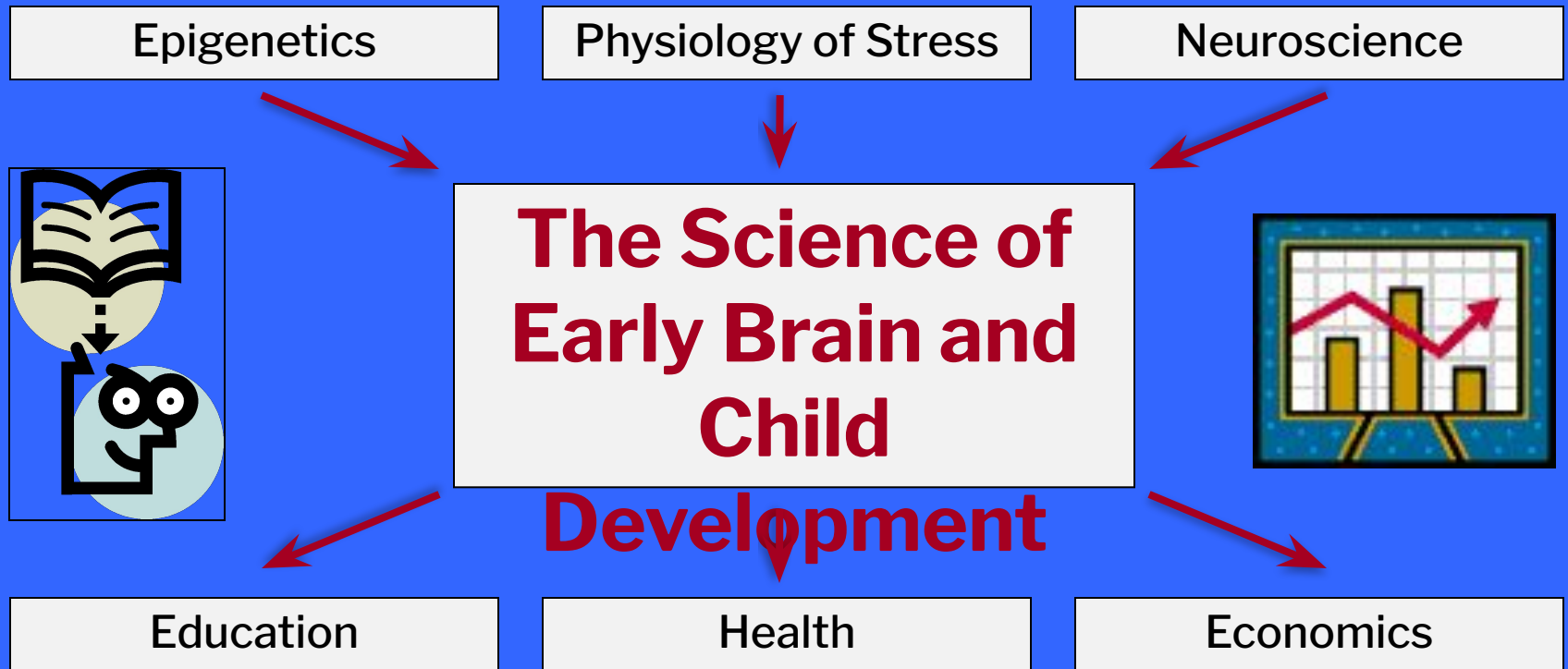


Ecology

Becomes **biology**,

And together they drive **development** across the lifespan

Critical Concept #4



One Science – Many

The critical challenge now is to **translate** game-changing advances in **developmental science** into effective **policies** and **practices** for families w/ children to improve **education**, **health** and **lifelong productivity**

Critical Concept #4

For young children,

Caregivers create the environment for brain development!

- Caregivers can turn off physiologic stress response by **addressing physiologic and safety needs**
- Turns off the physiologic stress response by **promoting healthy relationships and attachment**
- Notes and encourages **foundational coping skills** as they emerge

Early Childhood professionals are ideally placed!

- Promote this sort of “Purposeful” Parenting
- Advocate for a **public health approach** to address toxic stress

The Orchid Children
David Dobbs
The Atlantic
December 2009



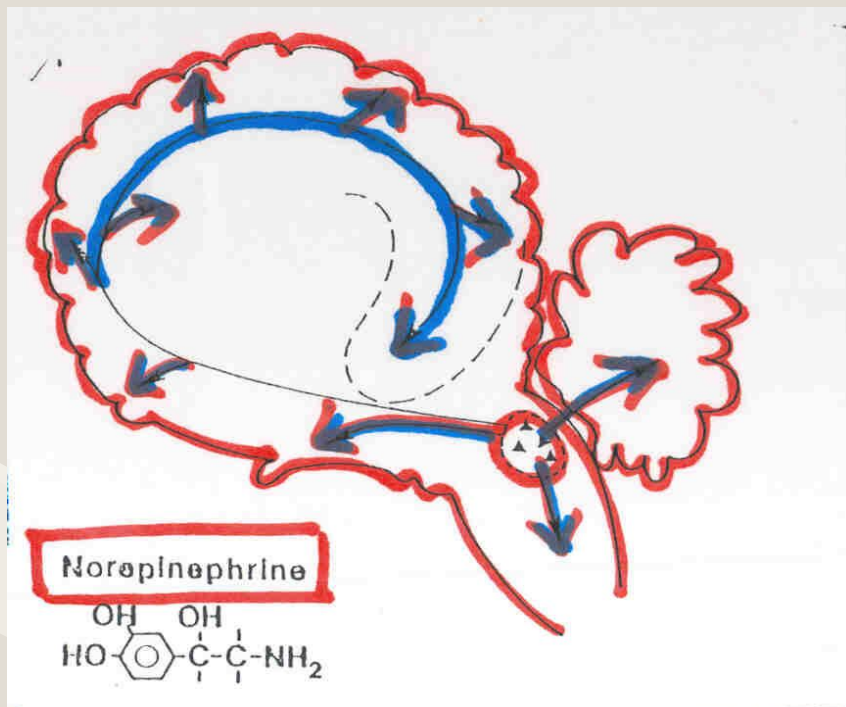
Most of us have genes that make us as hardy as dandelions: able to take root and survive almost anywhere. **A few of us, however, are more like the orchid: fragile and fickle, but capable of blooming spectacularly if given greenhouse care.** So holds a provocative new theory of genetics, which asserts that the very genes that give us the most trouble as a species, causing behaviors that are self-destructive and antisocial, also underlie humankind's phenomenal adaptability and evolutionary success. **With a bad environment and poor parenting, orchid children can end up depressed, drug-addicted, or in jail—but with the right environment and good parenting, they can grow up to be society's most creative, successful, and happy people.**

The Developing Brain

- Neuronal division
- Migration
- Differentiation
- Synaptogenesis
- Dependent on environmental and micro-environmental cues
- Disruption of these cues are going to impact all these stages in the developing fetus/infant
- Watershed Developmental phases connected to proximal to caudal development of neurotransmitter systems



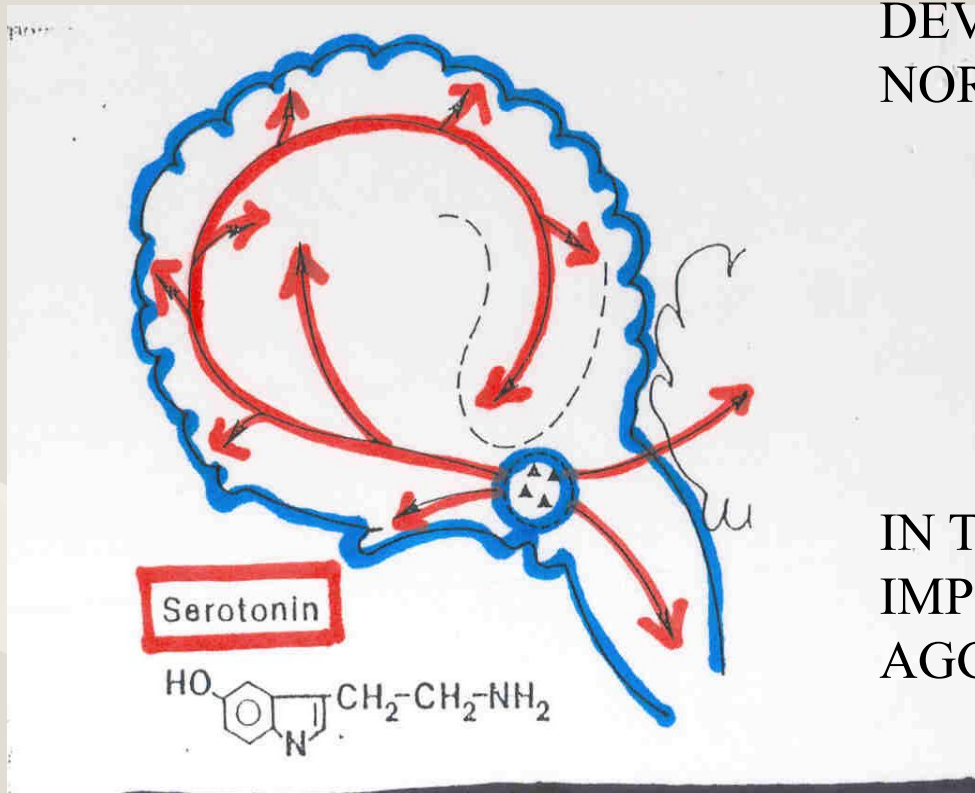
NORADRENERGIC NEURONS:



- In the developing brain: migration/ organization of cortical neurons
- In the developed brain: MOOD, ANXIETY, AROUSAL
-

Serotonin

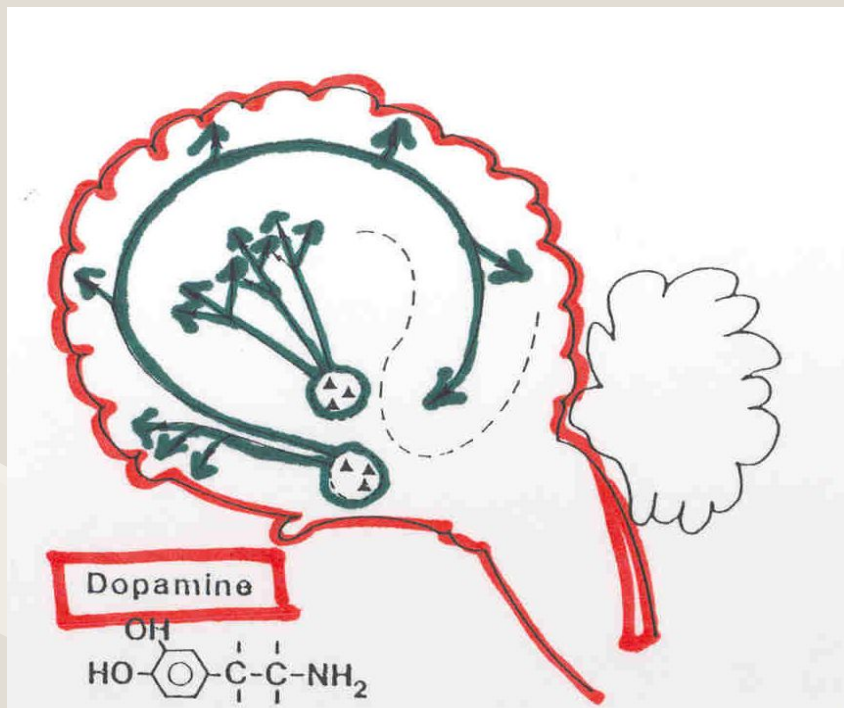
IN PERINATAL PERIOD
MODULATES BRAIN
DEVELOPMENT WITH
NOREPINEHRINE.



IN THE DEVELOPED BRAIN
IMPLICATED IN MOOD,
AGGRESSION, REM SLEEP

- DOPAMINERGIC
NEURONS

-
- Reward systems
- Cognitive integration
- Sustained attention

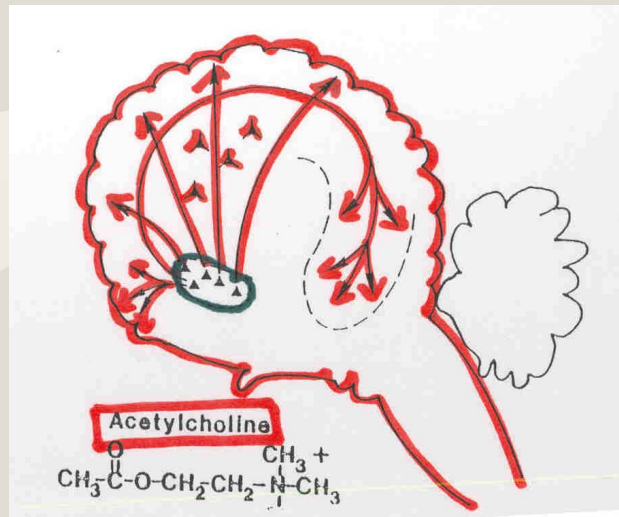


CHOLINERGIC NEURONS

- Fxn: memory, higher cognitive func.
- Alzheimers: degen. chol. adren. neurons

GABAMINERGIC NEURONS

-
- Fxn: SEDATION, ANXIETY, SEIZURES
-



Glucocorticoids increase with Stress

- Prenatally, brain is hypo-responsive to circulating levels of corticosteroids: “protected”
- Certain overwhelming stresses will overcome this & activate the stress response
- They reduce brain weight, DNA content
- They interfere with the formation of functioning synapses and dendritic spines
- Behaviorally: alteration in social behavior

Critical Concepts



- 3RD trimester fetal brain development
- Critical and Sensitive periods in development
- Trauma can be neglect or abuse which produce different phenotypes
- A sensitized neuron will respond to lesser and lesser intensity of stimulus
- Full blown response to minor stress is a characteristic of a sensitized neuron

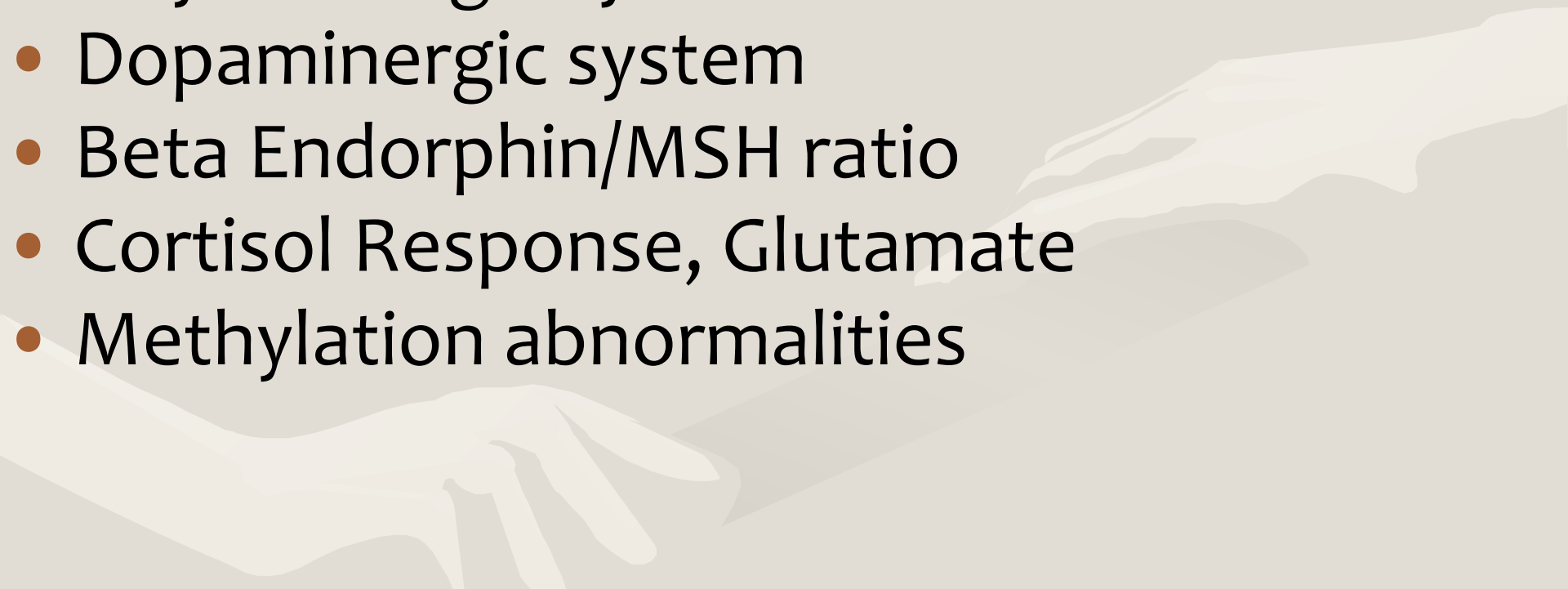
Sensitization

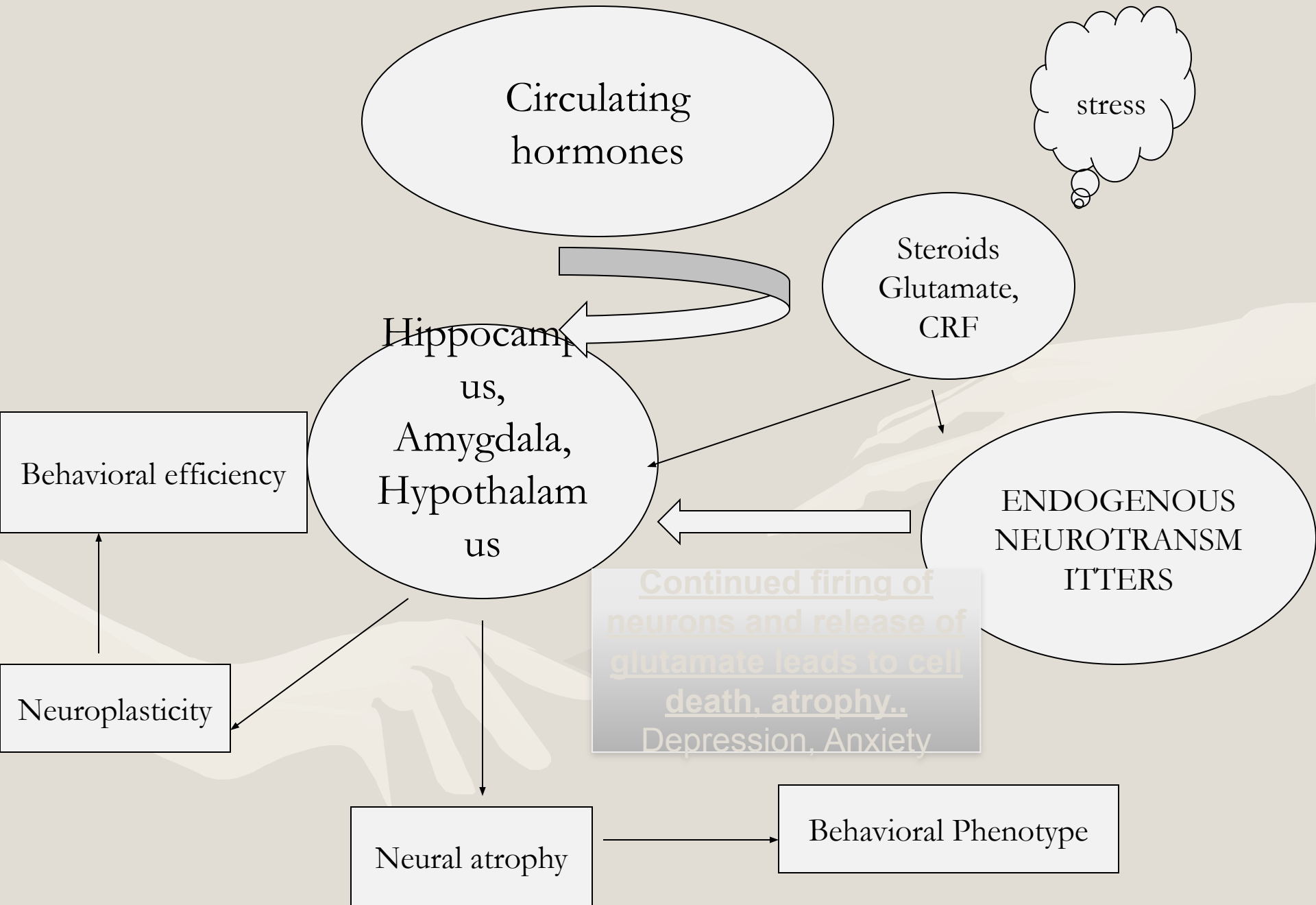


- Intense reactions affect neurotransmitter release, intracellular messengers systems which affect gene transcription and protein formation
- The mature brain internalizes a fear response as a “STATE” memory BUT
- **In the developing brain**, these experiences organize neural systems resulting in “TRAITS” that will be stoked into response each time a trauma is re-experienced

Other than the usual suspects...



- ***Putative systems affected by environment***
 - Oxytocinergic system
 - Dopaminergic system
 - Beta Endorphin/MSH ratio
 - Cortisol Response, Glutamate
 - Methylation abnormalities
- 
- A faint, stylized illustration of two hands reaching towards each other, one from the left and one from the right, positioned behind the text. The hands are rendered in a light, semi-transparent style, suggesting a sense of connection or support.



1. *Stress effects on the HPA axis*

- Triggered by isolation, separation, noxious, or novel stimuli; Cortisol response is often excessive, chronically elevated, or blunted in serious neglect, depression, or PTSD
- Excess cortisol is toxic to the hippocampus and immune system (McEwen, 1992)



2. Oxytocinergic system

Neuropeptide from the paraventricular and supraoptic nuclei

Released into blood stream via posterior pituitary

Peripheral action on uterine contraction and milk ejection

Centrally projects to VS, N. Accumbens, VTA, Medial Preoptic Area, strial terminalis: “ALL CONNECTED TO MATERNAL SOCIAL BEHAVIOR”

Functions of Oxytocin

- Facilitates Physical Proximity and nurturant care between the mother and infant.....pup grouping, pup retrieval, nest building and licking
- In the amygdala: has anxiolytic effects/ critical for social recognition
- In hippocampus: long term spatial memories which assist in pup retrieval, foraging..... peripheral vaginal stimulation produces central oxytocin release which lead to maternal behavior and minimizes rejection of the pups

Functions of Oxytocin

- MOST FASCINATING !!!
- Stimulates the onset and maintenance of maternal behavior
- BUT
- Also programs the development of the oxytocin system in female offspring; also mediates maternal behavior in adulthood
- These changes in OTR expression appear to be mediated by DNA methylation within the Estrogen Receptor Alpha gene

Functions of Oxytocin

- Early Maternal Care Giving = well developed Oxytocinergic system
- Non maternal rearing = reduced CSF oxytocin
- Women with high childhood emotional neglect = low CSF oxytocin level, and correlated with all type of maltreatment but not Physical abuse
- CSF Oxy Levels inversely correlated with emotional neglect scores on CTQ
- Salivary oxytocin levels in mother and infant strongly correlated and based on maternal infant synchrony

Summary

Oxytocin

- OT is likely a major anti-stress agent, and mediator for the transduction of early experiences into long-term behaviors
- OT is released by components of social interaction: safe touch, massage, breast or genital stimulation, pair bonding, acts of giving, mediation of “trust”
- Exposure to OT via positive mothering impacts on future CRH receptor density, OTR, and future mothering behavior
- Blocking OT can increase cortisol and stress reactivity, and prevent pair-bonding
- OT and/or social bonding suppresses cortisol to promote faster wound healing (Detillion 2004)



3. Dopaminergic System

- Neurotransmitter system associated with motivated behavior in mom and offspring; stimulus reward systems
- Striatum via the VTA, SN (MID BRAIN)....., PFC, ACG....., meso-cortico-limbic pathways (UNPREDICTABLE REWARDS) and Nigrostriatal pathways (PREDICTABLE ERRORS)
- information collated from the (Ventromedial) Limbic, (central) associative and (dorsolateral) motor areas = motor and behavioral responses, affective and cognitive responses
- Dopamine production in the NA of the VS= RESPONSIVE CARE GIVING IN RATS.....
- Lesions: disrupted pup retrieval, low L/G, lo maternal behavior

Dopaminergic System

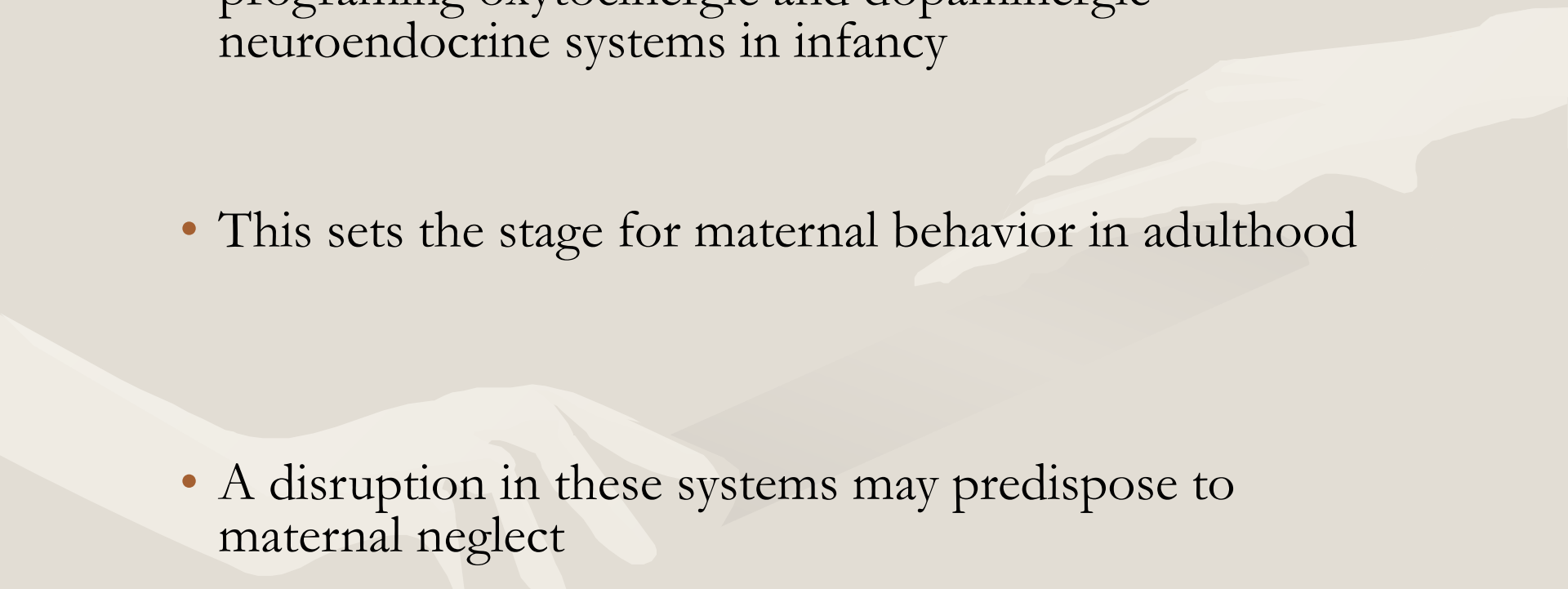
- These dopaminergic circuits are influenced by early developmental stimulation
- Prolonged maternal separation and isolation rearing = reduced dopamine transporter binding in VS, increased release of dopamine in response to acute stress
- Low self reported maternal care = elevated dopamine response to stress
- Hi L/G moms also had hi dopamine release **but to infant cues and NOT stress**; their physiological stress response is dampened

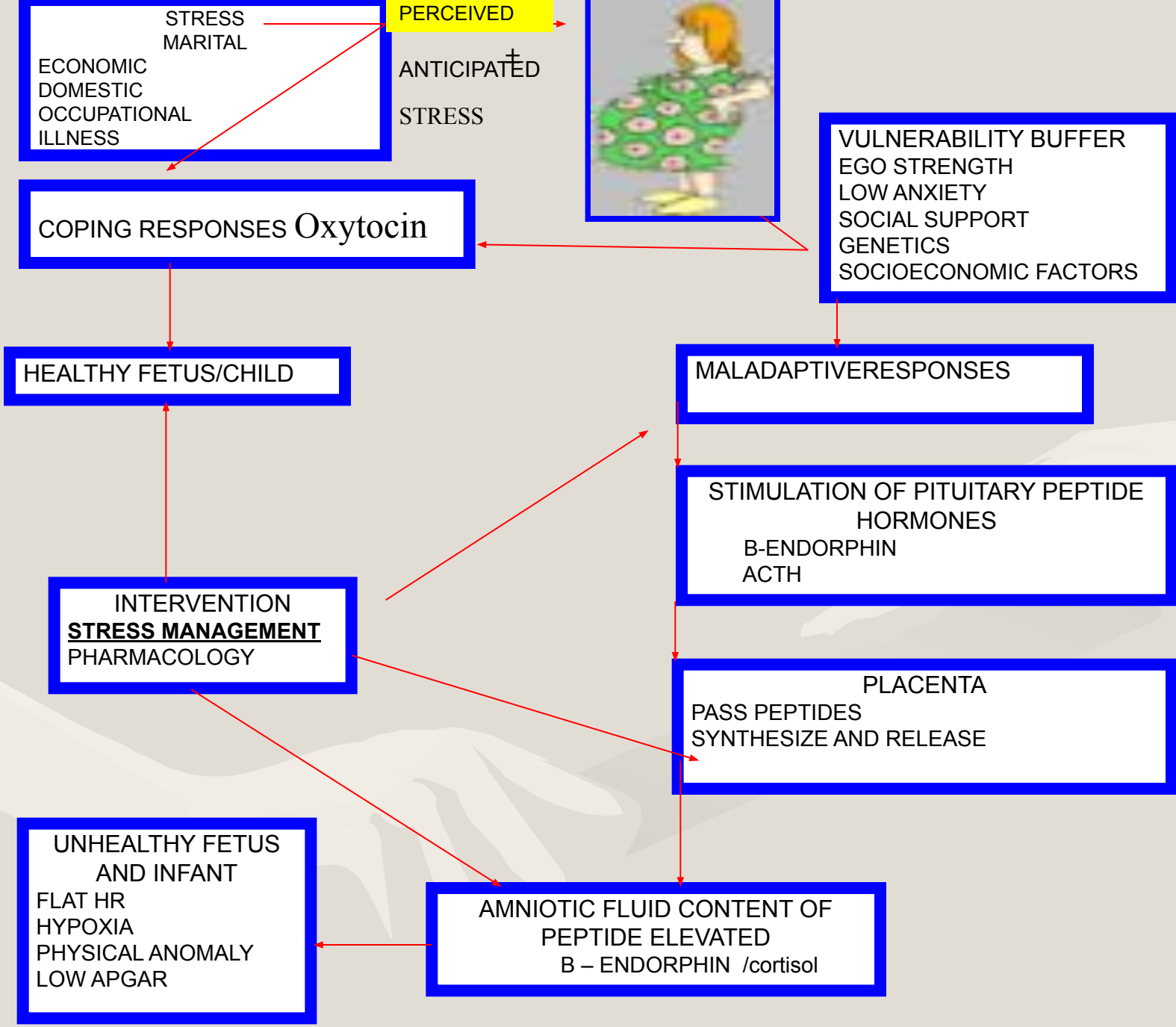
- Oxytocin and dopamine systems are structurally and functionally connected
- The stronger they are the higher the maternal care giving behavior
- In pregnancy and lactation: both oxytocin and dopamine levels increase in the SN
- Infant cues such as suckling= OTC release in hypothalamus= dopamine reward system = long term preference for social cues

ADDICTION AND MATERNAL NEGLECT

- In addiction: oxytocin in Mesocorticolimbic area, hypothalamus and VS are reduced
- Increased sensitivity to cocaine (psychostimulants) that activate dopaminergic neuron
- Oxytocin may ameliorate addiction and drug withdrawal effects
- ? Connection between addiction and maternal neglect

In Summary.....

- Early Maternal caregiving plays an important role in programming oxytocinergic and dopaminergic neuroendocrine systems in infancy
 - This sets the stage for maternal behavior in adulthood
 - A disruption in these systems may predispose to maternal neglect
- 



COPING RESPONSES Oxytocin

VULNERABILITY BUFFER
EGO STRENGTH
LOW ANXIETY
SOCIAL SUPPORT
GENETICS
SOCIOECONOMIC FACTORS

HEALTHY FETUS/CHILD

MALADAPTIVERESPONSES

INTERVENTION
STRESS MANAGEMENT
PHARMACOLOGY

STIMULATION OF PITUITARY PEPTIDE HORMONES
B-ENDORPHIN
ACTH

PLACENTA
PASS PEPTIDES
SYNTHESIZE AND RELEASE

UNHEALTHY FETUS AND INFANT
FLAT HR
HYPOXIA
PHYSICAL ANOMALY
LOW APGAR

AMNIOTIC FLUID CONTENT OF PEPTIDE ELEVATED
B - ENDORPHIN /cortisol

Addressing **Toxic** Stress



- **Primary / Universal Prevention**

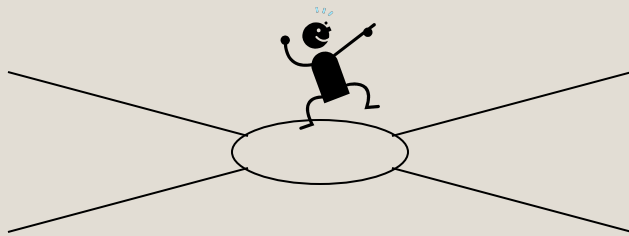
- Proactive, universal interventions to make stress **positive**, instead of tolerable or toxic
- Acknowledges that preventing all childhood adversity is **impossible** and even **undesirable**
- **Actively building resiliency** (“immunizing” through positive parenting, 7C’s of resilience, promoting optimism, “One Minute” social-emotional learning)
- **SE Buffers** for caregivers allow the physiologic stress response to return to baseline

Promoting the Five R's of Early Childhood Education

- **READING** together - daily
- **RHYMING**, playing and cuddling
- **ROUTINES** – help children know what to expect of us - what is expected of them
- **REWARDS** for everyday successes – PRAISE is a powerful reward
- **RELATIONSHIPS**, reciprocal and nurturing – foundation of healthy child development



WHAT are we DOING?!



Universal Primary Preventions

Bright Futures
Connected Kids
Social-Behavioral Milestones
Relationships as a “vital” sign
Basic EB CD Competencies

Targeted Interventions

Screening for risks
(assess the ecology)
Refer to/advocate for EBI
Collaborating/Developing EBI
Mid-level Competencies

Evidence-Based Treatments

Screening for diagnoses
Common factors approach
Refer for/advocate for EBT
Collaborating/Developing EBT
Advanced Competencies

Addressing **Toxic** Stress



- **Treatment** of the consequences
 - Evidence-based treatments
 - Trauma Focused Cognitive Behavioral Therapy
 - Parent-Child Interactive Therapy
 - **Reactive** – some “damage” already done!
 - Very **COSTLY**
 - Efficacy linked to age and chronicity
 - Declining **brain plasticity**?
 - Insufficient **number** of / **access** to providers
 - Persistent **STIGMA**
 - “**Character Flaws**” vs “**Biological Mal-adaptations**”

SUMMARY

- **What can I do?**
 - **Understand** the **ecobiodevelopmental framework** (advocate for a collaborative, public health approach to address toxic stress)
 - **Help** children figure out **how to turn off** their stress response (parent/child skills)
 - **Recognize** the relationship as a vital sign

SUMMARY

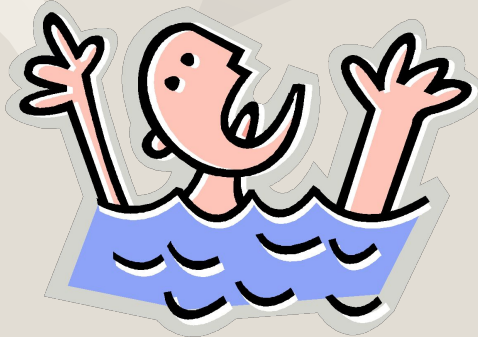
- What can I do?
 - **Develop** purposeful partnerships with **Pediatric healthcare providers**
 - **Incorporate practice process to screen, refer, and follow all children**
 - **Intervene early** for those children who appear **unable to turn off** their stress response (secondary and tertiary prevention)

SUMMARY

- What can I do?
 - Provide parents information on Adverse Childhood Experiences
 - Understand and learn about parents' adverse childhood experiences
 - Refer parents for resources to help them address their own stress and health concerns.

A Public Health Parable:

- Man by the river hears someone **drowning**
- Being a good swimmer, he **rescues** the person
- Before catching his breath, he hears **another** in need, and **another** and **another**...
- The man, exhausted, begins to **walk away**
- Asked where he's going, he responds...

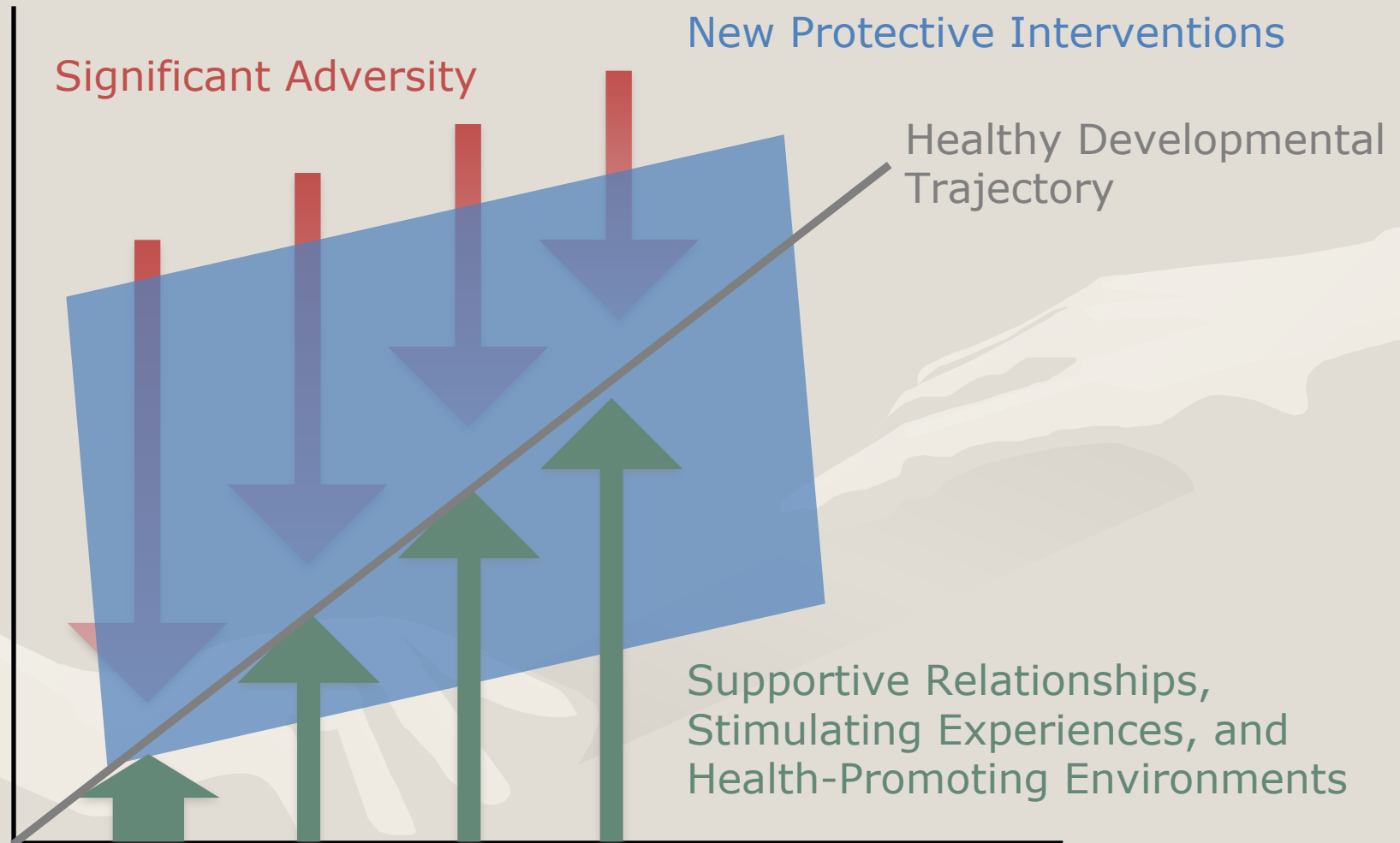


A Public Health Parable:

“I’m going **upstream
to prevent others
from falling in!!”**



Building an Enhanced Theory of Change that Balances Enrichment and Protection

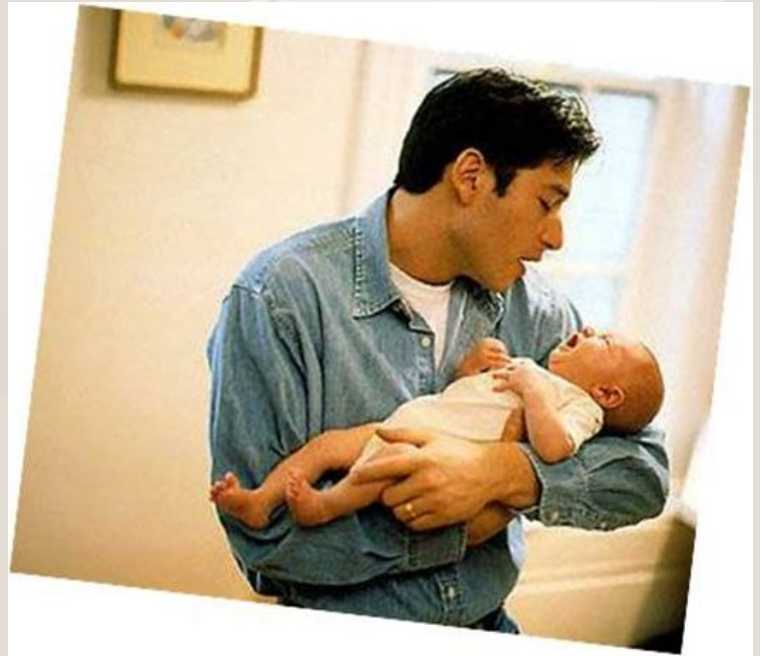


We're in the “building health and developmental assurance” business.....

Physical health

Developmental health

Relational health



CONCLUSION:

It is easier to **build strong children**
than to **repair broken men.**

Frederick Douglass

