



# Formación en Lactancia y Salud Mental

*Psicología de la Lactancia*

Dirigida por Ibone Olza,  
Carmela Baeza y Esther R. Matos

Información e inscripciones  
[saludmentalperinatal.es](http://saludmentalperinatal.es)



Instituto Europeo de  
Salud Mental Perinatal

# Introducing NURTURESCIENCE a new model with ancient roots.



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*(USA equiv: MD, MPH, PhD)*

Karolinska Institute,  
Sweden.

Introducing NURTURESCIENCE a  
new model with ancient roots.



**NINO**  
Nurturescience  
for Improved  
Neonatal Outcomes

[www.ninobirth.org](http://www.ninobirth.org)

# Introducing NURTURESCIENCE a new model with ancient roots.



Instituto Europeo de  
Salud Mental Perinatal

... with focus on long  
term mental health  
benefits.

# Introducing NURTURESCIENCE a new model with ancient roots.

**nurture** noun

nur·ture | \ 'nər-cher \

## Definition of *nurture* (Entry 1 of 2)

1 : TRAINING, UPBRINGING

// With proper focus during *early nurture*, one can grow into a secure being ...



SINCE 1828

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nurture

DICTIONARY

THESAURUS

# Introducing NURTURESCIENCE a new model with ancient roots.

## nurture **noun**

nur·ture | \ 'nər-cher \ 

### Definition of *nurture* (Entry 1 of 2)

**1** : TRAINING, UPBRINGING

// With proper focus during *early nurture*, one can grow into a secure being ...

— Ella Pearson Mitchell

**2** : something that nourishes : FOOD

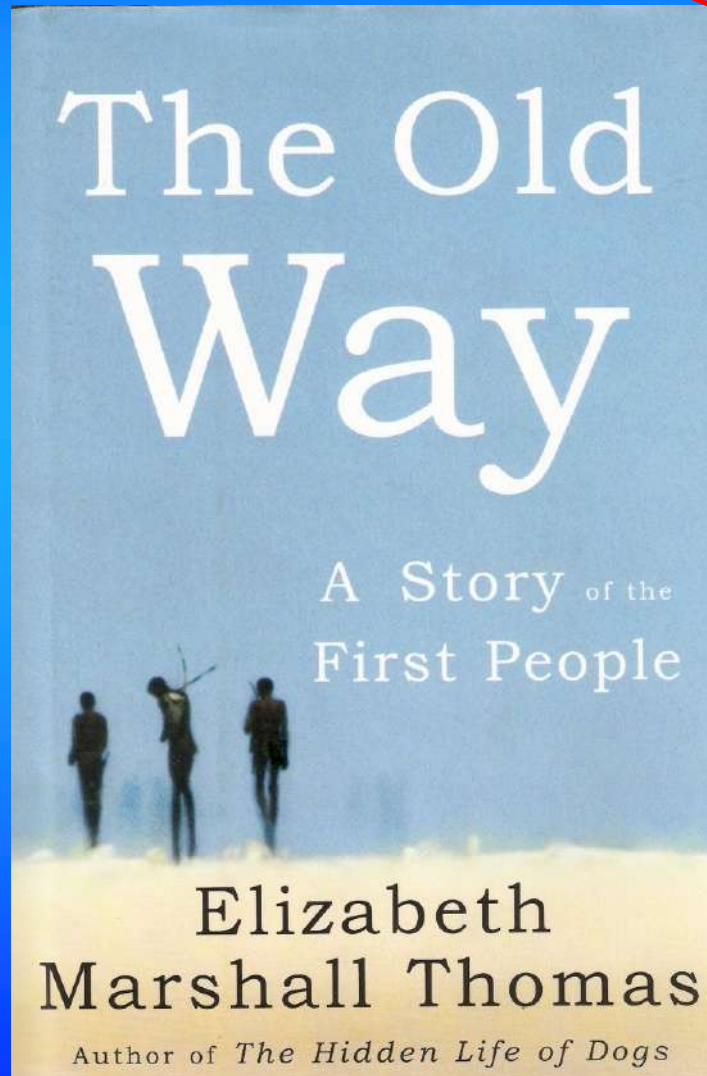
// ... fed him well, and nourished himself, and took *nurture* for the road ...

— R. D. Blackmore

**3** : the sum of the environmental factors influencing the behavior and traits expressed by an organism

// Is our character affected more by nature or by *nurture*?

Introducing NURTURESCIENCE a  
new model with ancient roots.



*Other Ways  
of Being Born  
and Growing*

# The Old Way

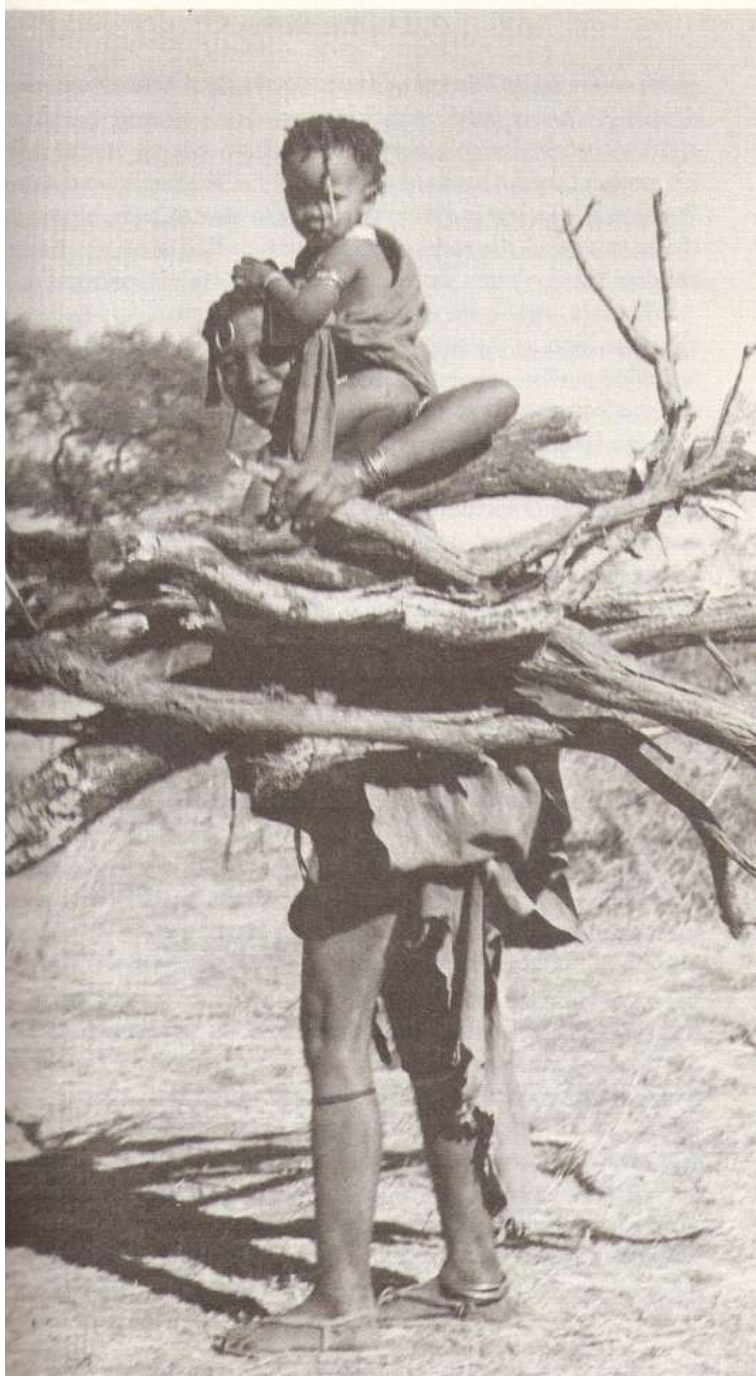
A Story of the  
First People

Elizabeth  
Marshall Thomas

Author of *The Hidden Life of Dogs*

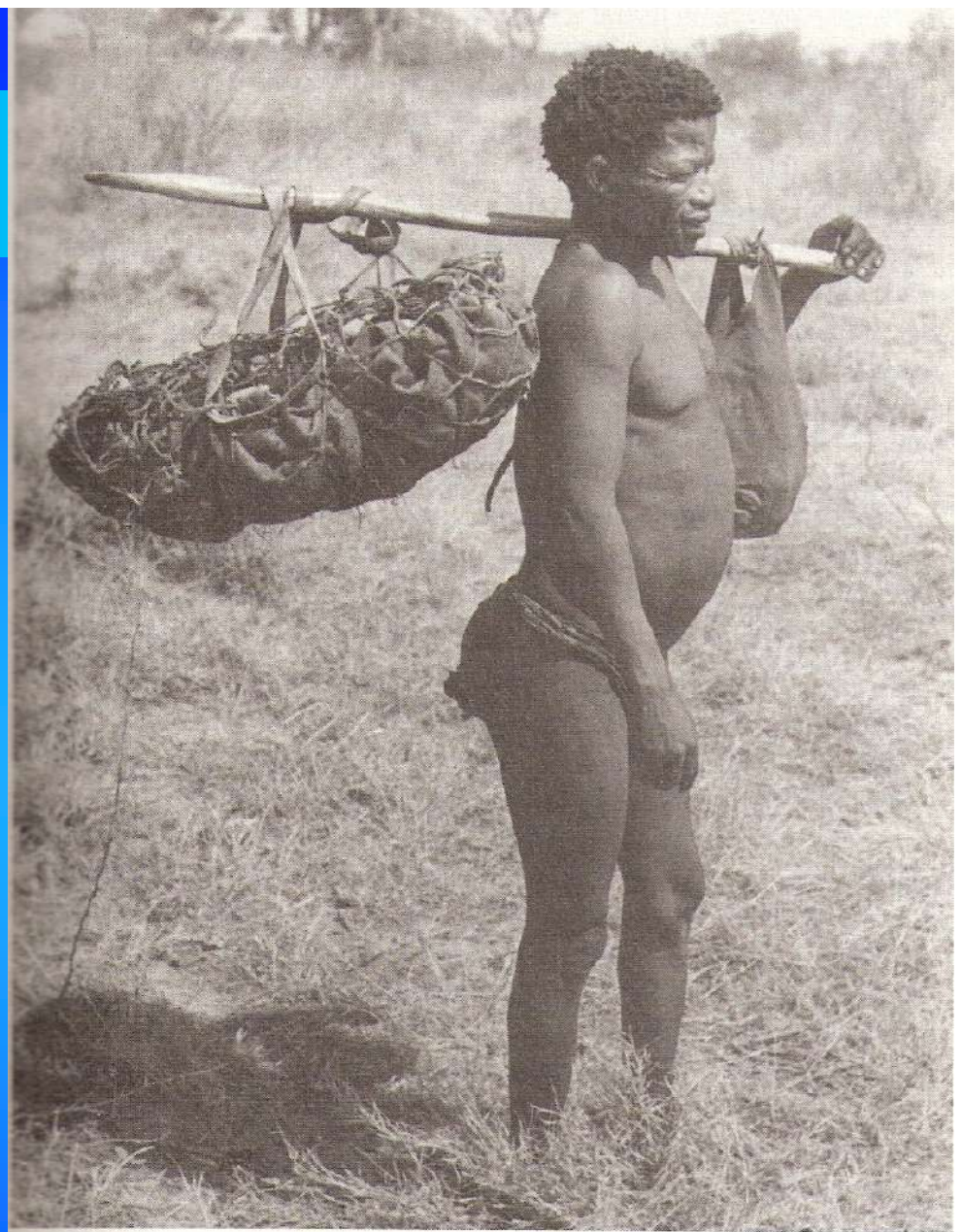




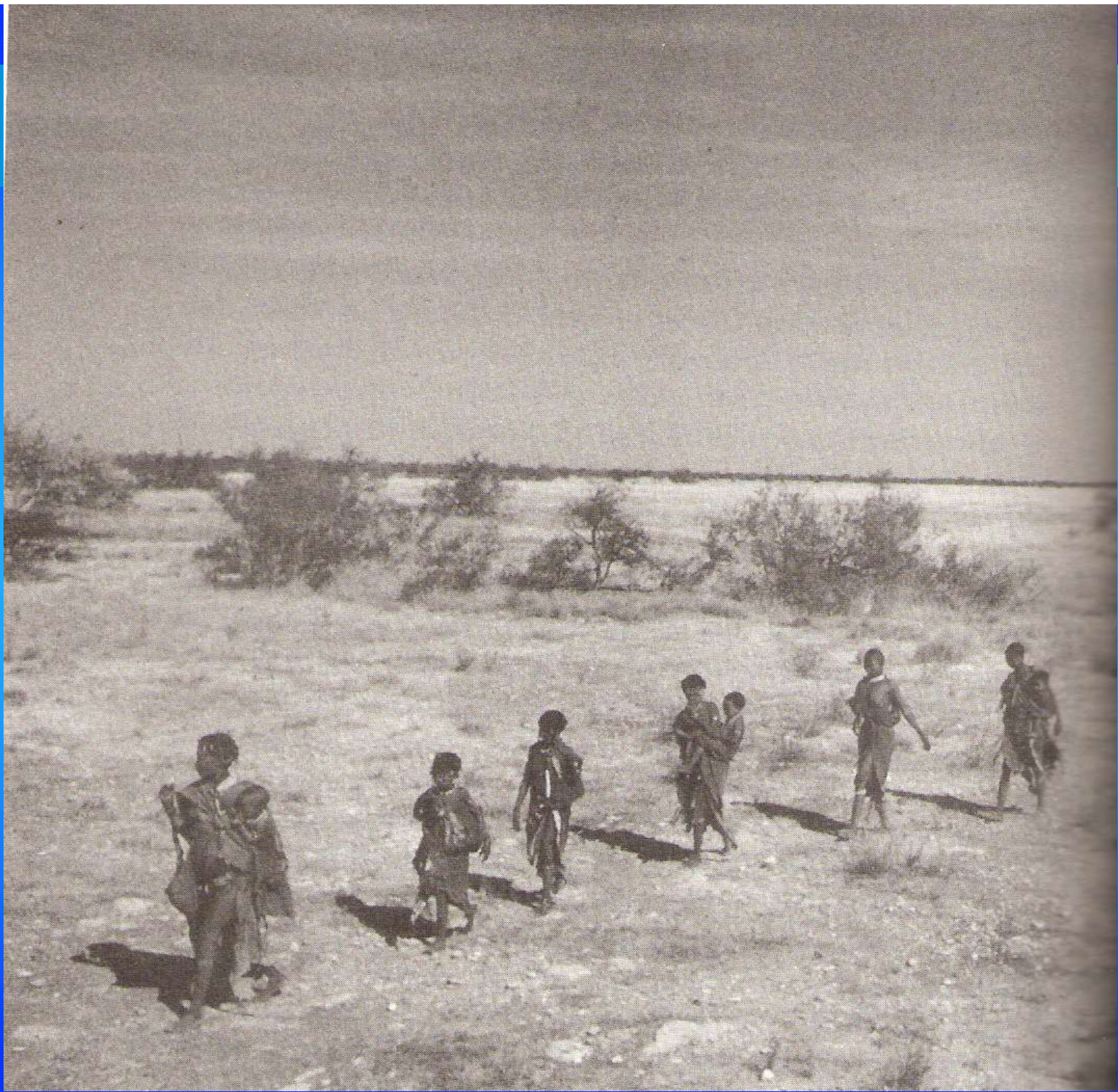




≠Toma once said of himself,  
"From the day I was born, I was born for meat."



≠Toma returns from a foraging trip carrying a net lined with skin and filled with nuts. A gathering party of men and women would walk for several days over waterless country to pick clean the nut groves or the groundnut patches and would carry home their harvest in big leather bags that could hold from fifty to one hundred pounds of nuts.



# Hominines were prey at Sterkfontein, "Cradle of Mankind"

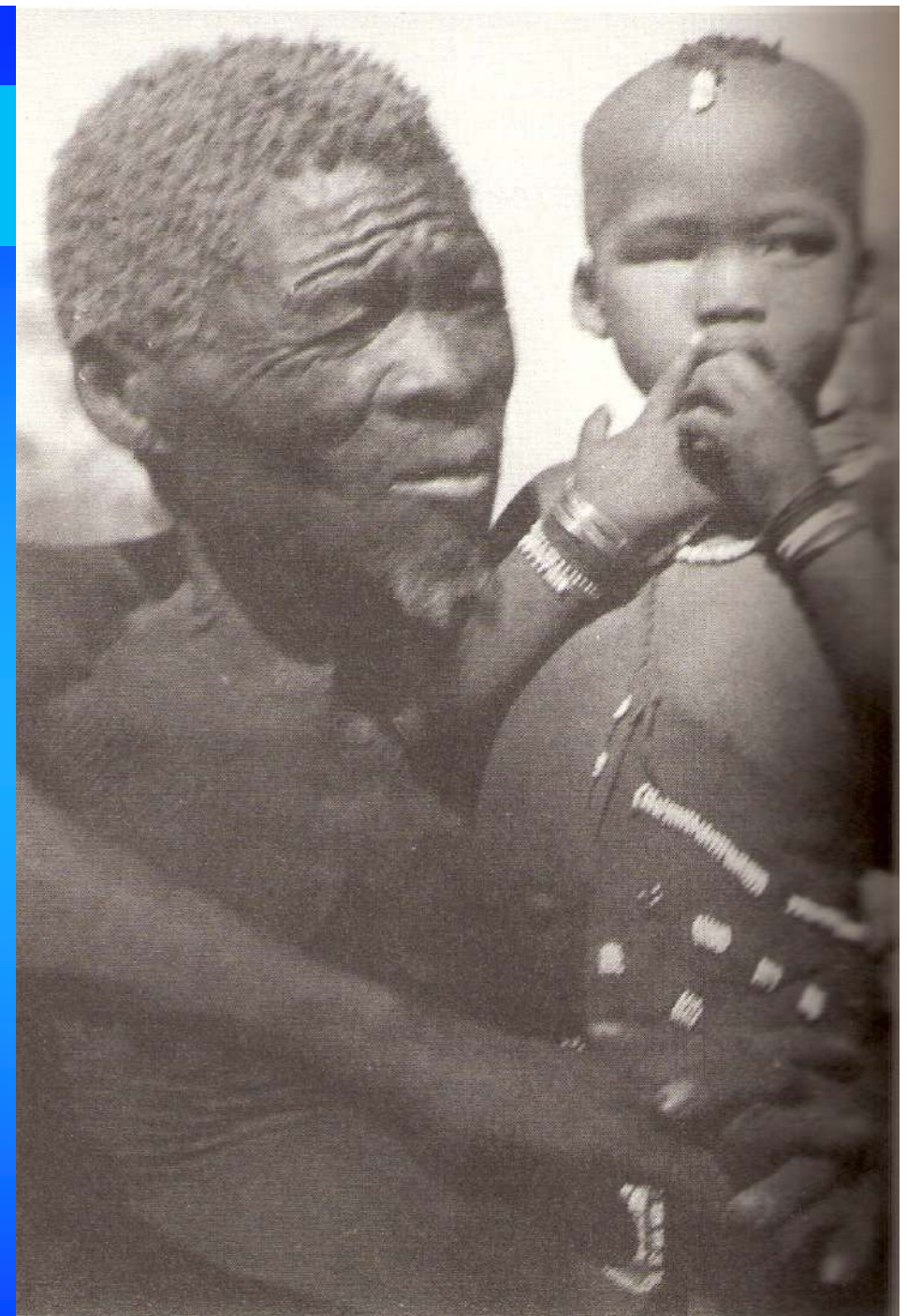






Immediate feeding  
response to crying

Father frequently  
and closely involved ...



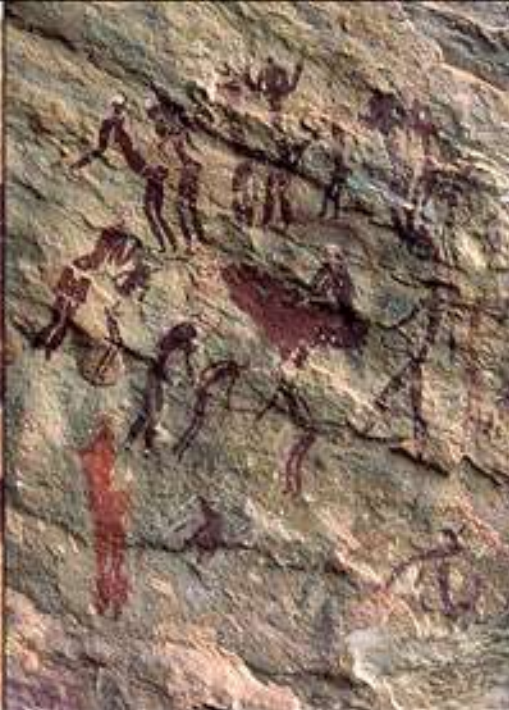


EXTREME EGALITARIANISM

EQUALITY (gender, age, capacity)

INTENSE SOCIAL COHESION

→ NO AGGRESSION !!!!!



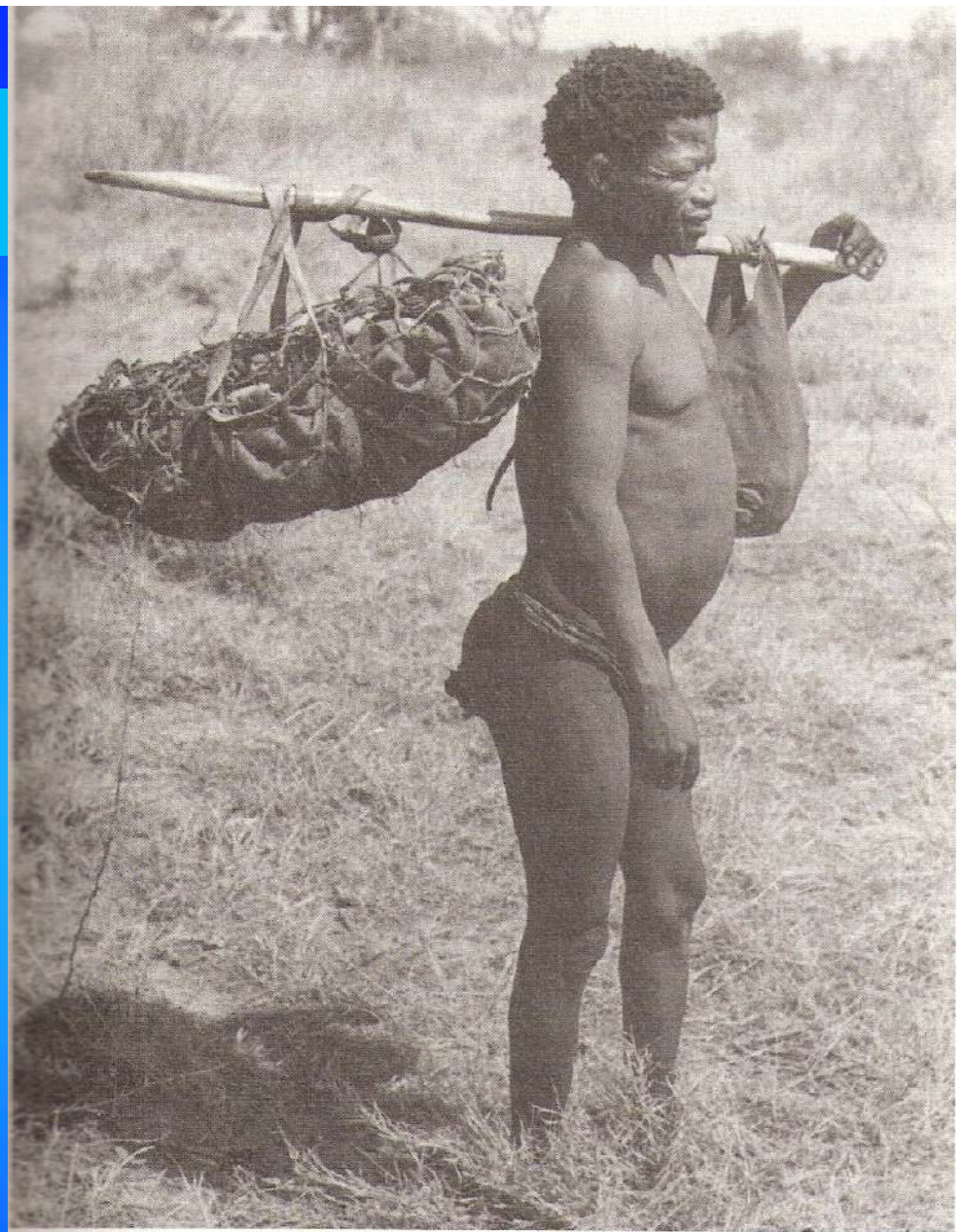


UNIQUE

hominin feature:  
carry food home  
to share ...

BERGMAN

'sharing phenotype'



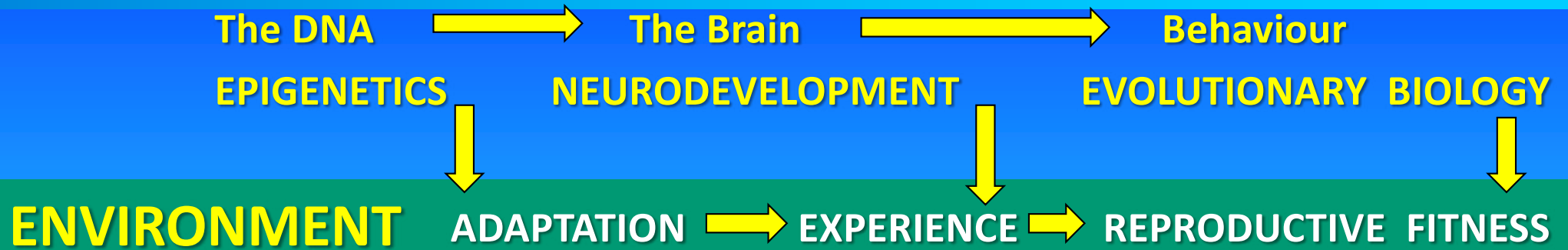
*≠Toma returns from a foraging trip carrying a net lined with skin and filled with nuts. A gathering party of men and women would walk for several days over waterless country to pick clean the nut groves or the groundnut patches and would carry home their harvest in big leather bags that could hold from fifty to one hundred pounds of nuts.*

## THE HUNTER GATHERER (cont)

Infant care patterns in such societies  
(which are closest to our origins):

- 1 Infant carried most of time
- 2 Mother sleeps with infant same bed
- 3 Immediate feeding response to crying
- 4 Breastfeeding 24 months or more
- 5 Father frequently and closely involved ...

# NURTURESCIENCE



- 1 Infant carried most of time
- 2 Mother sleeps with infant same bed
- 3 Immediate feeding response to crying
- 4 Breastfeeding 24 months or more
- 5 Father frequently and closely involved ...

a new model with ancient roots.

# DURATION OF HUMAN SUBSISTENCE PATTERNS



a new model with ancient roots.

Introducing NURTURESCIENCE a  
new model with ancient roots.

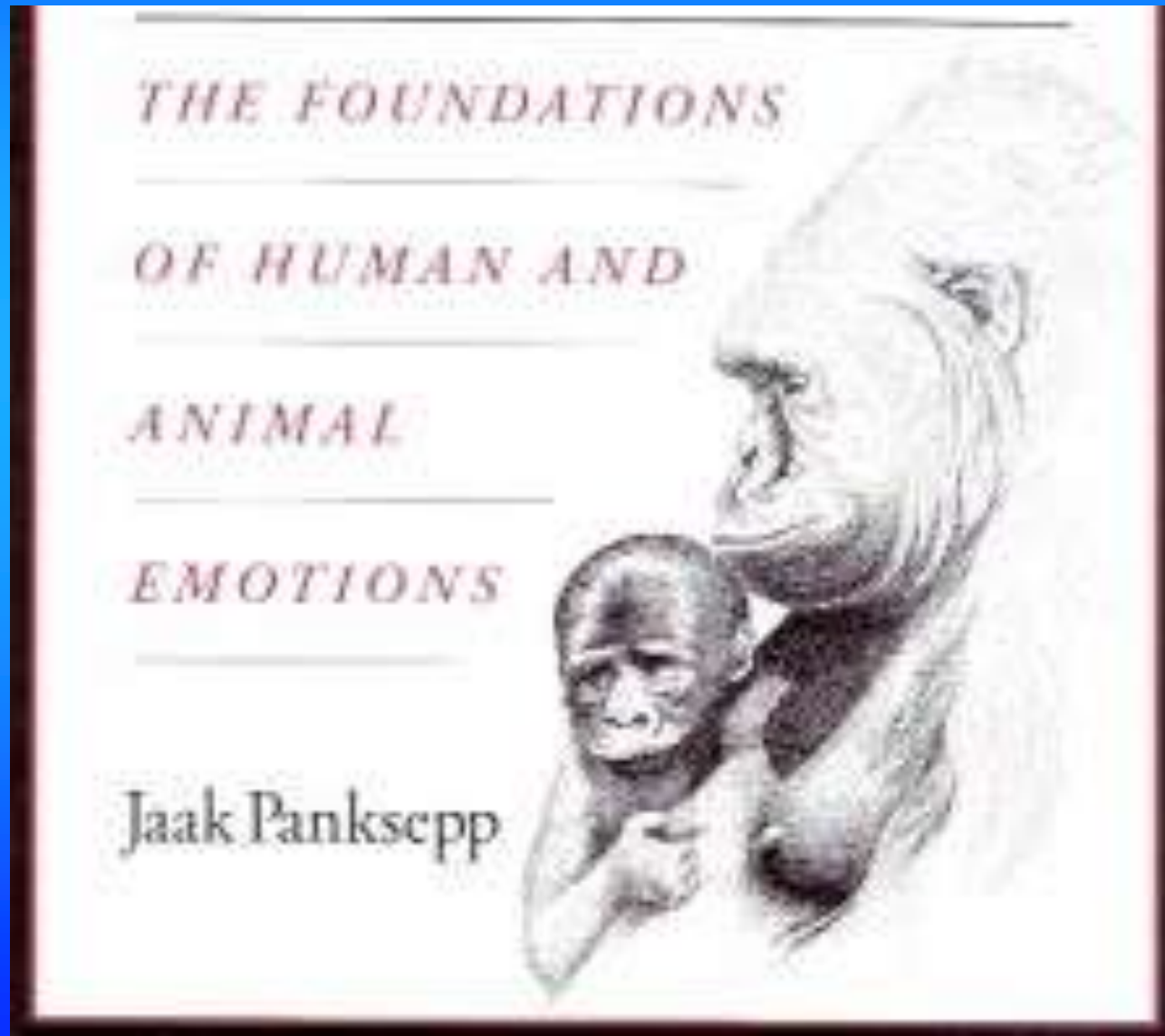
ZERO SEPARATION  
for 30,000,000 years

SEPARATION for 100 years



a new model with ancient roots.

# Introducing NURTURESCIENCE a new model with ancient roots.



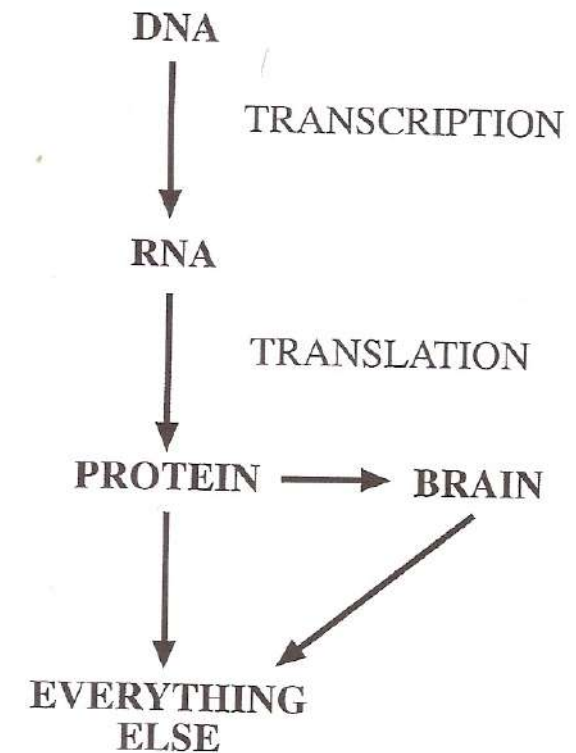
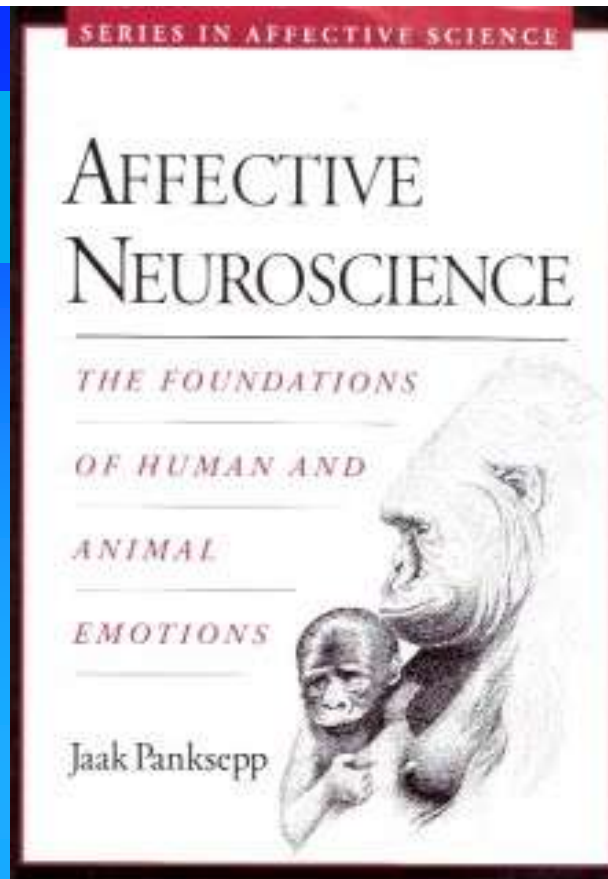


Figure 6.1. Summary of the current “central dogma” that underlies the analysis of all biological processes, including those that mediate basic psychobiological

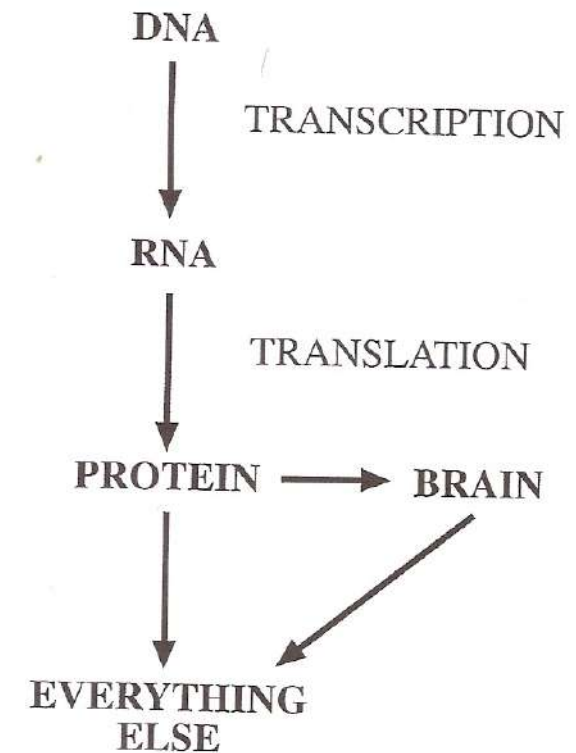
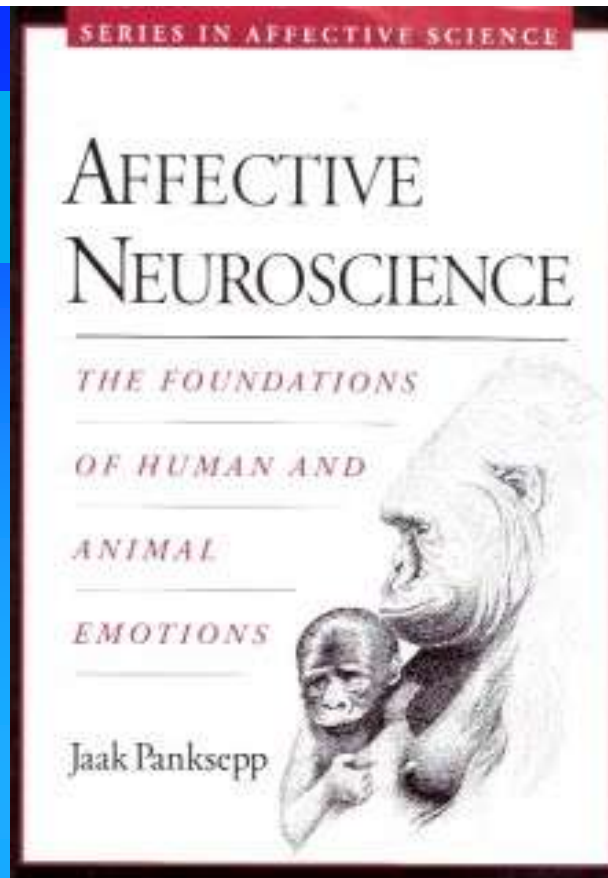
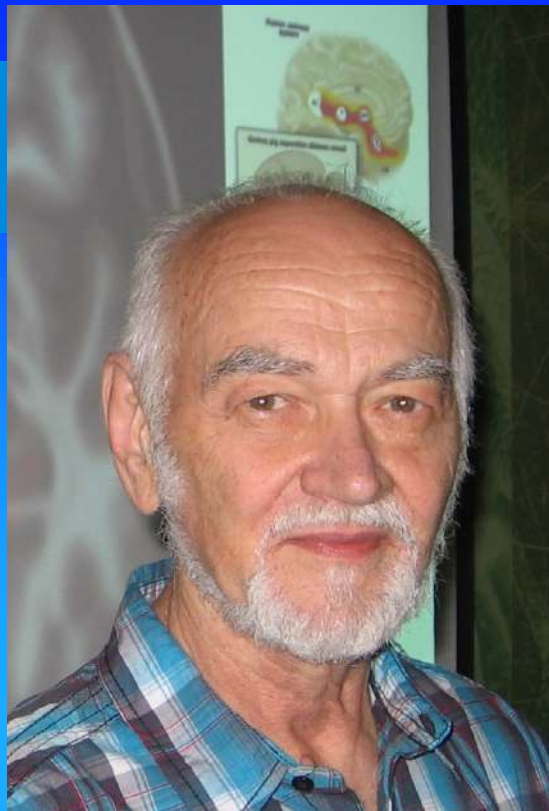


Figure 6.1. Summary of the current “central dogma” that underlies the analysis of all biological processes, including those that mediate basic psychobiological processes. The only major concept missing from this schematic is the environment, and these influences permeate all phases of these transactions.



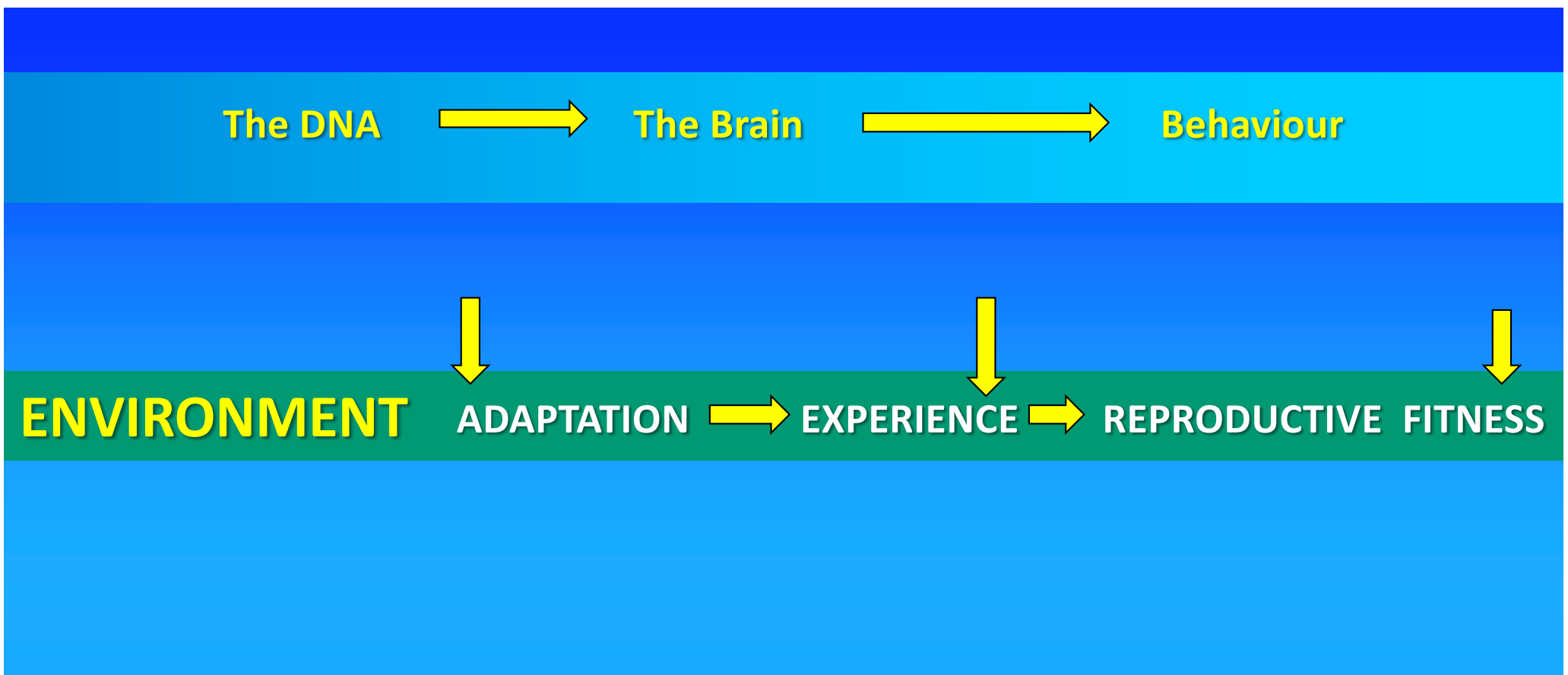


Figure 6.1. Summary of the current “central dogma” that underlies the analysis of all biological processes, including those that mediate basic psychobiological processes. The only major concept missing from this schematic is the environment, and these influences permeate all phases of these transactions.

The DNA → The Brain → Behaviour

Genome → Connectome → Behaviour

EPIGENETICS

NEURODEVELOPMENT

EVOLUTIONARY BIOLOGY

ENVIRONMENT

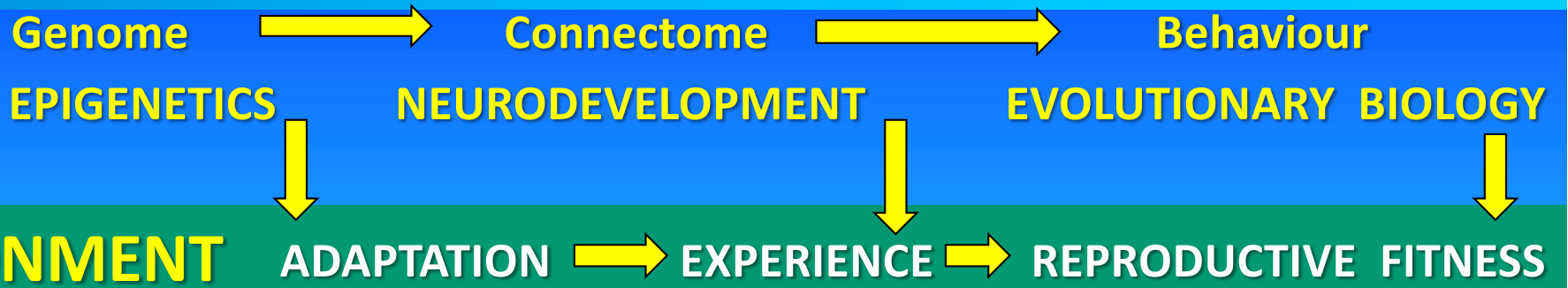
ADAPTATION

EXPERIENCE

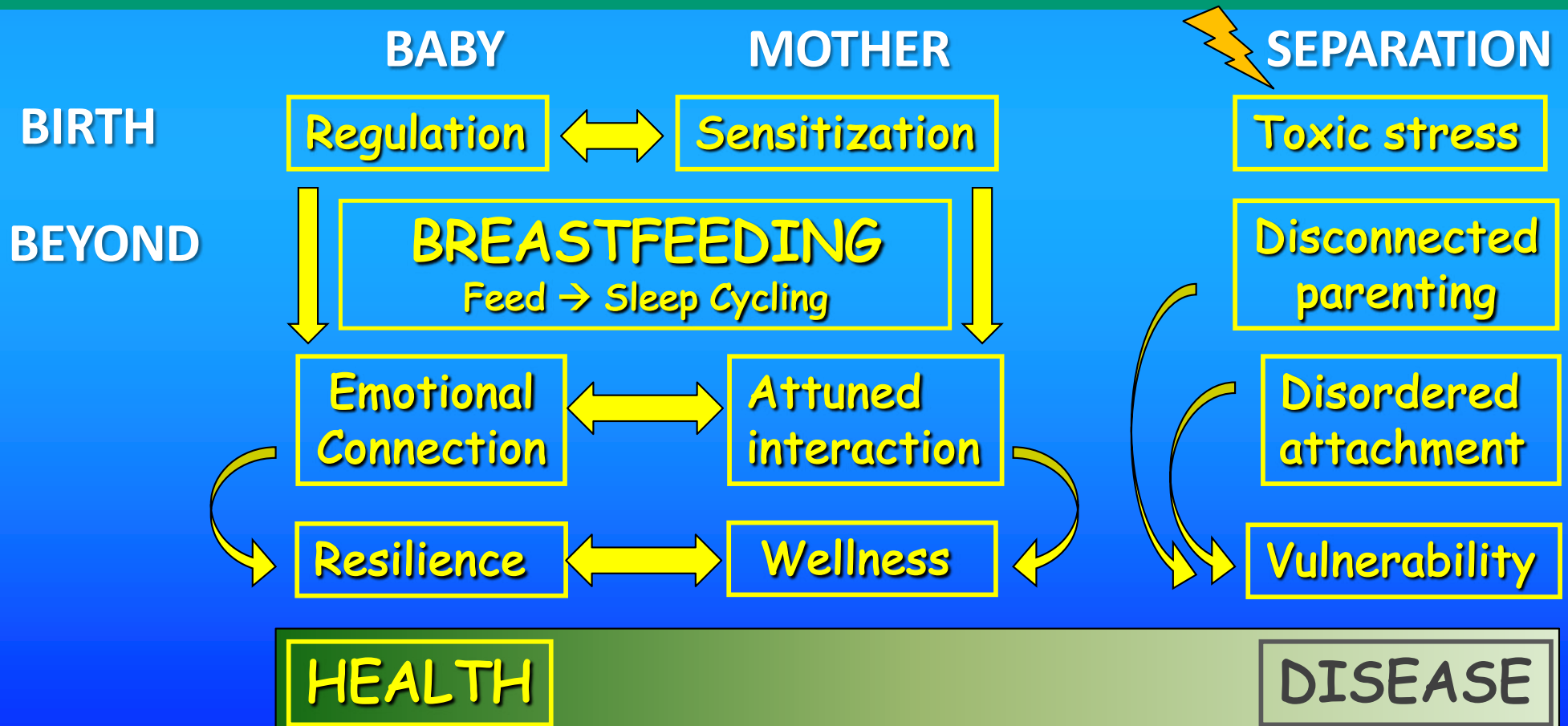
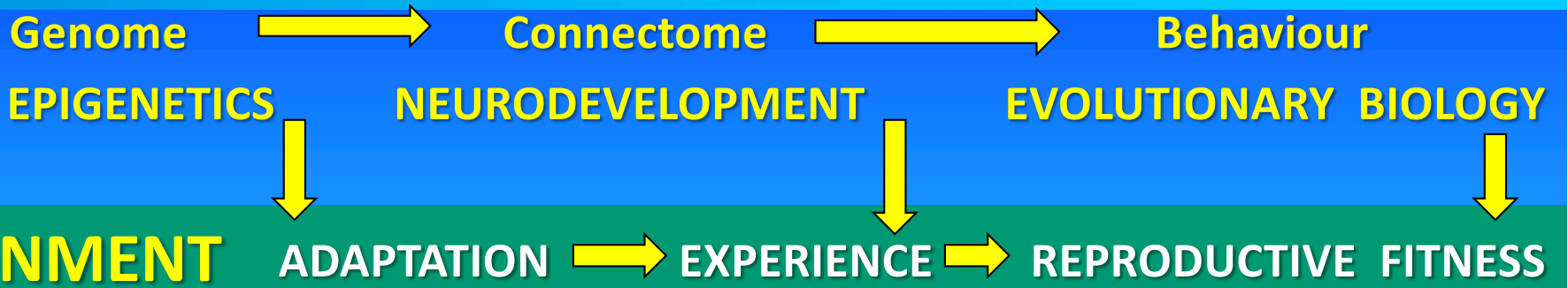
REPRODUCTIVE FITNESS



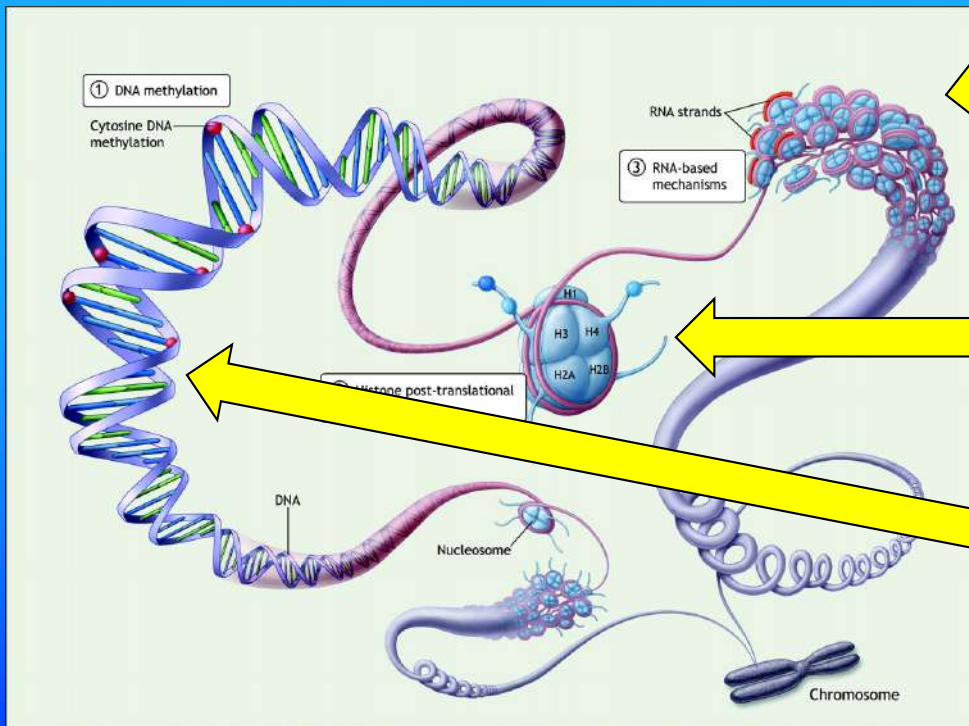
# NURTURESCIENCE



# NURTURESCIENCE



# NURTURESCIENCE



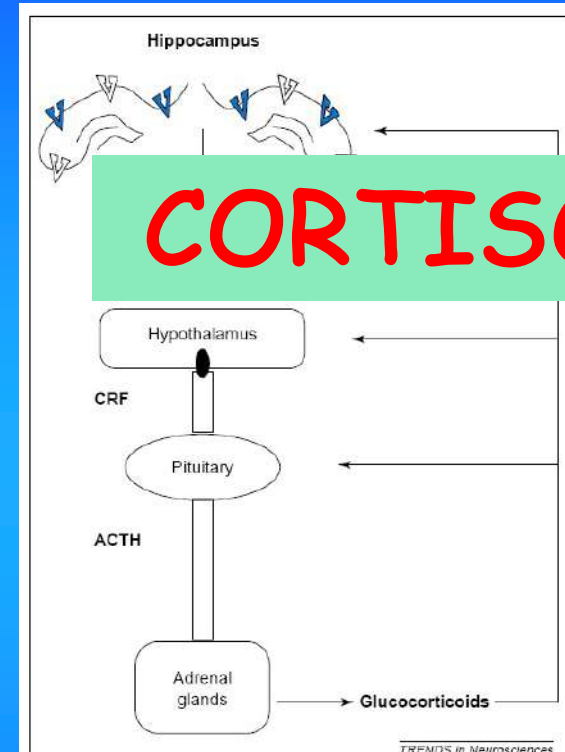
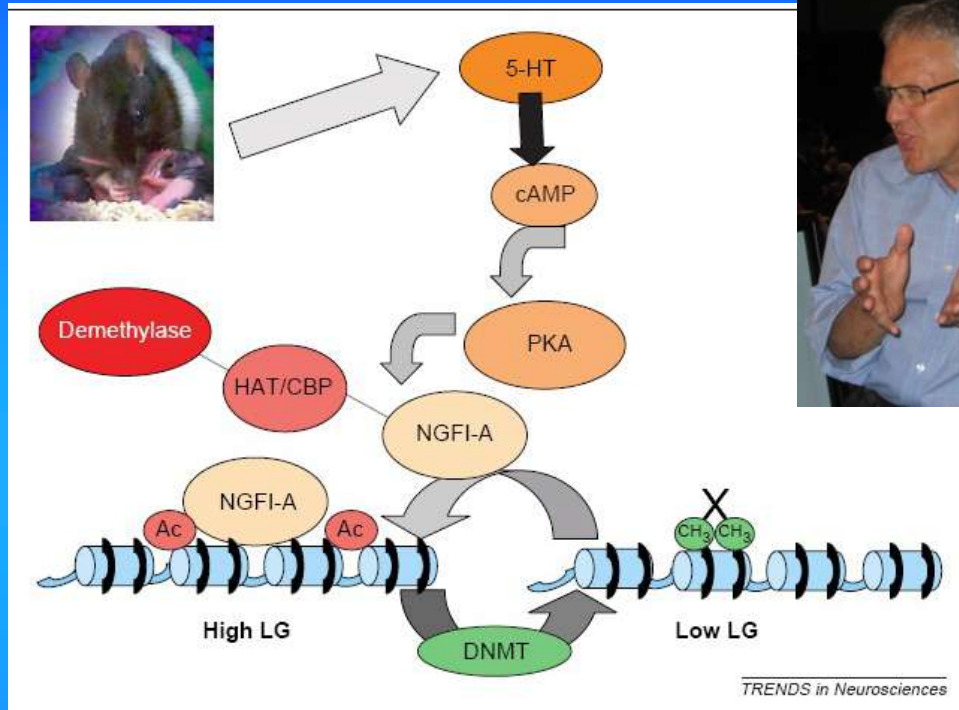
MICRO-RNA

HISTONE MODIFICATION

DNA METHYLATION

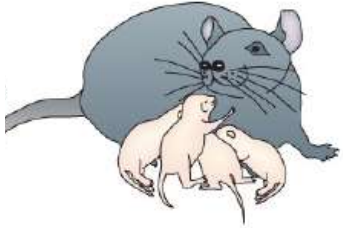
# MICHAEL MEANEY

# epigenetics



Unsafe environment activates HPA axis (autonomic nervous system, ANS).

High licking and grooming



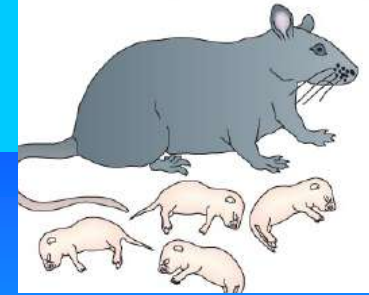
**MOTHER**

**HG - High Grooming**

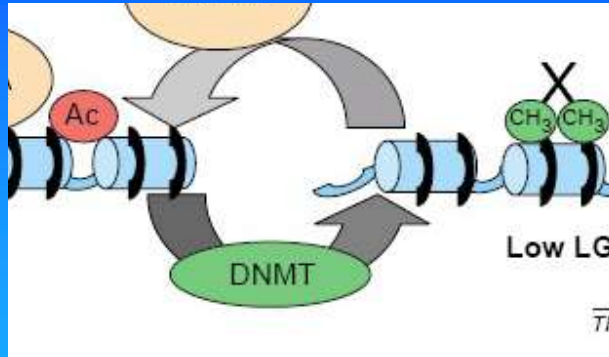
**MOTHER**

**Low Grooming LG**

Low licking and grooming



**HG BABY**



**LG BABY**

**Healthy adult**

**UNHEALTHY adult**

**Makes MOTHER**

**Makes MOTHER**

**HG - High Grooming**

**Low Grooming - LG**

**HG BABY**



**HG BABY**



**LOW Grooming care**

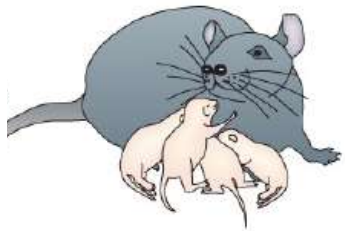
**CORTISOL**

**UNHEALTHY adult**

**Makes MOTHER**

**LOW Grooming LG**

High licking and grooming



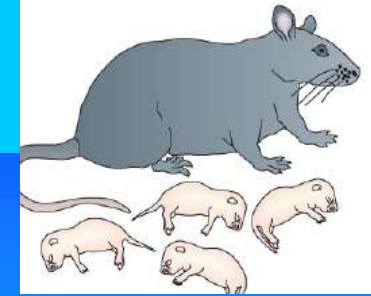
**MOTHER**

**HG - High Grooming**

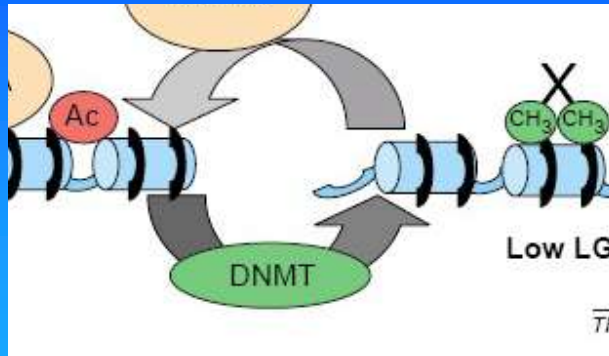
**MOTHER**

**Low Grooming LG**

Low licking and grooming



**HG BABY**



**LG BABY**

**Healthy  
adult**

**UNHEALTHY  
adult**

**Makes MOTHER**

**HG – High Grooming**

**Makes MOTHER**

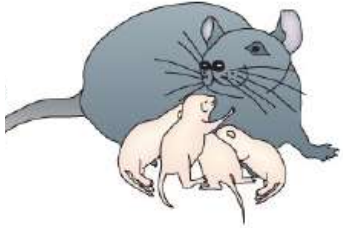
**Low Grooming - LG**

**Early stress alters gene expression,  
with health impact across lifespan.**

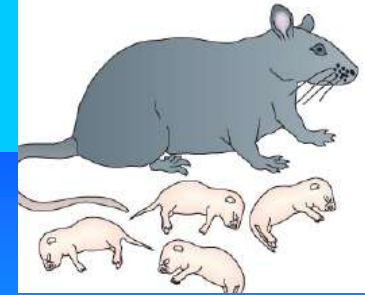


# Earliest care at birth matters

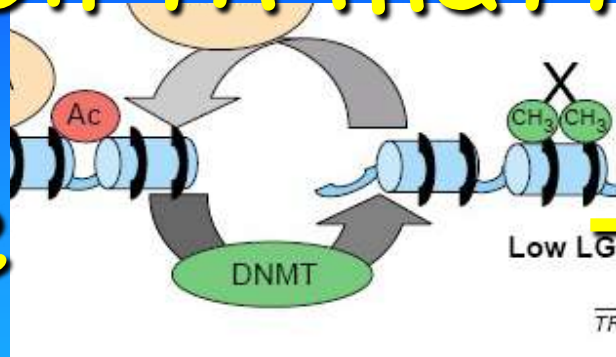
High licking and grooming



Low licking and grooming



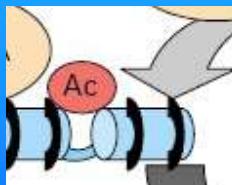
Same gene



switched

Makes MOTHER  
HG – High Grooming

Makes MOTHER  
Low Grooming - LG



LG BABY

HIGH grooming care

LG BABY

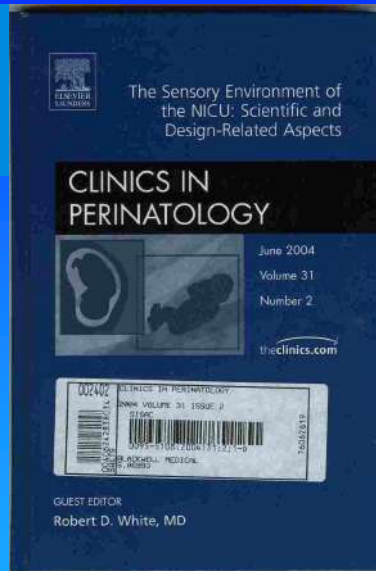


Low LG

HEALTHY  
adult

Makes MOTHER  
HIGH Grooming HG

OXYTOCIN



**Clinics in Perinatology,**  
**June 2004, Vol 31(2) page 210**  
**Stanley Graven**  
*Early neurosensory visual  
development of fetus and newborn.*



**“It is a serious mistake to assume that the principles derived from careful animal studies do not apply to human infants.**

# The Neuroscience of Birth & Breastfeeding



**ENVIRONMENT**    ADAPTATION → EXPERIENCE → REPRODUCTIVE FITNESS

“It is a serious mistake to assume that the principles derived from careful animal studies do not apply to human infants.

The risk of suppression or disruption of *needed neural processes* ...

is very significant and potentially lasts a life time.

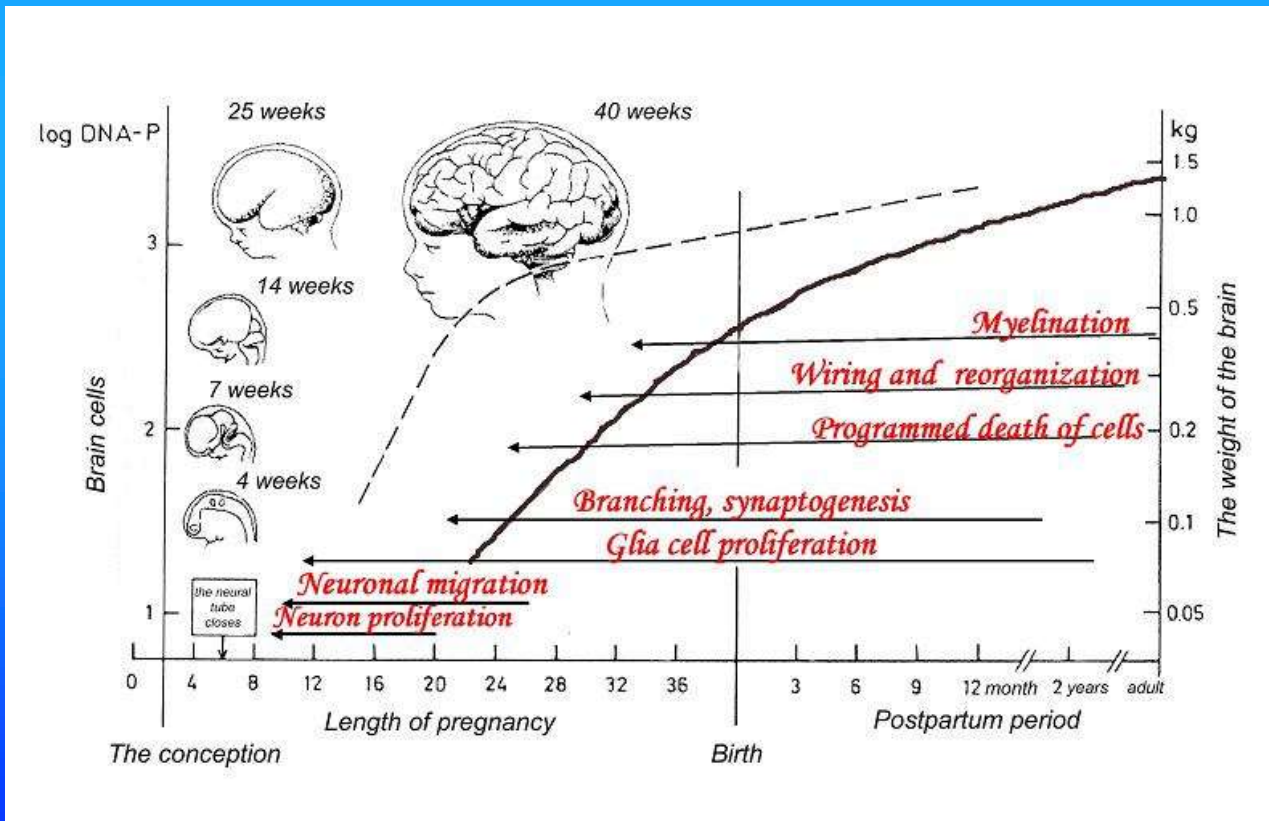
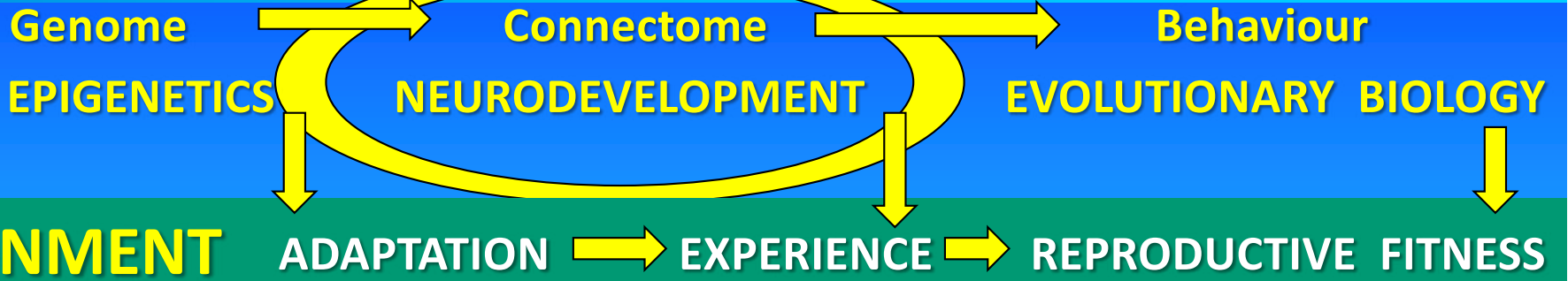
# The Neuroscience of Birth & Breastfeeding



ENVIRONMENT → ADAPTATION → EXPERIENCE → REPRODUCTIVE FITNESS

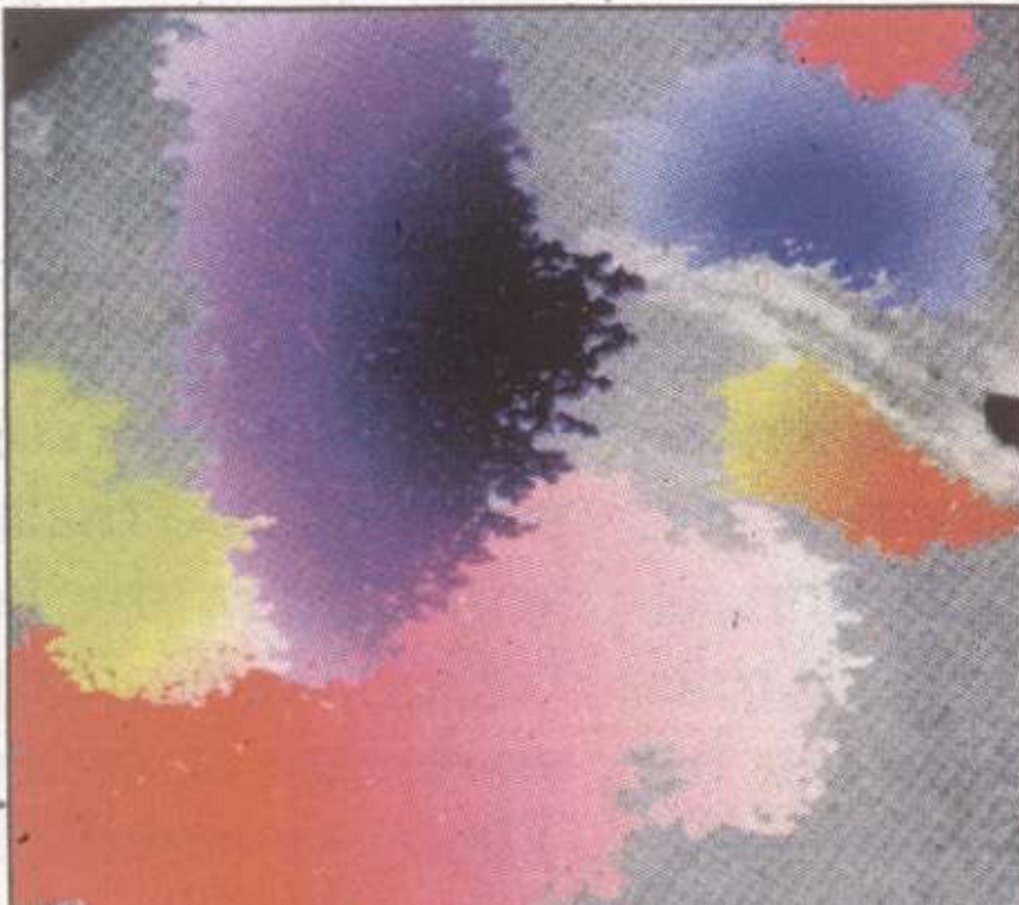
*“needed neural processes”*

# NURTURESCIENCE

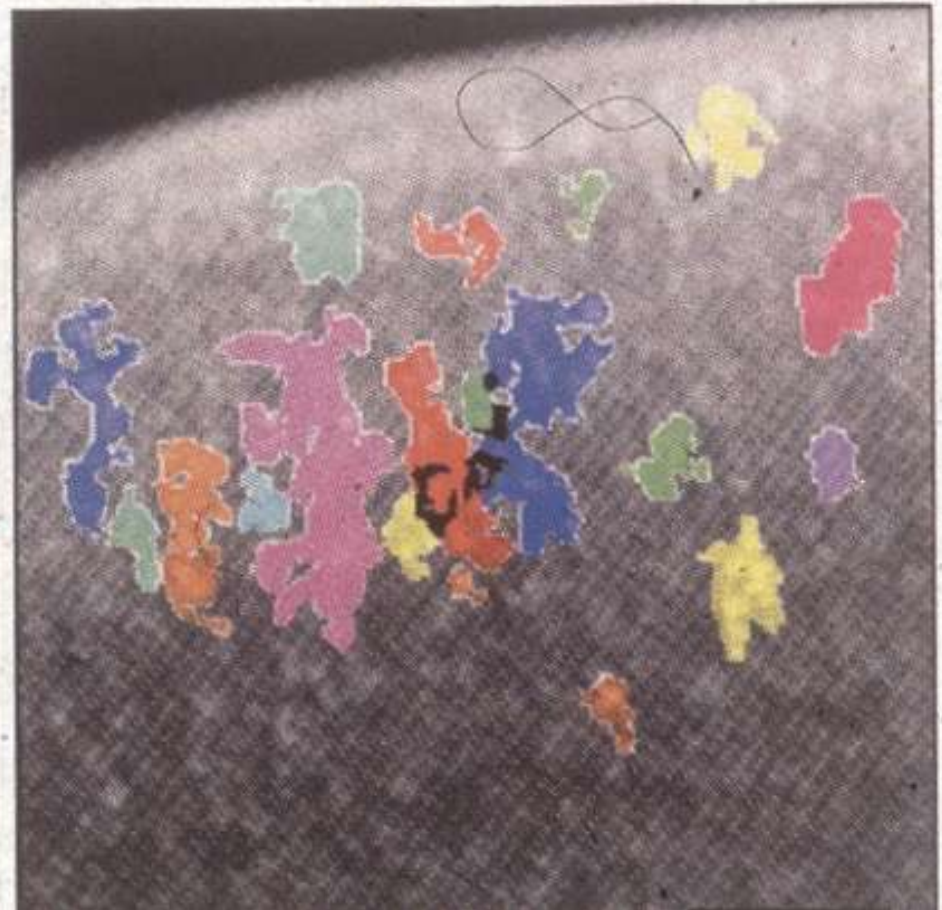


“Neurons that fire together wire together while those which don't, won't”  
*Hebb/Carla Shatz*

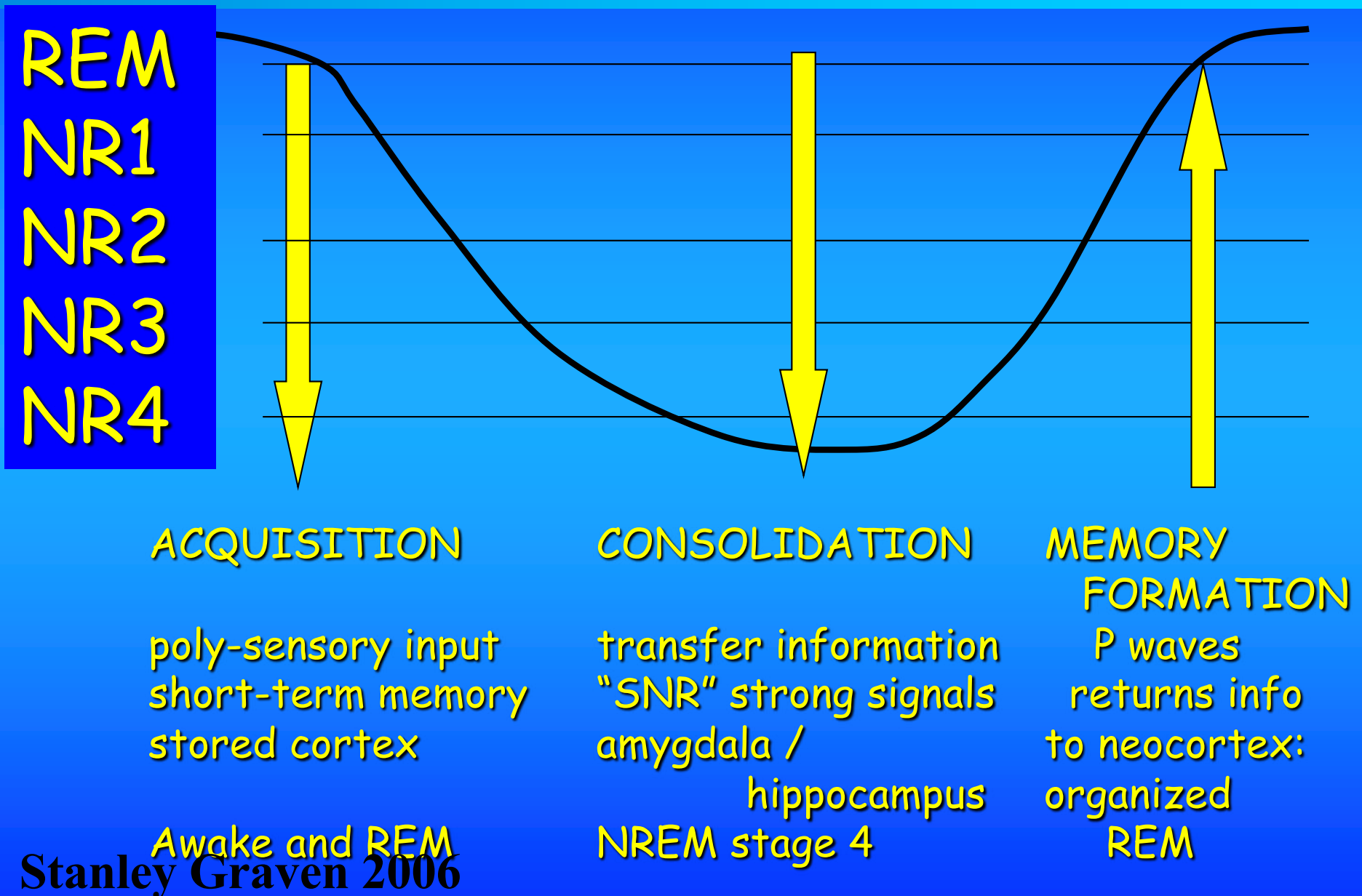
Retina



Cortex



# BRAIN WIRING



Stanley Graven 2006

# Sleep, Hormones, and Memory

Jan Born, PhD<sup>a,\*</sup>, Ullrich Wagner, PhD<sup>b</sup>

Obstet Gynecol Clin N Am 36 (2009) 809–829



**Sleep**



This article follows the hypothesis that a primary function of sleep pertains to the consolidation of memory. In recent years, this view has received substantial support from a rapidly growing number of experiments performed in various species and at different levels of behavioral, cellular, and molecular analysis.<sup>2–7</sup>

In adult:  
sleep pertains  
to memory



# Sleep, Hormones, and Memory

Jan Born, PhD<sup>a,\*</sup>, Ullrich Wagner, PhD<sup>b</sup>

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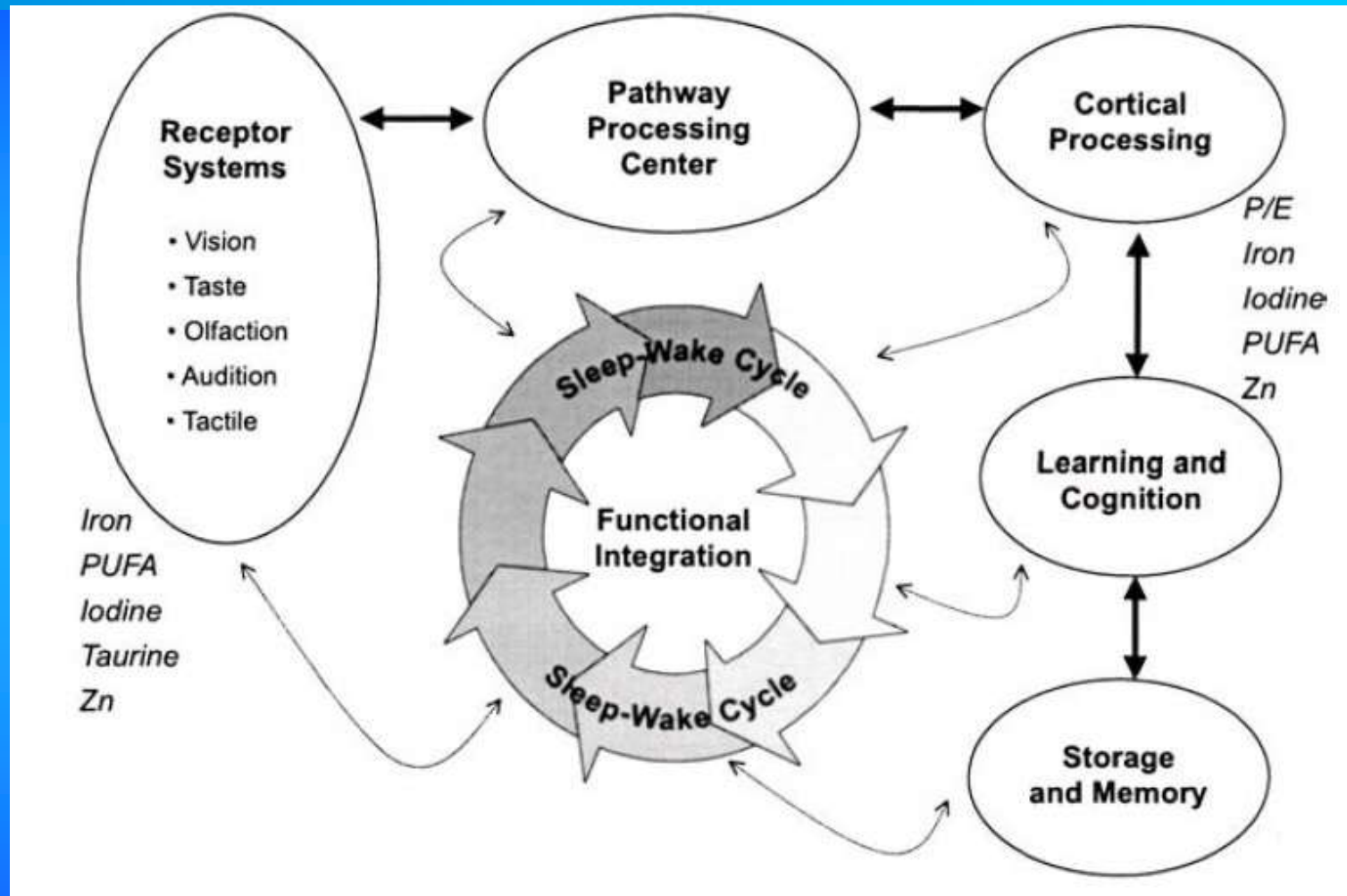
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In adult:  
sleep pertains  
to memory

In child:  
neurodevelopment  
(brain wiring)  
1<sup>st</sup> 1000 days

# BRAIN WIRING

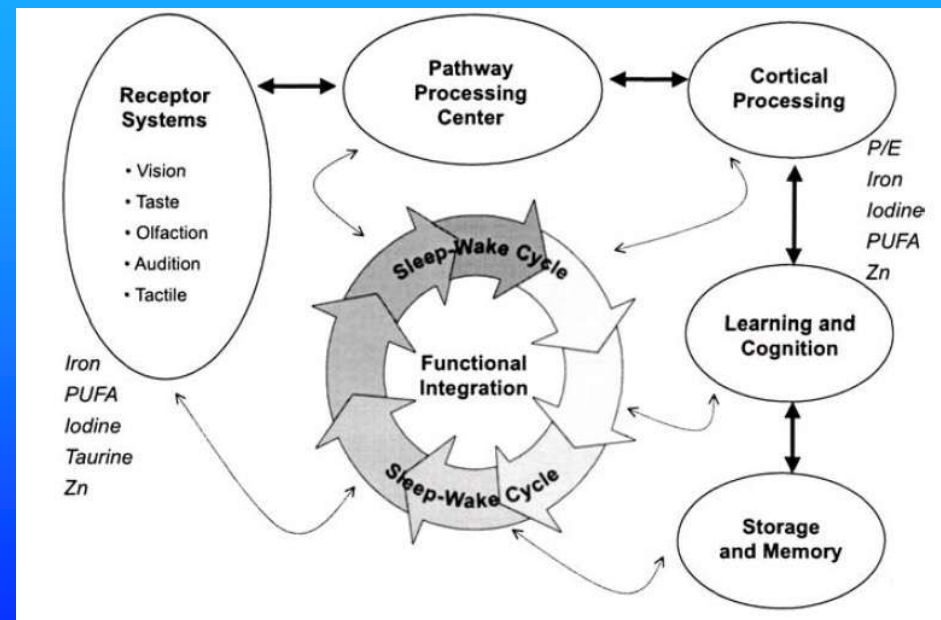


**Fig 4.** Schematic representation of the interaction between sensory receptors and CNS functions within the framework of the sleep-wake cycle. Nutrients with proven effects on sensory receptors and/or cortical processing are included (*PUFA*, polyunsaturated fatty acids; *Zn*, zinc; *P/E*, protein/energy).



# Brain Architecture and Skills are Built in a Hierarchical “Bottom-Up” Sequence

- **Neural circuits that process basic information are wired earlier than those that process more complex information.**



Slide by: Jack P. Shonkoff, M.D.



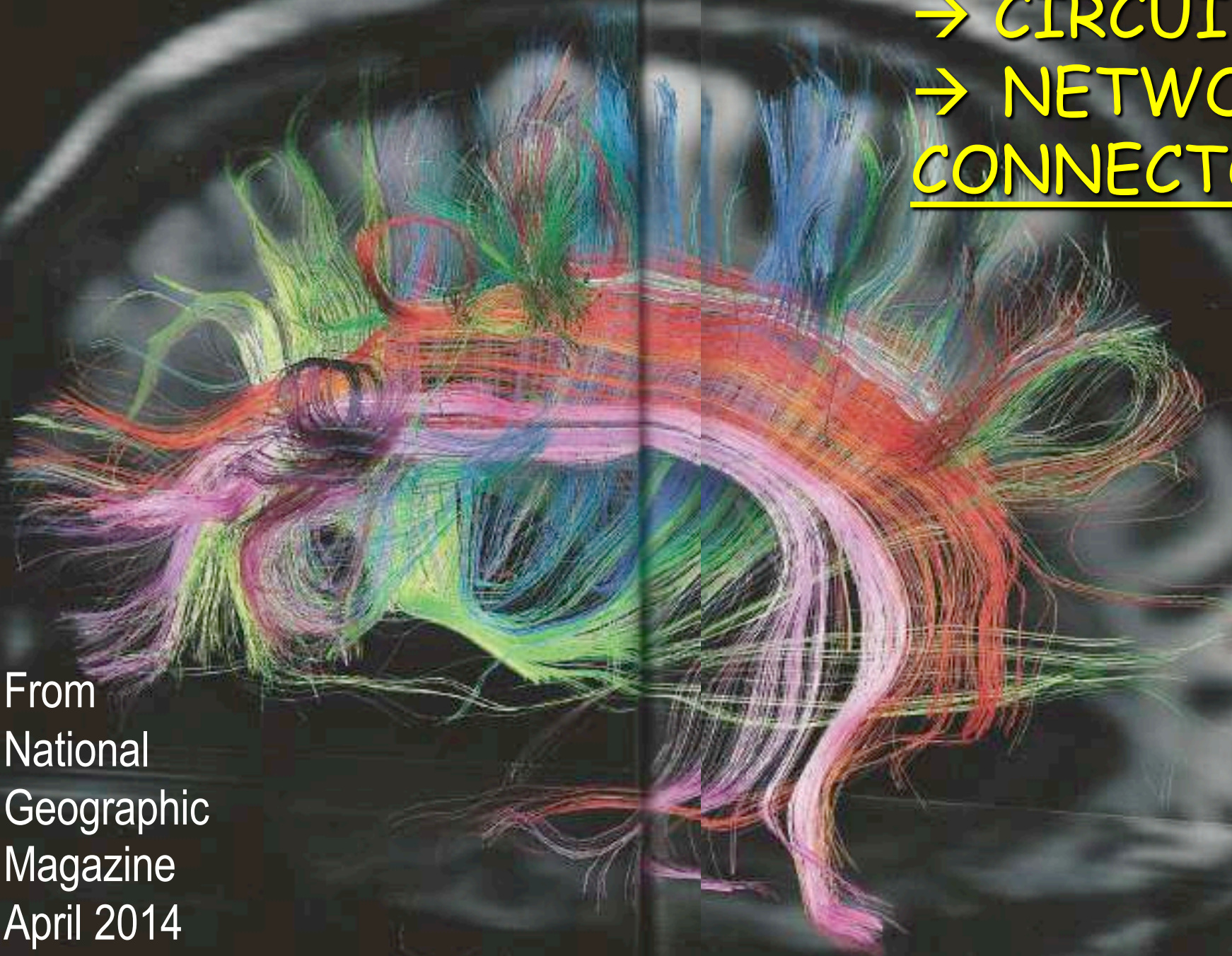
# Brain Architecture and Skills are Built in a Hierarchical “Bottom-Up” Sequence

- **Neural circuits that process basic information are wired earlier than those that process more complex information.**
- **Higher circuits build on lower circuits, and skill development at higher levels is more difficult if lower level circuits are not wired properly.**

# TRACTOGRAPHY

PATHWAYS  
→ CIRCUITS  
→ NETWORKS  
CONNECTOME

From  
National  
Geographic  
Magazine  
April 2014



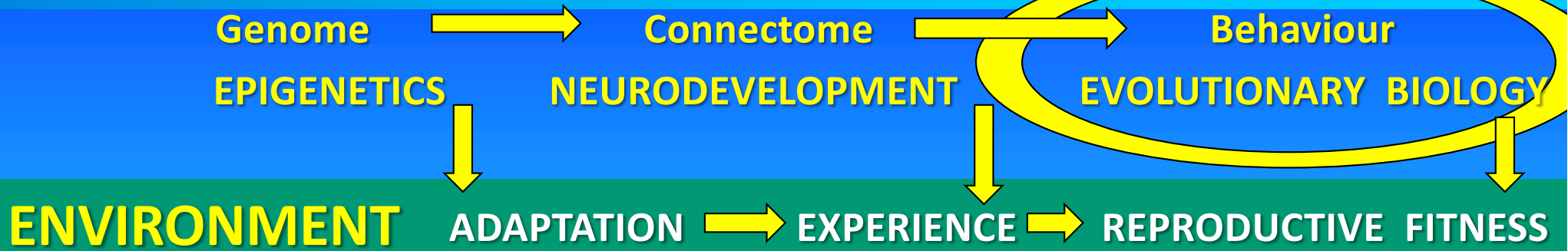
# NURTURESCIENCE



# NURTURESCIENCE



# NURTURESCIENCE



## Newborn behaviour to locate the breast when skin-to-skin: a possible method for enabling early self-regulation

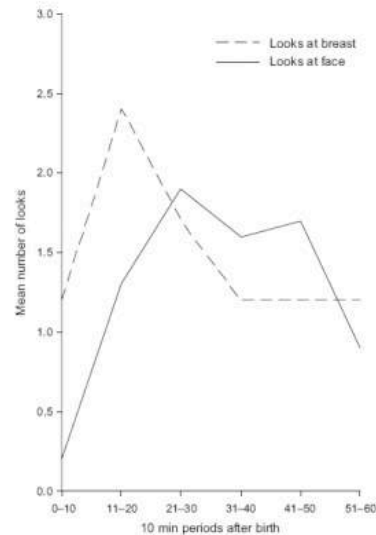
A-M Widström (ann-marie.widstrom@ki.se)<sup>1</sup>, G Lijia<sup>2</sup>, P Aaltomaa-Michalakis<sup>3</sup>, A Dahlid<sup>4</sup>, M Lintula<sup>4</sup>, E Nissen<sup>5,6</sup>

DOI:10.1111/j.1651-2227.2010.01983.x

Newborns' location of the breast



**Figure 1** (A) The baby looks at the breast 15 min old. (B) The baby looks at the mother 21 min old. Photo: Thomas Annersten.



**Figure 2** The infant's mean number of looks at either mother's breast or face is shown for 10-min periods during the first hour after birth.

**Table 1** Definition of phases/behaviours identified

Phases	Behaviours
Birth cry	Intense crying just after birth
Relaxation phase	Infant resting/recovering. No activity of mouth, head, arms, legs or body
Awakening phase	Infant begins to show signs of activity. Small thrusts of head: up, down, from side-to-side. Small movements of limbs and shoulders
Active phase	Infant moves limbs and head, is more determined in movements. Rooting activity, 'pushing' with limbs without shifting body
Crawling phase	'Pushing' which results in shifting body
Resting phase	Infant rests, with some activity, such as mouth activity, sucks on hand
Familiarization	Infant has reached areola/nipple with mouth positioned to brush and lick areola/nipple
Suckling phase	Infant has taken nipple in mouth and commences suckling
Sleeping phase	The baby has closed its eyes



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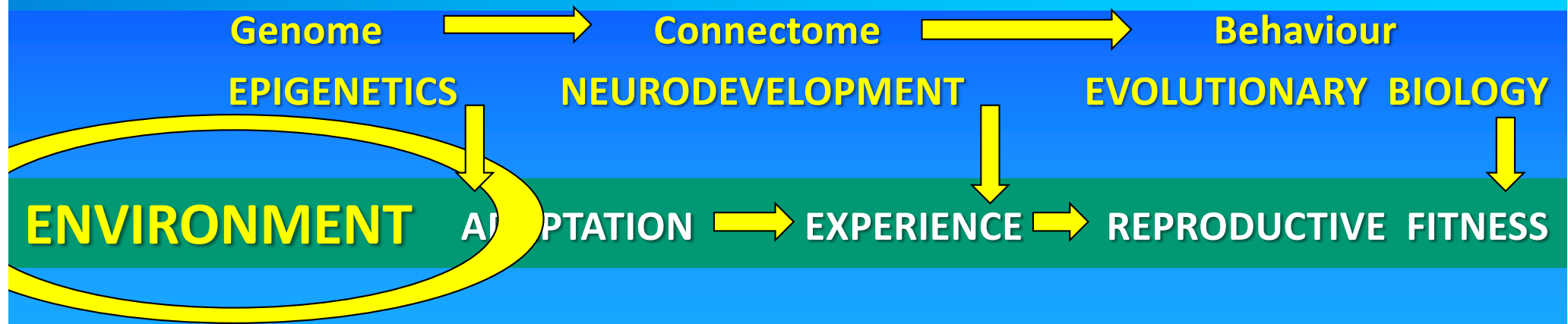
# NURTURESCIENCE



HIGHLY CONSERVED  
NEURO-ENDOCRINE  
BEHAVIOR

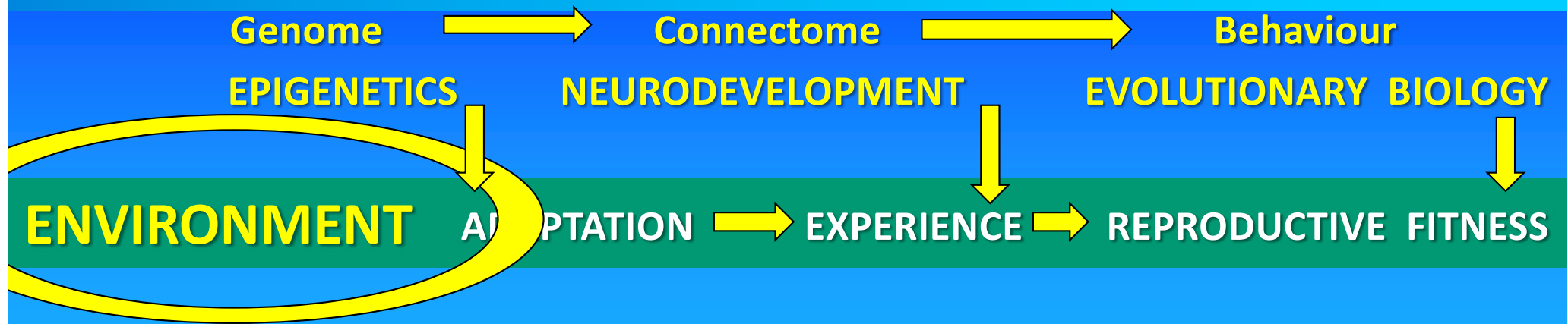
ZERO SEPARATION  
for 30,000,000 years

# NURTURESCIENCE



“For species such as primates, the mother IS the environment.”  
Sarah Blaffer Hrdy, Mother Nature (1999)

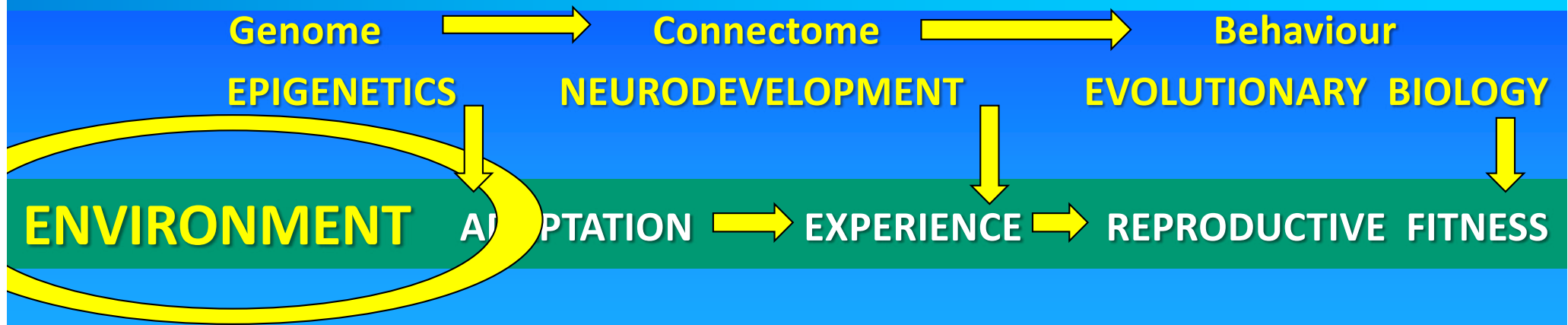
# NURTURESCIENCE



Nothing an infant can or  
cannot do makes sense,

except in light of mother's body

# NURTURESCIENCE



Skin-to-skin contact

except in light of mother's body

# NURTURESCIENCE

Essentially ecological:



Skin-to-skin contact

except in light of mother's body

# NURTURESCIENCE

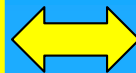
Essentially ecological:

ENVIRONMENT → ADAPTATION → EXPERIENCE → REPRODUCTIVE FITNESS

BABY


MOTHER

BONDING



Sensitization

ecology

/ɪˈkɒlədʒi, ɛˈkɒlədʒi/ 

*noun*

The branch of biology that deals with the relations of organisms to one another and to their physical surroundings.

(from Greek: οἶκος, "house", or "environment"; -λογία, "study of")

Introducing NURTURESCIENCE a  
new model with ancient roots.

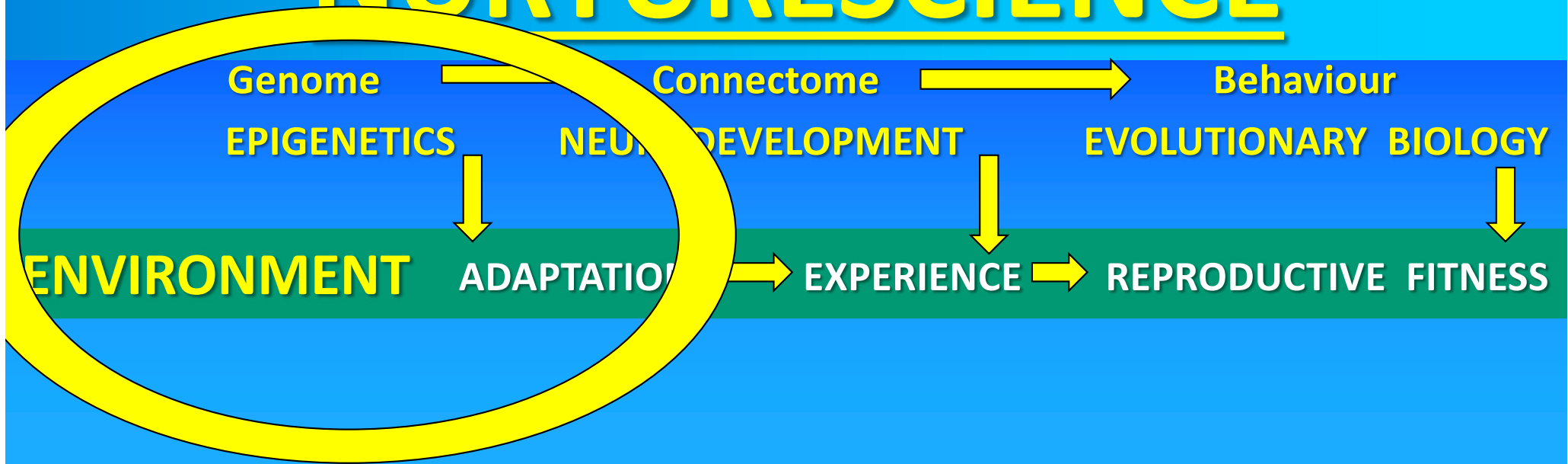
NURTURE and NATURE  
was all there was.

"Womb ecology becomes world ecology."  
(APPPAH)

The branch of biology that deals with the relations of  
organisms to one another and to their physical surroundings.

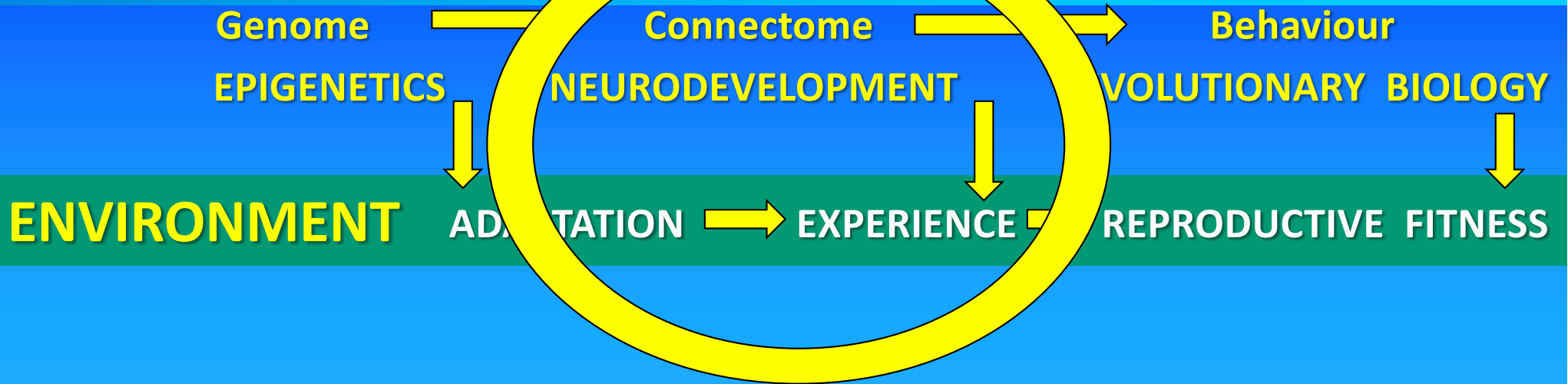


# NURTURESCIENCE



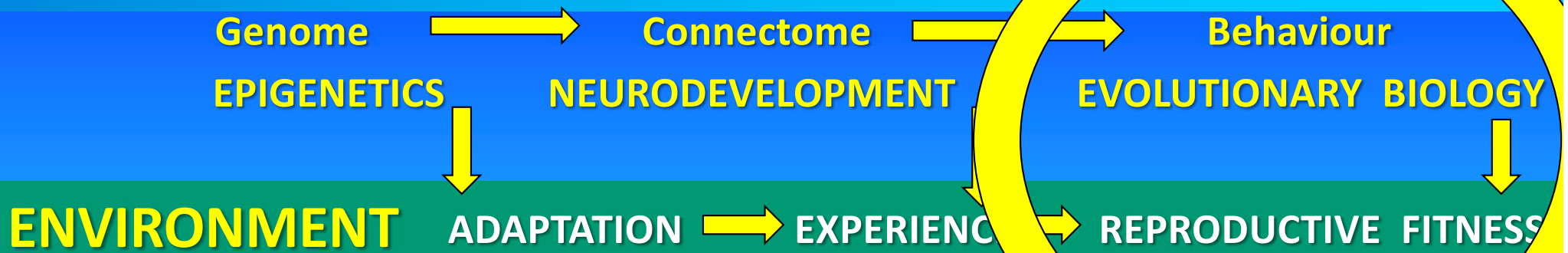
*“buffering protection  
of adult support”*

# NURTURESCIENCE



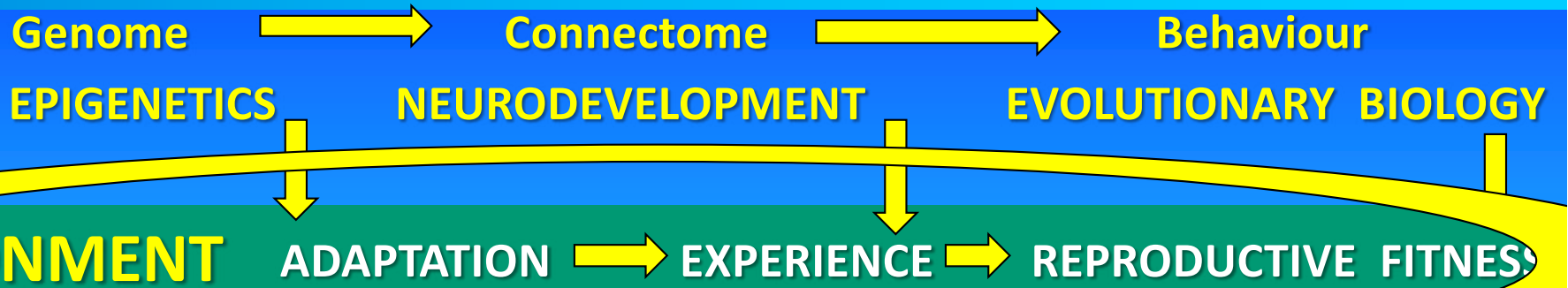
*“needed neural processes”*

# NURTURESCIENCE



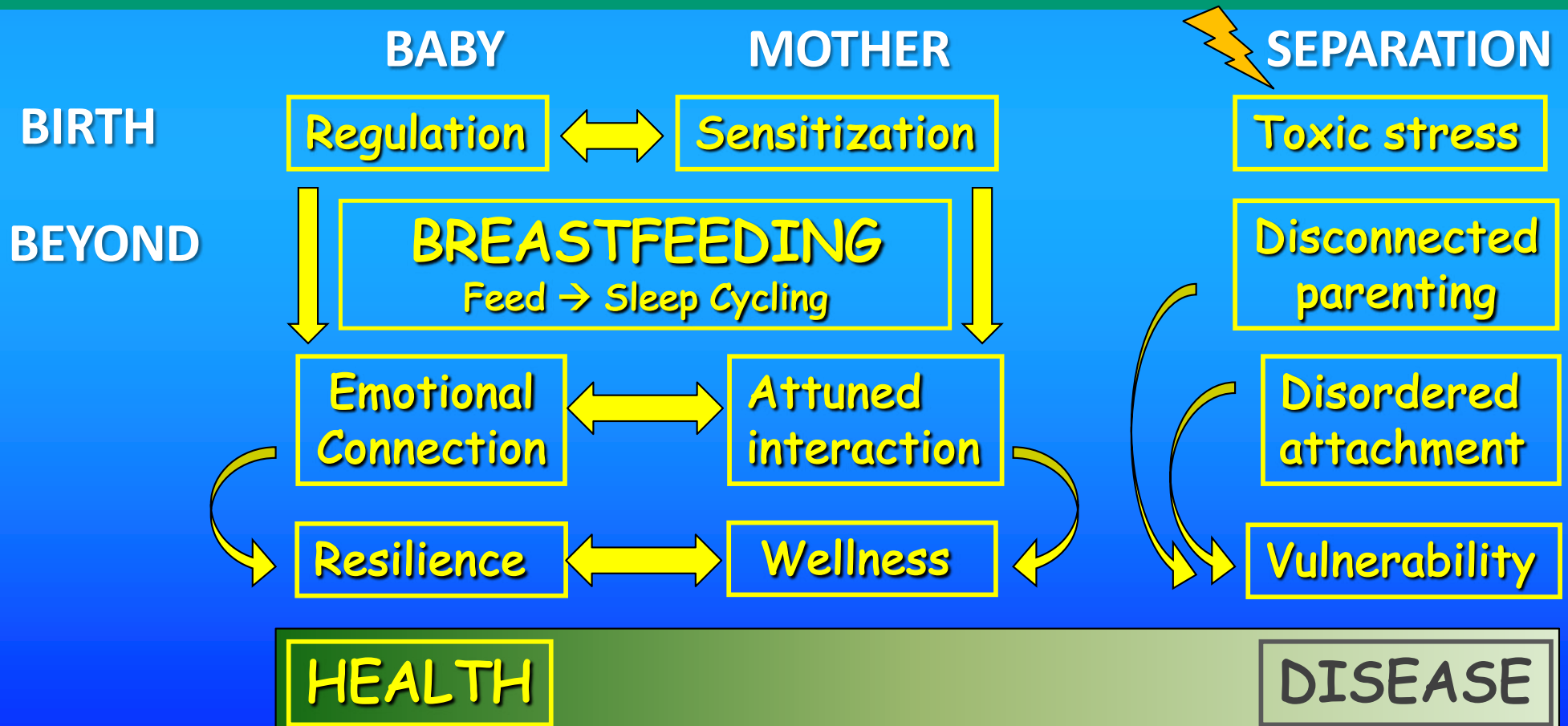
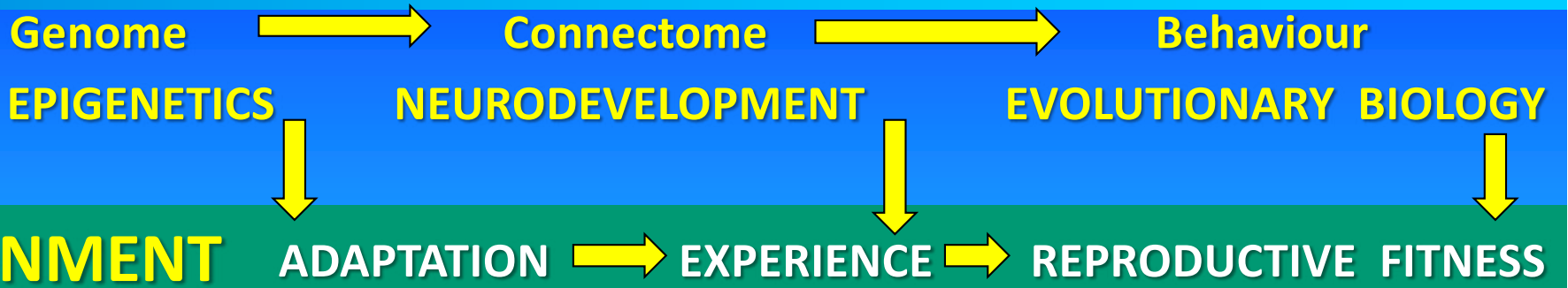
*“except in the light of mother’s body.”*

# NURTURESCIENCE

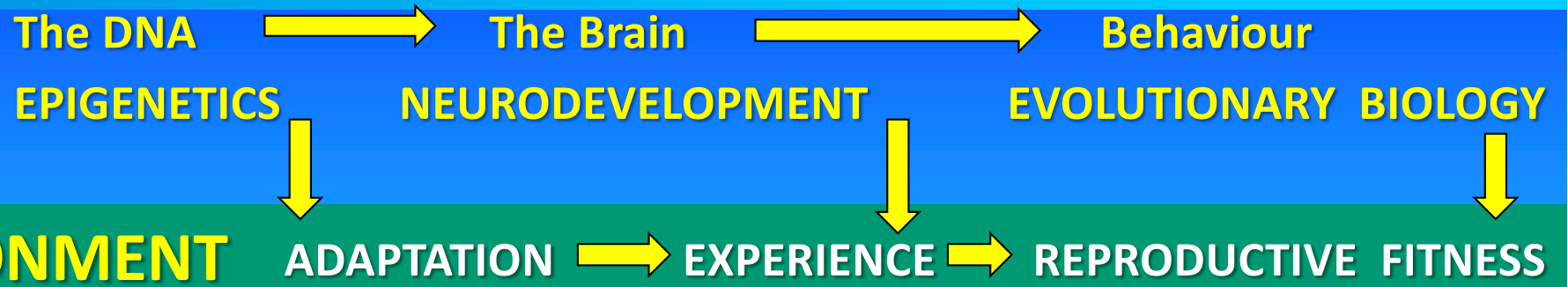


*ZERO  
SEPARATION*

# NURTURESCIENCE



# NURTURESCIENCE

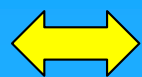


BABY

MOTHER

BIRTH

Regulation



Sensitization

BEYOND



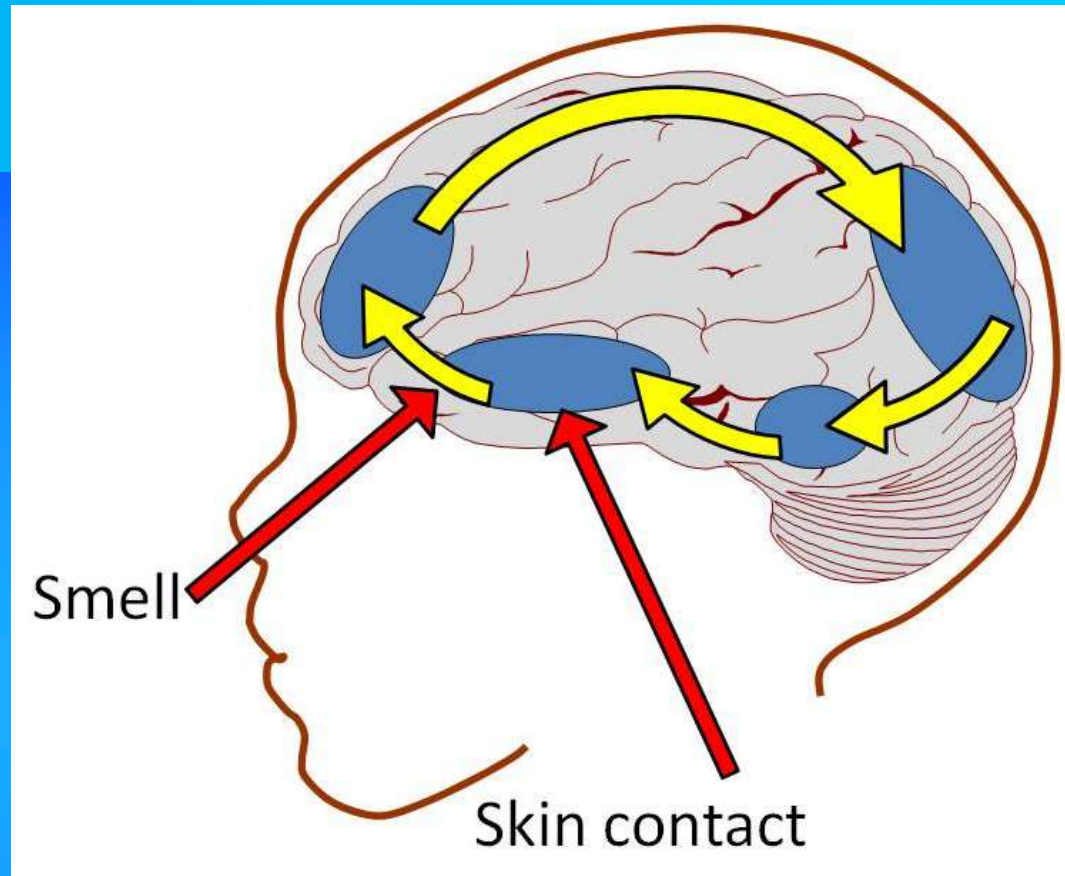
Emotional  
Connection



Attuned  
interaction

AT BIRTH,

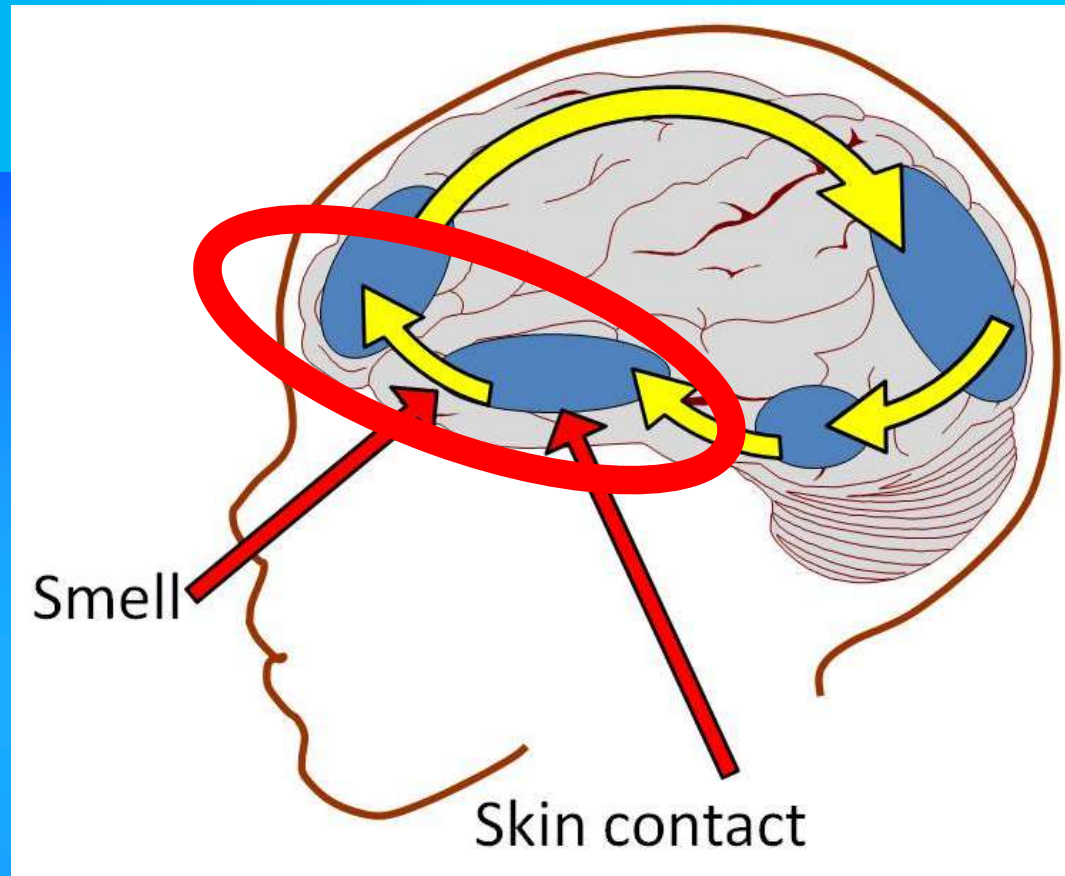
the brain has  
TWO  
CRITICAL  
SENSORY  
NEEDS:



SMELL & CONTACT  
connect direct to the amygdala

# THE NEWBORN BRAIN

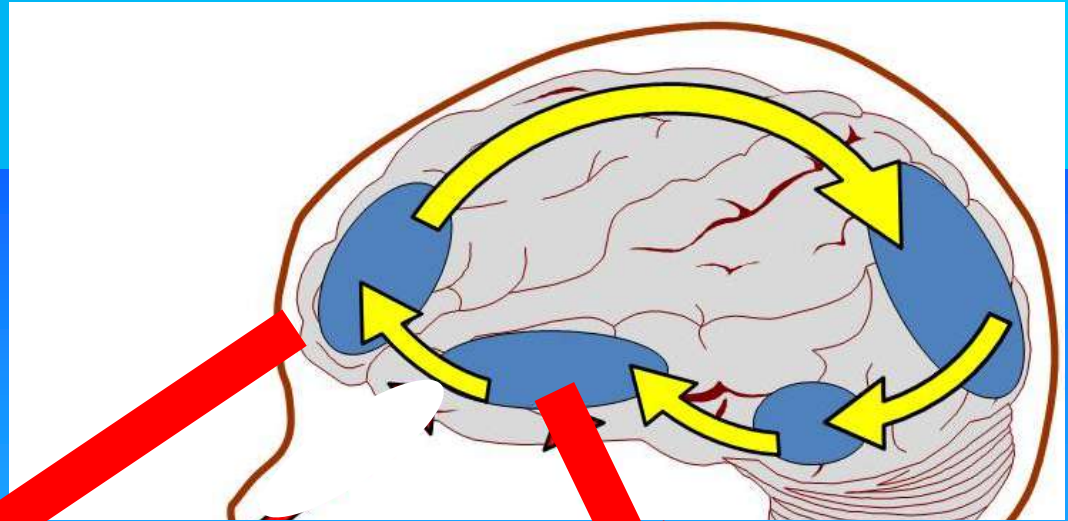
SKIN-TO-SKIN  
CONTACT  
fires and wires



the amygdala-prefronto-orbital  
cortical pathway (PFOC)

Schore 2001





Prefrontal cortex

Executive  
function

AMYGDALA:

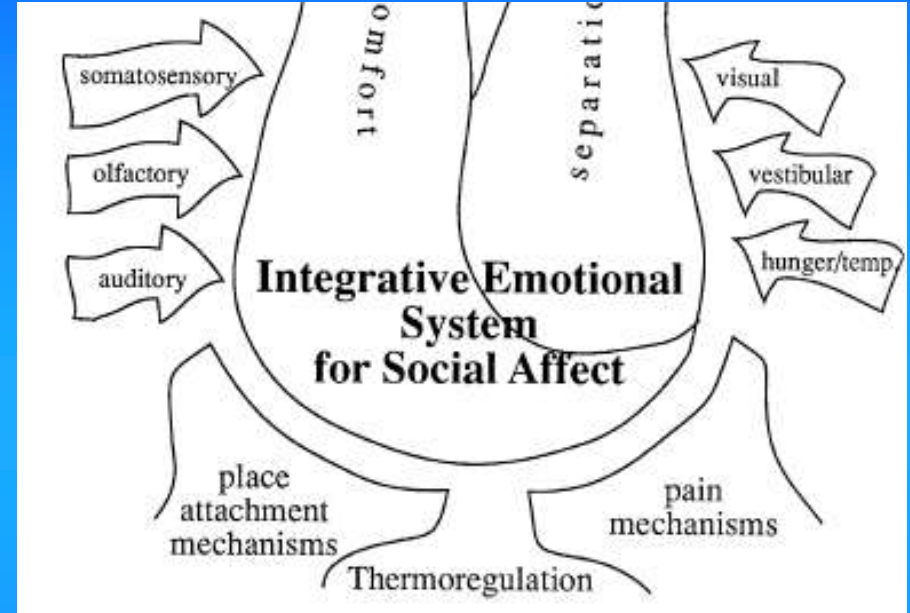
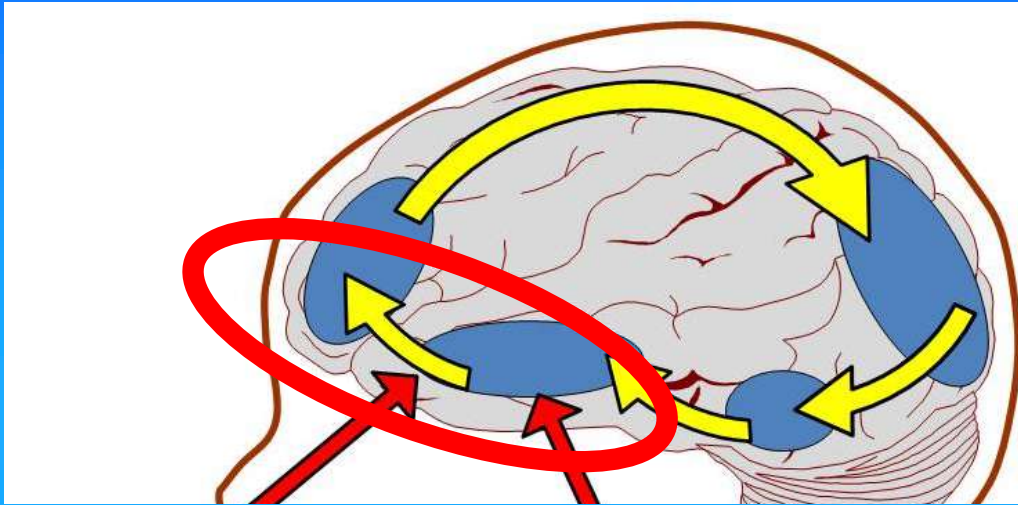
Emotional  
Processing  
Unit

CPU

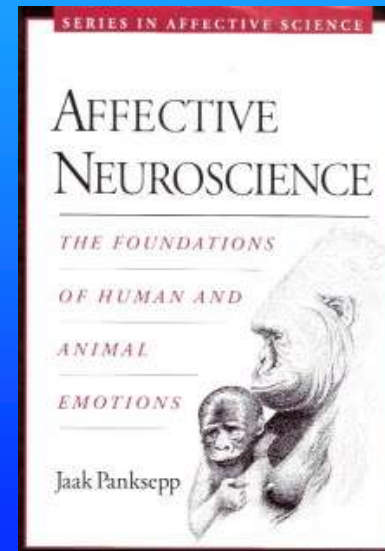
SOCIAL and EMOTIONAL  
INTELLIGENCE

# SOCIAL INTELLIGENCE

# EMOTIONAL INTELLIGENCE



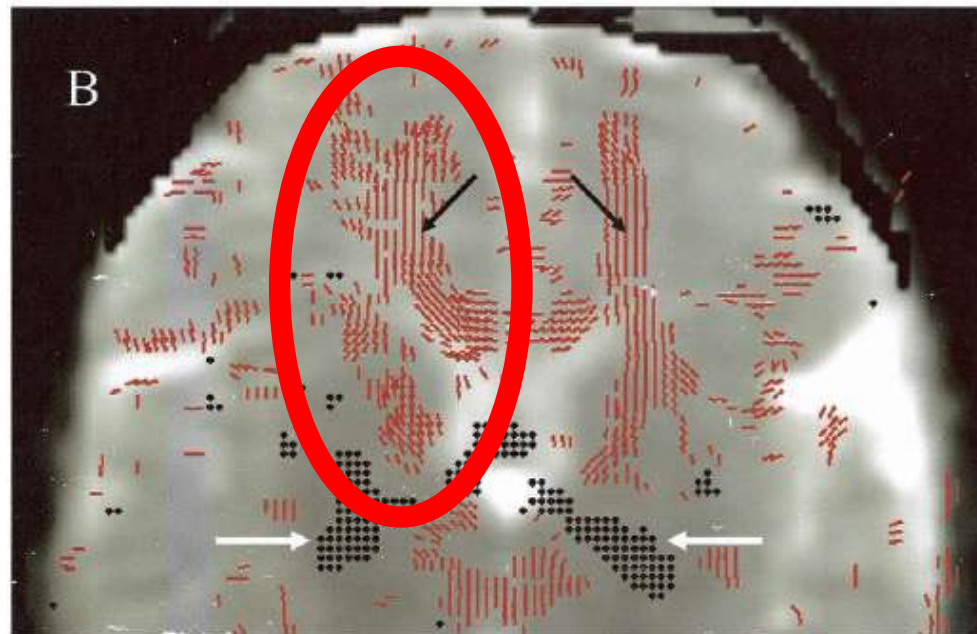
Behavioural  
activation system  
reward-based  
(dopamine)



# Early Experience Alters Brain Function and Structure

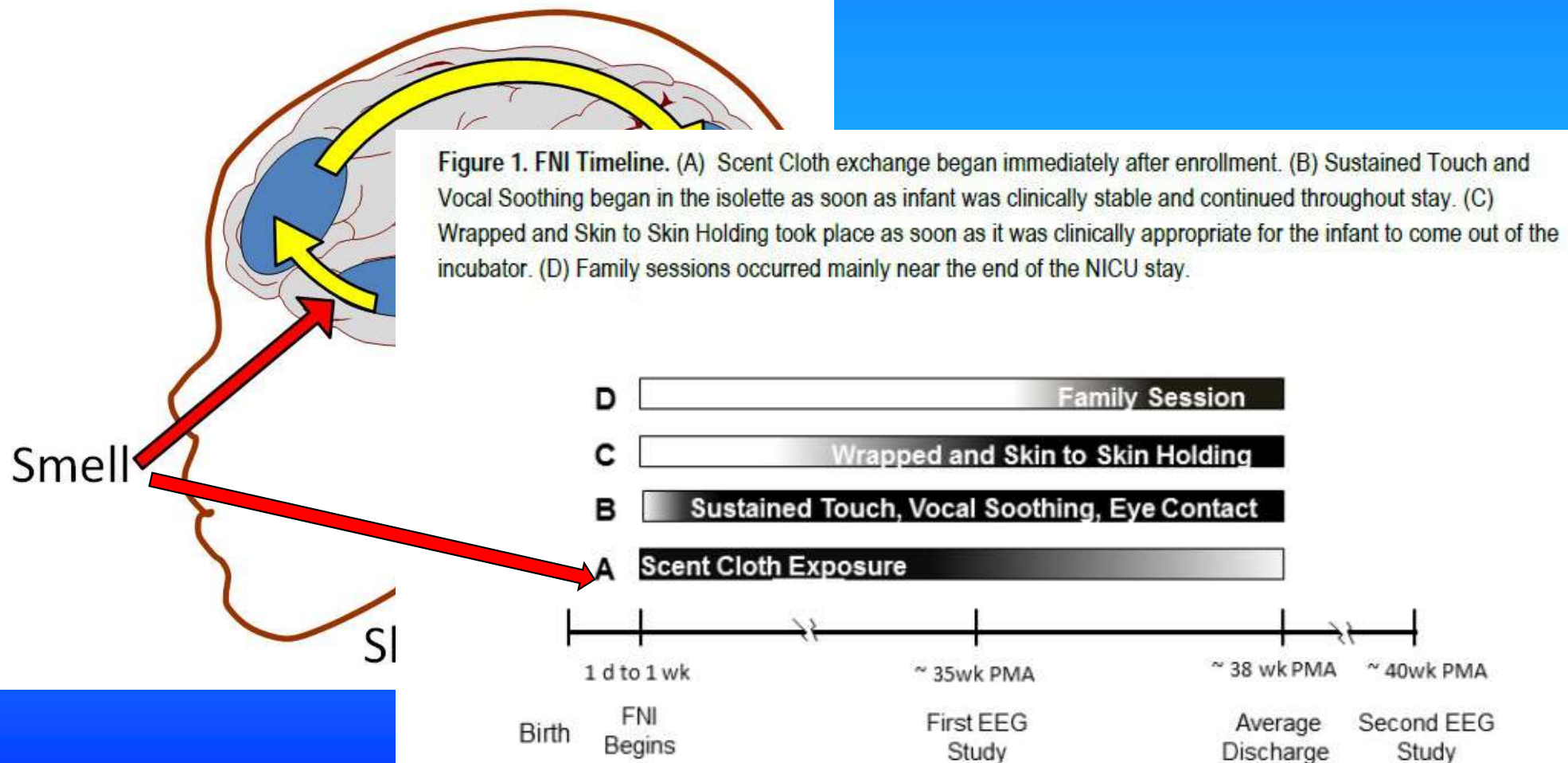
Heidelise Als, PhD\*; Frank H. Duffy, MD†; Gloria B. McAnulty, PhD\*; Michael J. Rivkin, MD\*†§;

Fig 3. MRI DTI: comparison of control and experimental group infants at 2 weeks' corrected age. Shown are examples of diffusion tensor maps from identical axial slices through the frontal lobes of a representative control group (A) and an experimental group (B) infant obtained at 2 weeks' corrected age. In each example, the principal eigenvectors (shown in red and black) overlaid the apparent diffusion coefficient (ADC) map to show anisotropy in white matter. The red lines denote eigenvectors located within the plane of the image, and the black dots indicate eigenvectors oriented mostly perpendicular to the image plane. The ratio of E1/E3 has been used as a threshold to show only eigenvectors at those voxels where E1/E3 exceeds a threshold value of 1.3 in both images. Note the greater anisotropy of white matter found in the experimental infant (B) as compared with the control infant (A) at the posterior limbs of the internal capsule (white arrows) and the frontal white matter adjacent to the corpus callosum (black arrows). The greater anisotropy found in the experimental infant (B) suggests more advanced white matter development in these regions as compared with white matter found in the control infant (A).

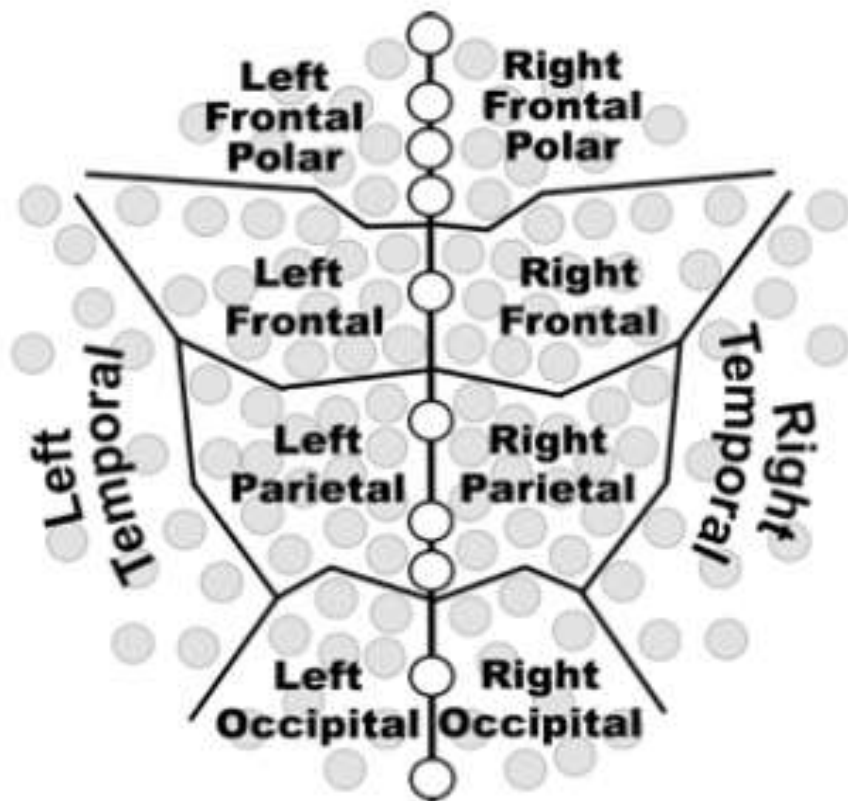




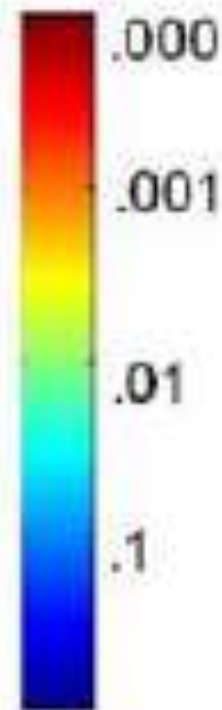
## Electroencephalographic activity of preterm infants is increased by Family Nurture Intervention: a Randomized Controlled Trial in the NICU



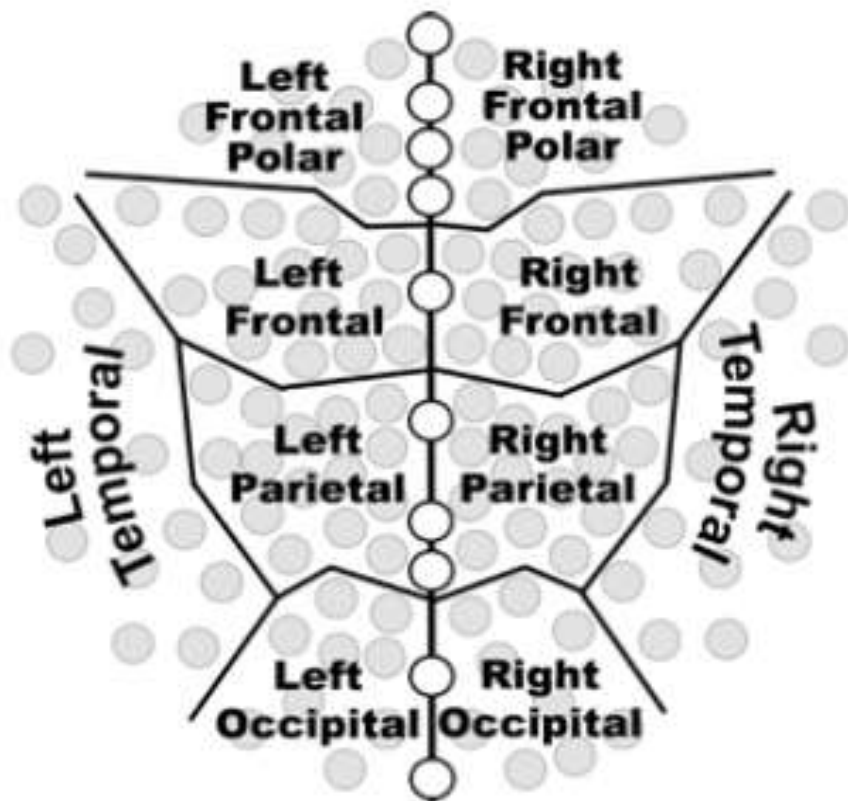
EG net. The 124 electrodes in the E  
analyses of the study. Note 10 midline



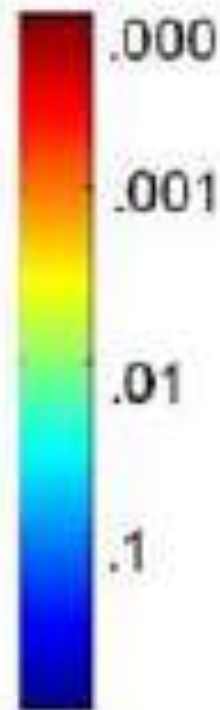
p-value



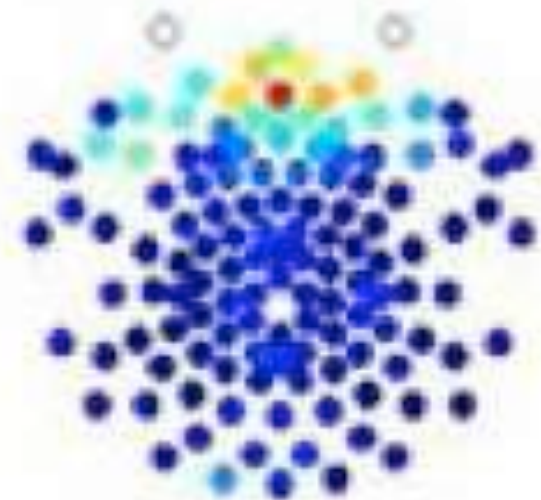
EG net. The 124 electrodes in the E  
analyses of the study. Note 10 midline



p-value



13-15 Hz



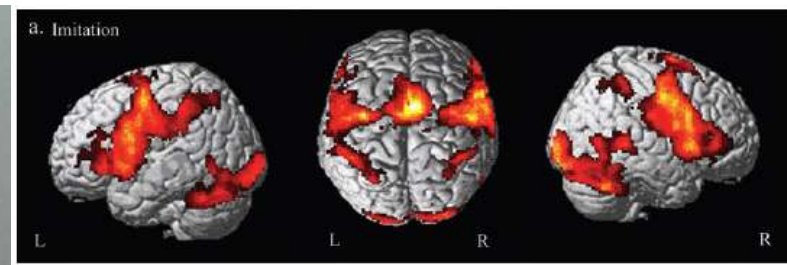
37-48 Hz



Cerebral Cortex May 2009;19:1124-1133  
doi:10.1093/cercor/bhn153  
Advance Access publication September 11, 2008

## Neural Basis of Maternal Communication and Emotional Expression Processing during Infant Preverbal Stage

infant self. Sixteen mothers underwent functional magnetic resonance imaging while observing and imitating faces of their own child and those of someone else's child. We found that the mirror neuron system, the insula and amygdala were more active during emotional expressions, that this circuit is engaged to a greater extent when interacting with one's own child, and that it is correlated with maternal reflective function (a measure of empathy). We also found, by comparing single emotions with each



As predicted, imitation and observation of facial expressions elicited activation of fronto-parietal mirror areas (vPMC-IFG-pars opercularis and IPL), STS, anterior insula, and amygdala.

Therefore, our results are in keeping with the *simulation theory* (or motor theory of empathy), according to which empathy is generated by inner imitation of actions of others (Gallese and Goldman, 1998).

**Lenzi 2009**



Kerstin  
Uvnas-Moberg

Ross 2009

## Interpersonal awareness Emotions



In humans, oxytocin increases gaze to the eye region of human faces and enhances interpersonal trust and the ability to infer the emotions of others from facial cues.



# Learning affective values for faces is expressed in amygdala and fusiform gyrus

Predrag Petrovic, Raffael Kalj  
Wellcome Trust Centre for Neuroima

To monitor the environment for soc  
and to a high degree shaped by res  
these evaluations are constructed i

CSdg+



CSdg-



CSag+



CSag-



le  
ch  
m

Petrovic 2008

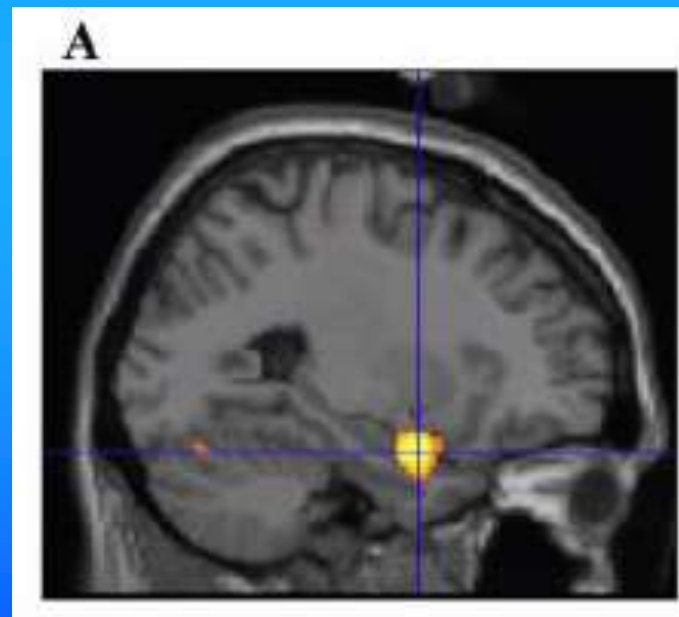
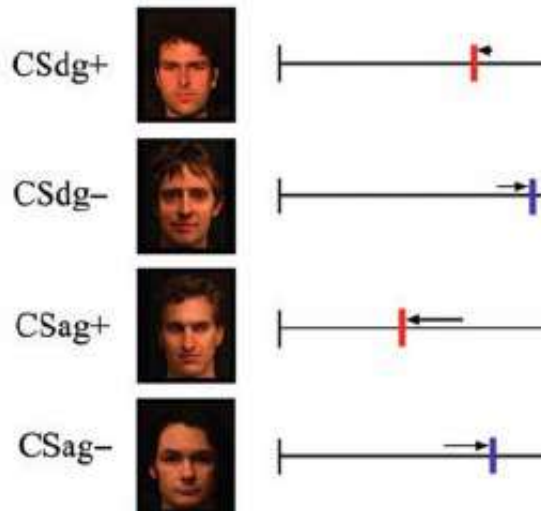
# Learning affective values for faces is expressed in amygdala and fusiform gyrus

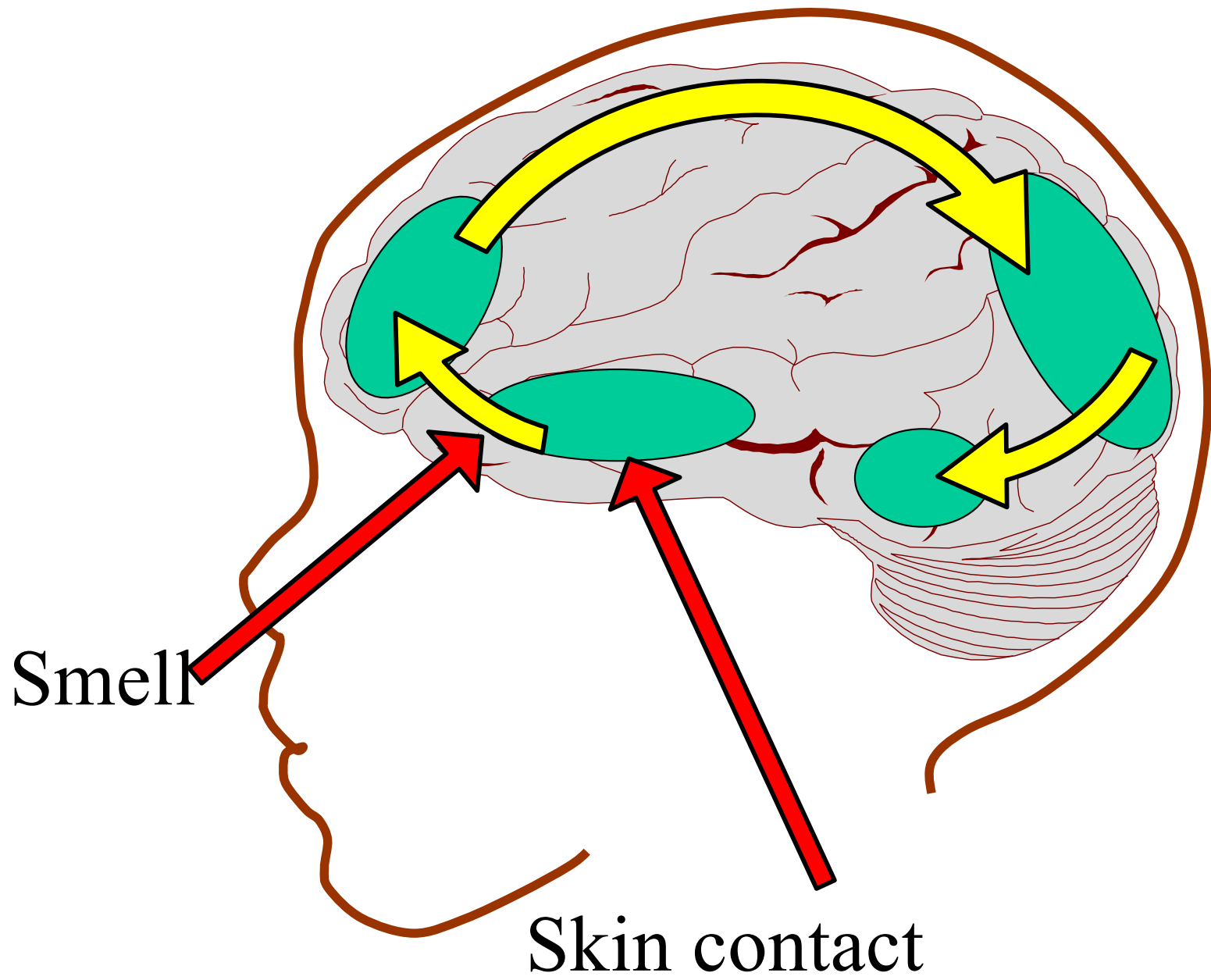
Predrag Petrovic, Raffael Kalisch, Mathias Pessiglione, Tania Singer, and Raymond J. Dolan

Wellcome Trust Centre for Neuroimaging, University College of London, 12 Queen Square, London, WC1N 3BG, UK

To monitor the environment for social threat humans must build affective evaluations of others. These evaluations are malleable and to a high degree shaped by responses engendered by specific social encounters. The precise neuronal mechanism by which these evaluations are constructed is poorly understood. We tested a hypothesis that conjoint activity in amygdala and fusiform

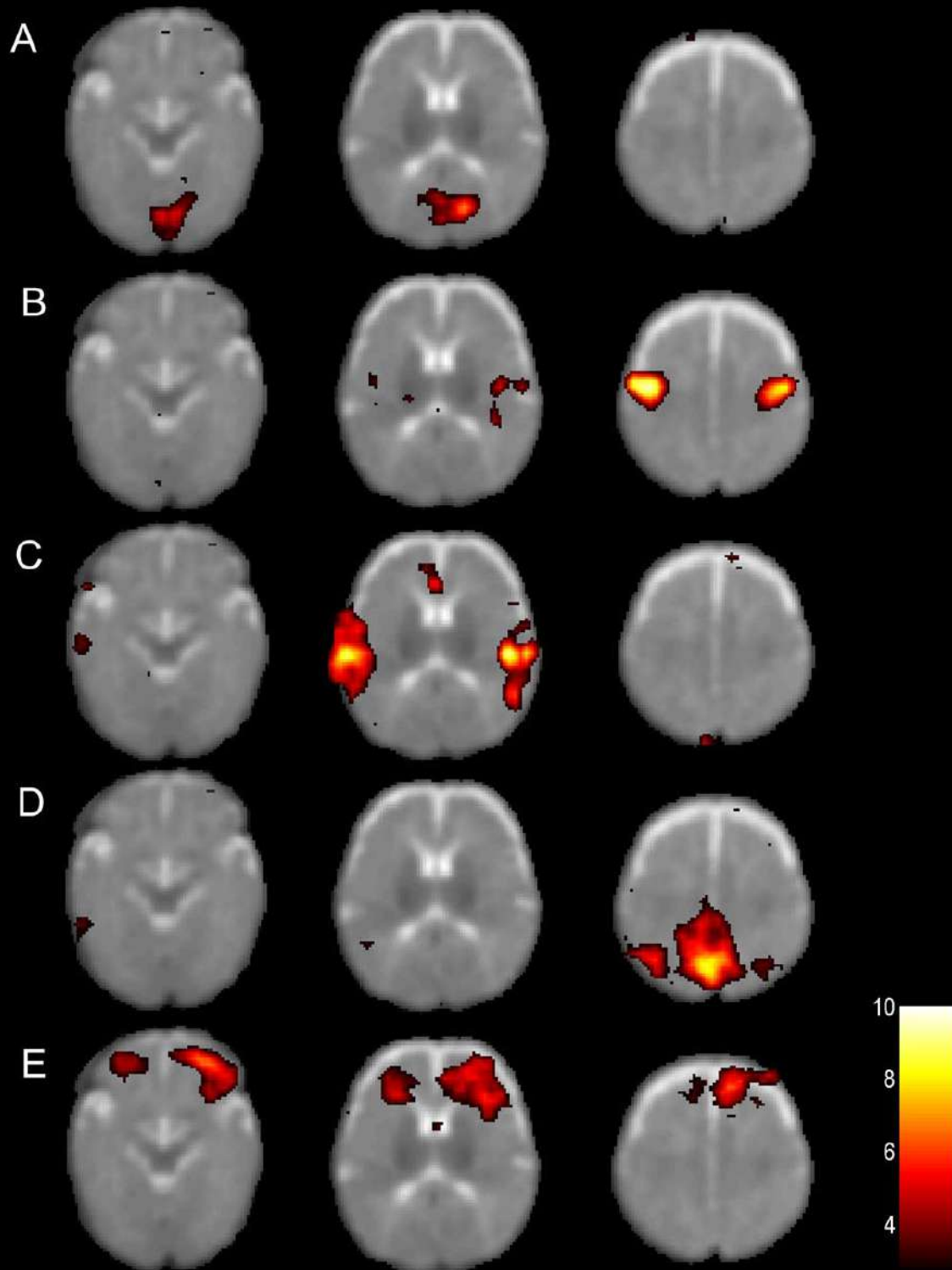
A. How sympathetic do you perceive this





Smell

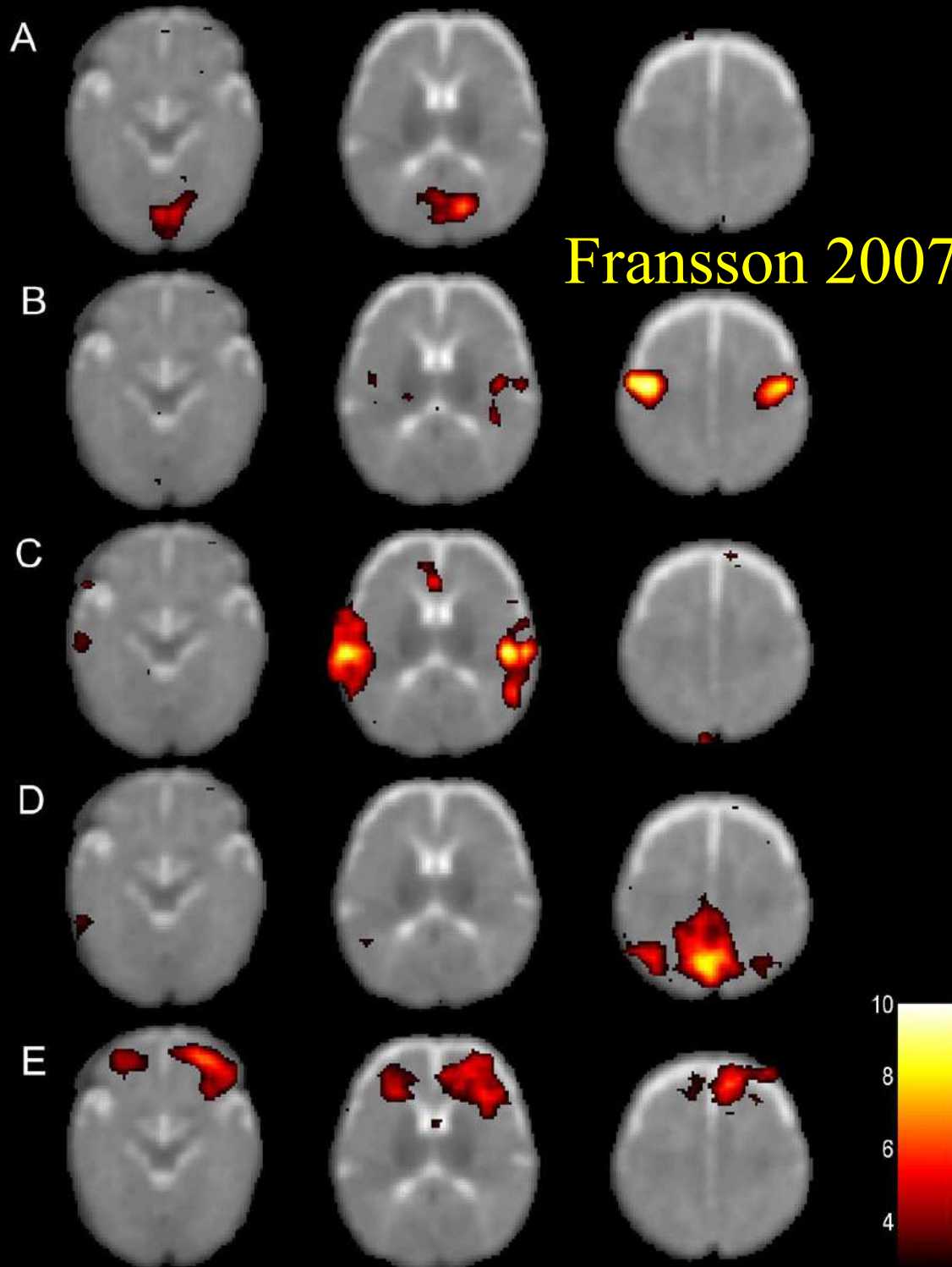
Skin contact



The infant  
brain is not  
blank!  
Resting activity  
-  
"stream of  
consciousness"

Fransson 2007

Fransson 2007



A primary visual areas,

B somatosensory motor cortex

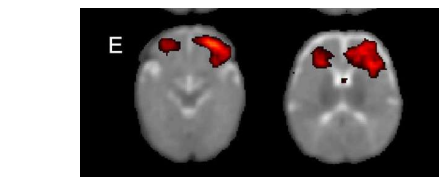
C primary auditory cortex

D parietal cortex & cerebellum

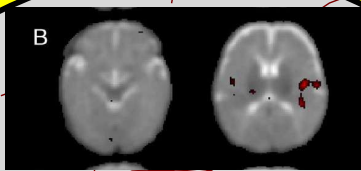
E medial anterior prefrontal cortex

# OXYTOCIN

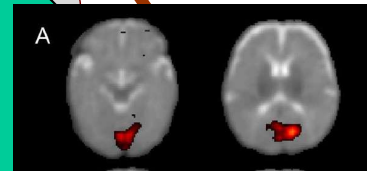
EMOTION  
CONTROL  
CENTRE



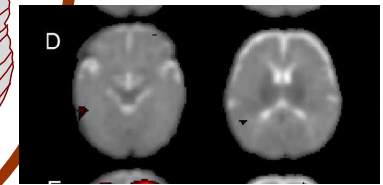
E prefrontal



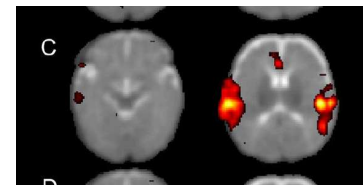
B somatosensory



A primary visual



D parietal  
& cerebellum

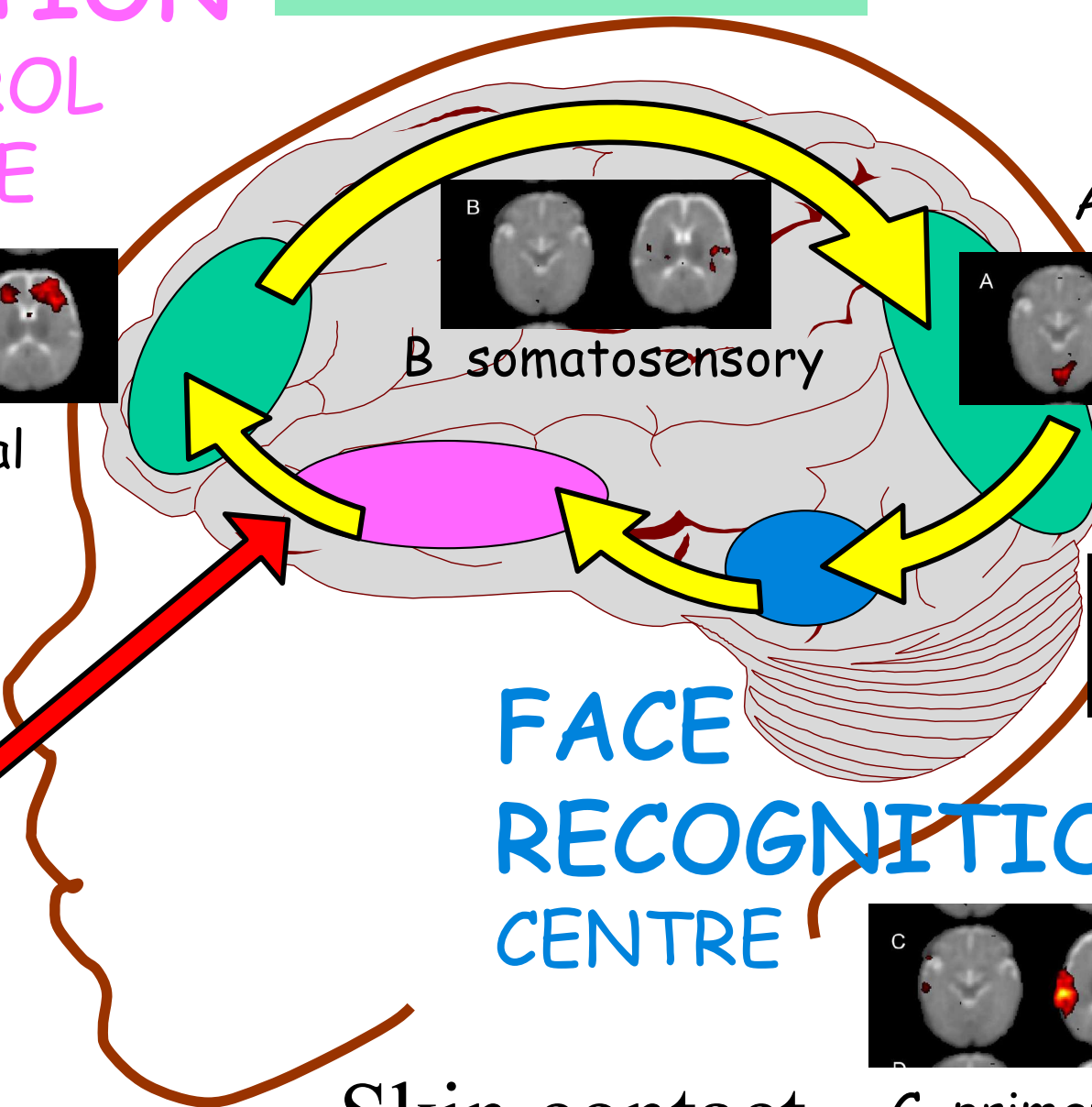


C primary auditory

FACE  
RECOGNITION  
CENTRE

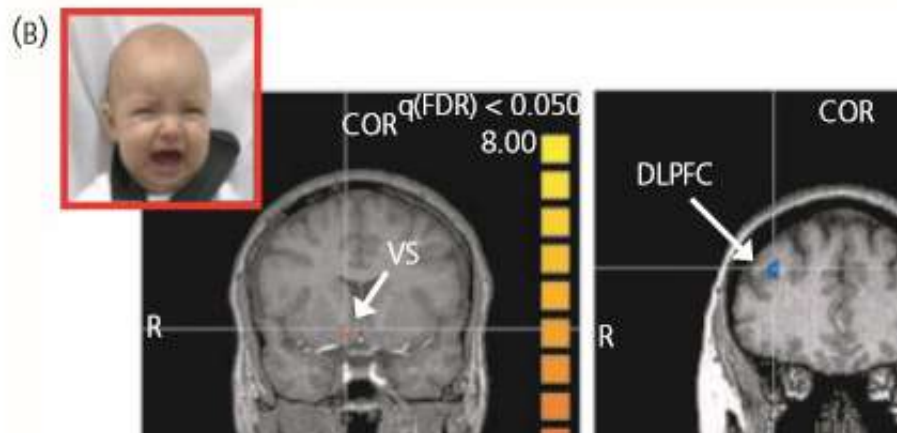
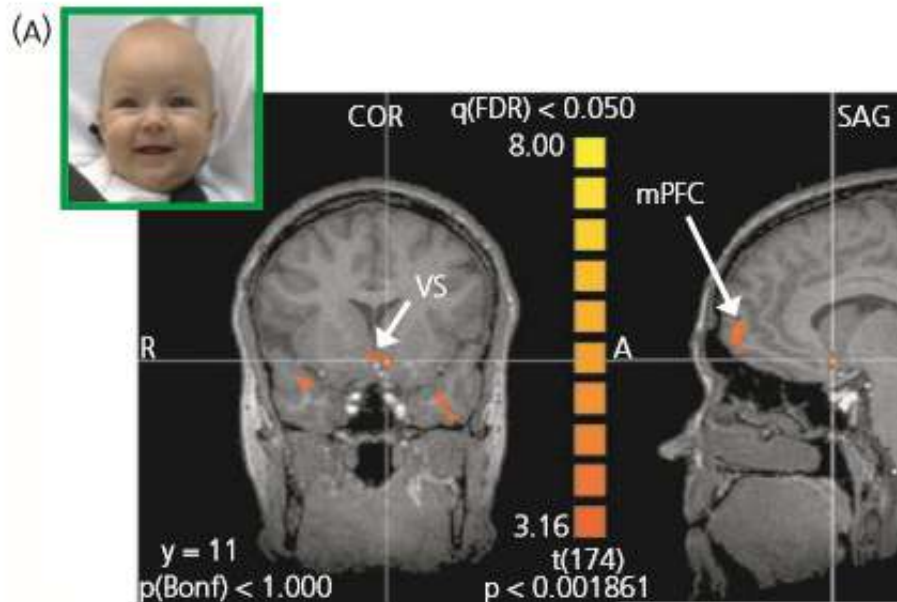
Smell

Skin contact



## How oxytocin and dopamine connect

From animal studies, we learn that oxytocinergic circuits are directly linked with the mesocorticolimbic dopamine pathway, with oxytocinergic neurones projecting from the hypothalamic PVN and MPOA to both the VTA and the VS (Fig. 3). The strength of these connections is associated with levels of maternal caregiving behav-



... infant cues - suckling, vocalisation and tactile stimulation - stimulate **OXYTOCIN** release in the hypothalamus, which may result in the activation of the **DOPAMINE** reward pathway leading to behavioural reinforcement

**SOCIAL  
CONTROL  
CENTRE**



**REWARD  
CONTROL  
CENTRE**



**OXYTOCIN**

**DOPAMINE**

Medial prefrontal cortex

Sensory cortex

Caudate nucleus

Glutamate

Oxytocin

Vasopressin

N-Methyl-D-aspartate receptor

N-Methyl-D-aspartate receptor

Glutamate

Oxytocin

Vasopressin

Nucleus accumbens

Glutamate

Oxytocin

Vasopressin

Cortisol

Hippocampus

Corticotropin-releasing hormone

N-Methyl-D-aspartate receptor

Glucocorticoid receptor

Corticotropin-releasing hormone

Orbitofrontal cortex

Norepinephrine

Norepinephrine

Dopamine

Norepinephrine

Dopamine

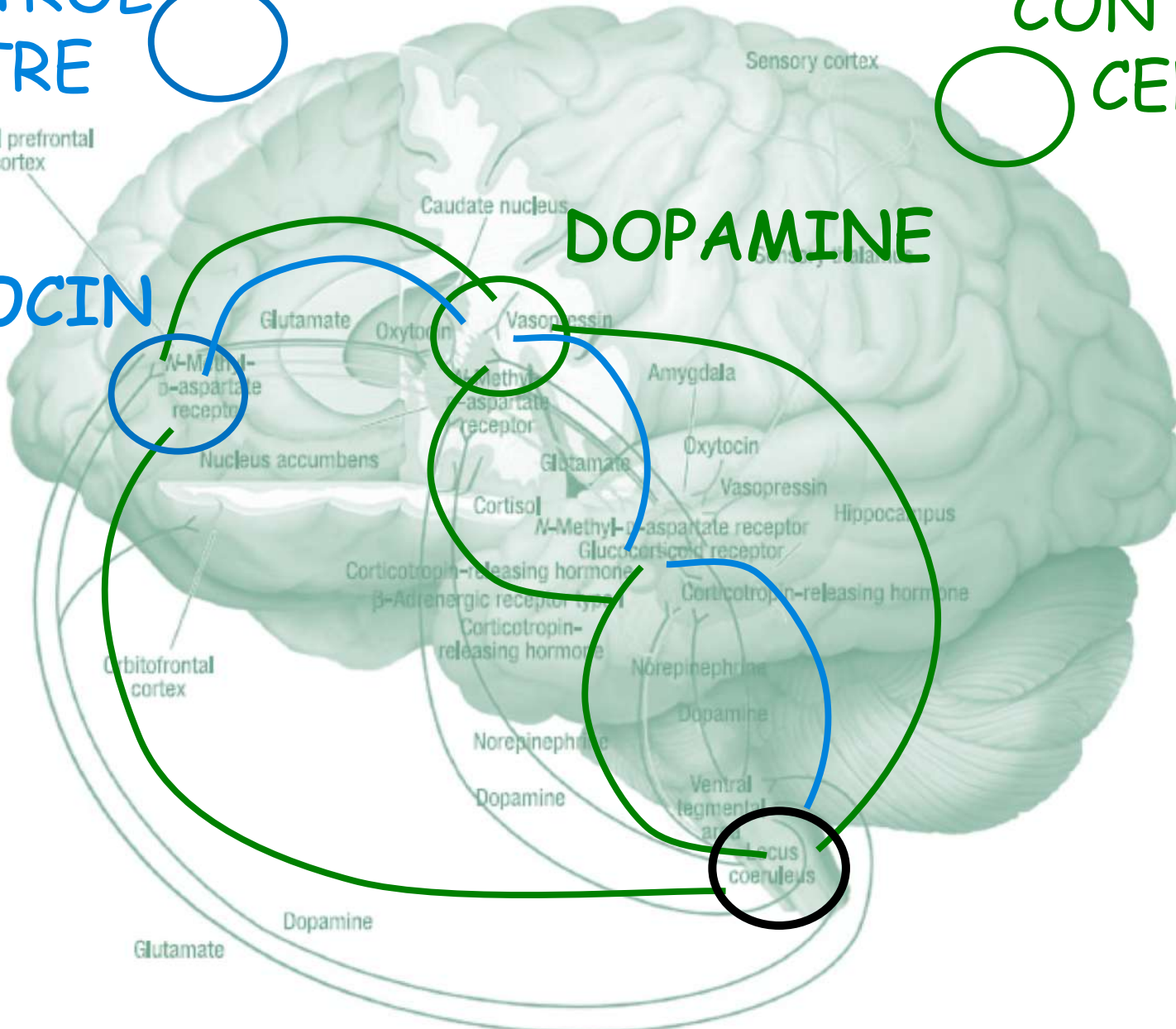
Dopamine

Ventral tegmental area

Locus coeruleus

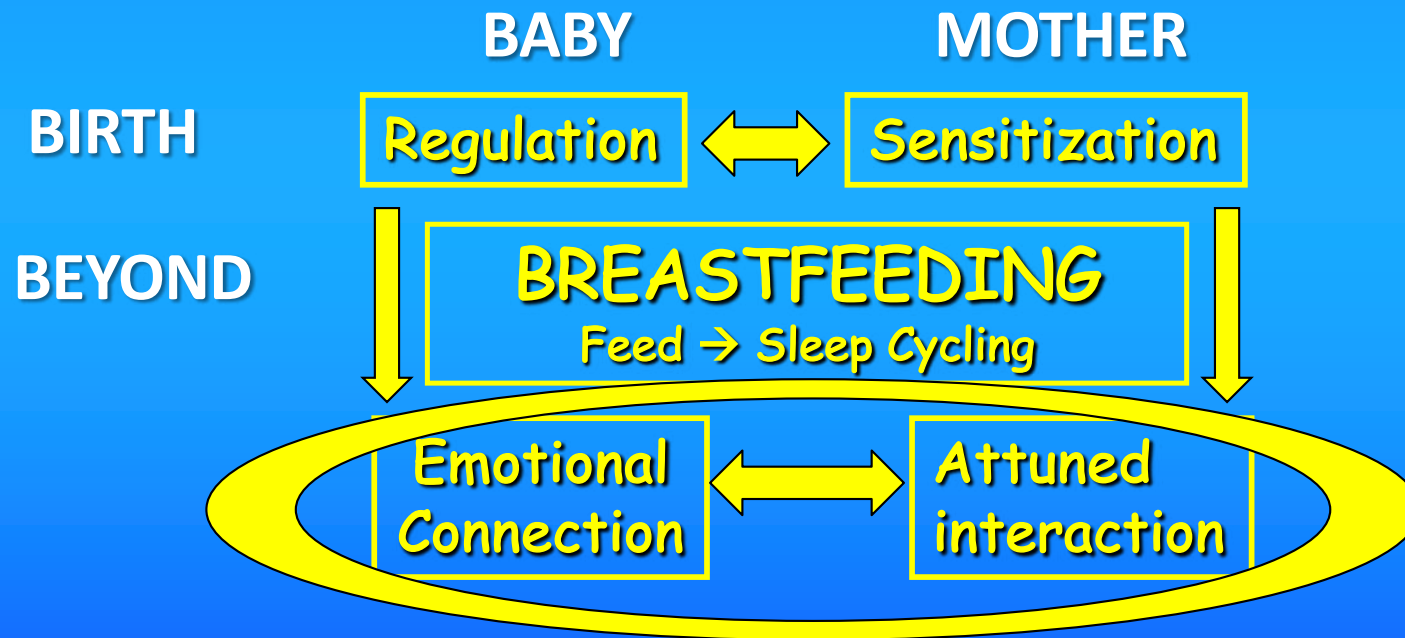
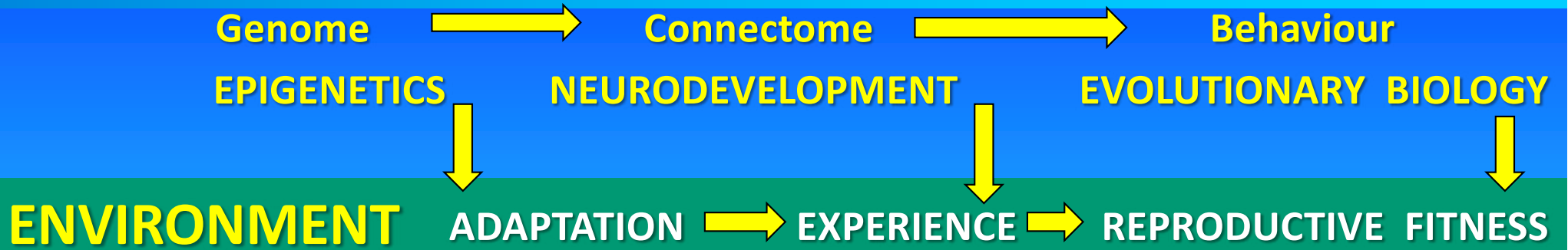
Glutamate

Dopamine

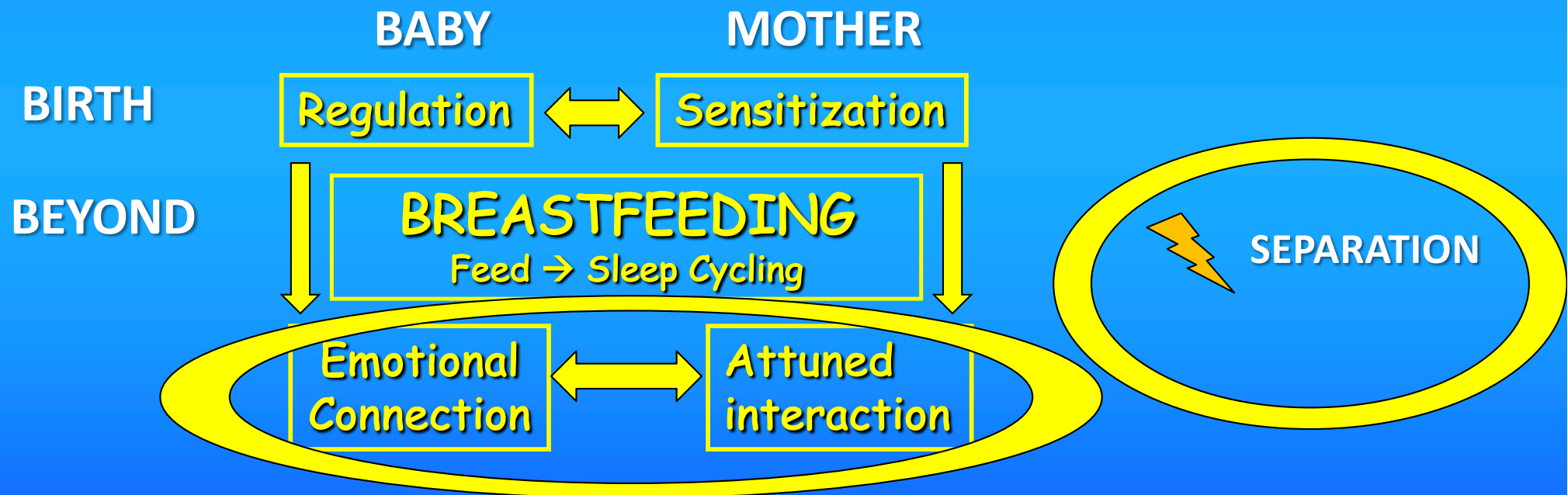
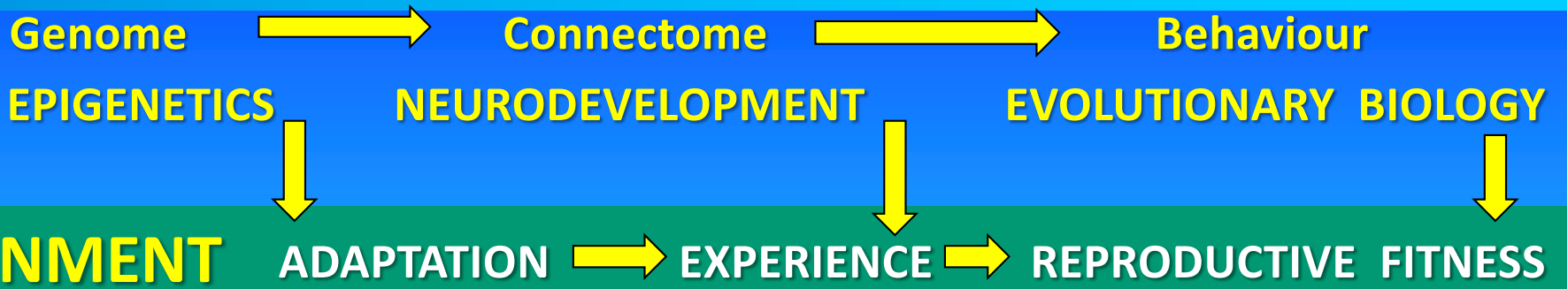




# NURTURESCIENCE

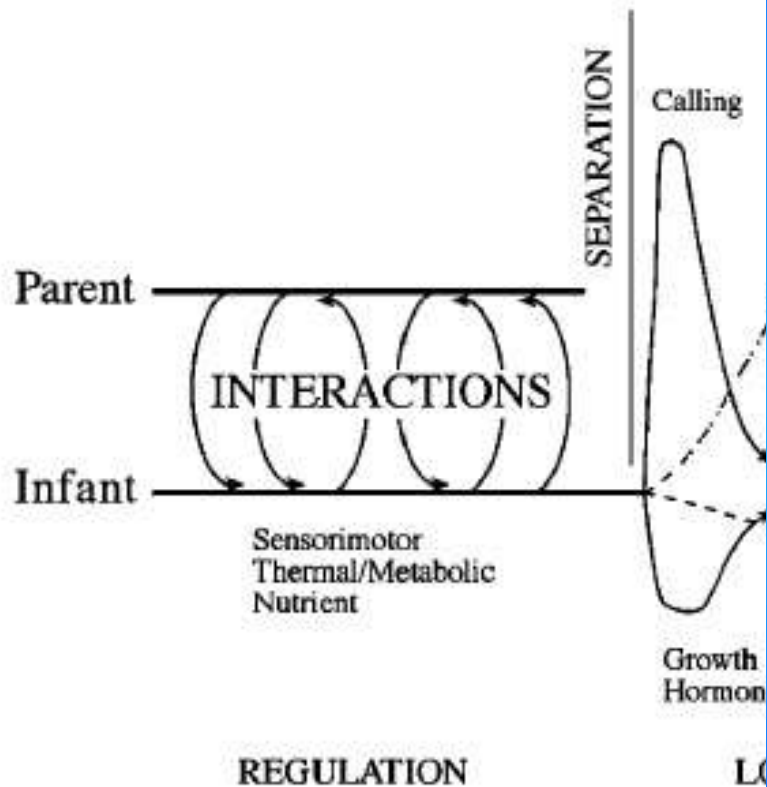


# NURTURESCIENCE



# WHY IS EARLY MATERNAL SEPARATION STRESSFUL?

## SEPARATION



absence

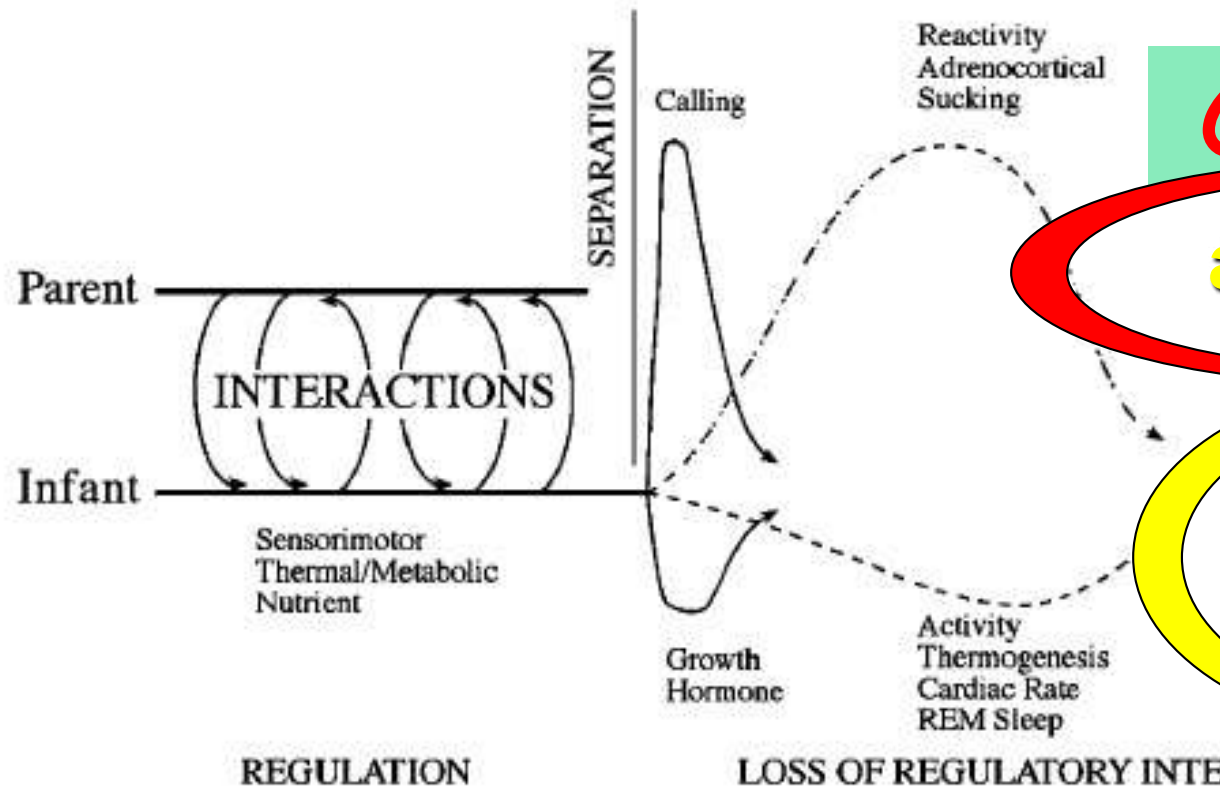
SEPARATION

OXYTOCIN

mother-infant relationship.

# WHY IS EARLY MATERNAL SEPARATION STRESSFUL?

## SEPARATION DYSREGULATES



CORTISOL

absence

SEPARATION

Toxic stress

OXYTOCIN

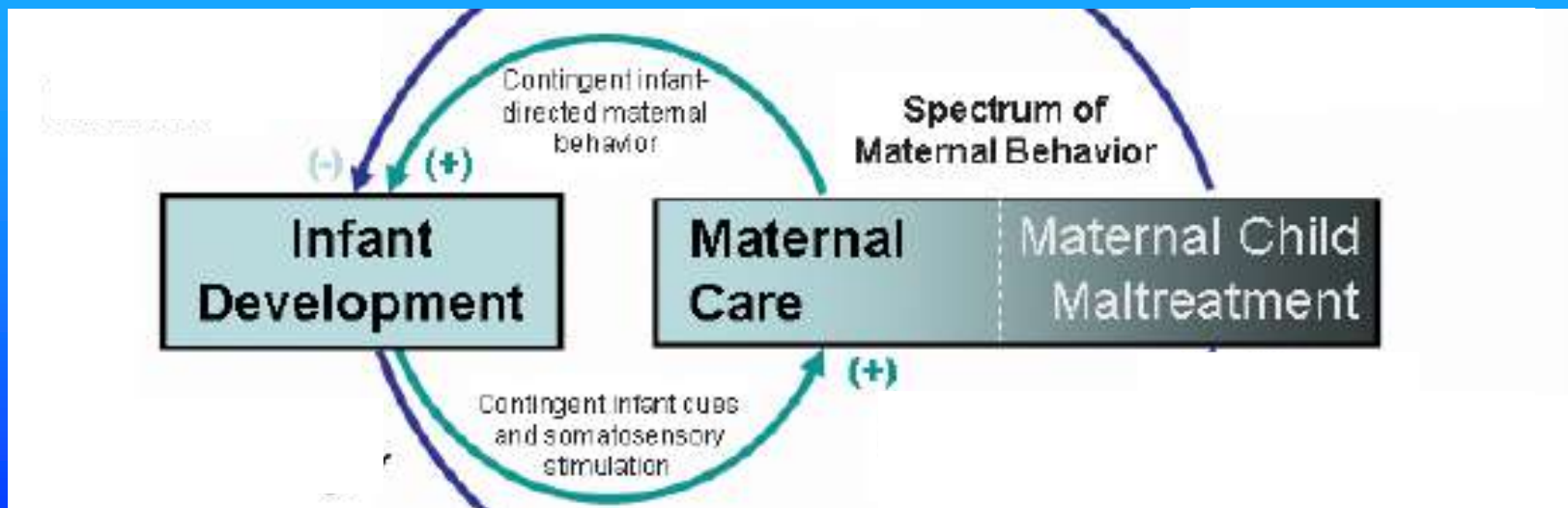
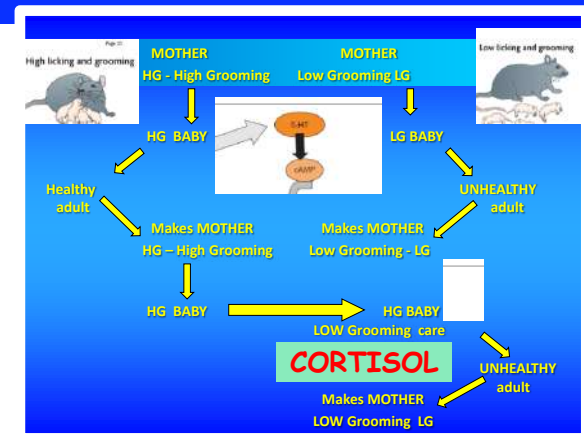
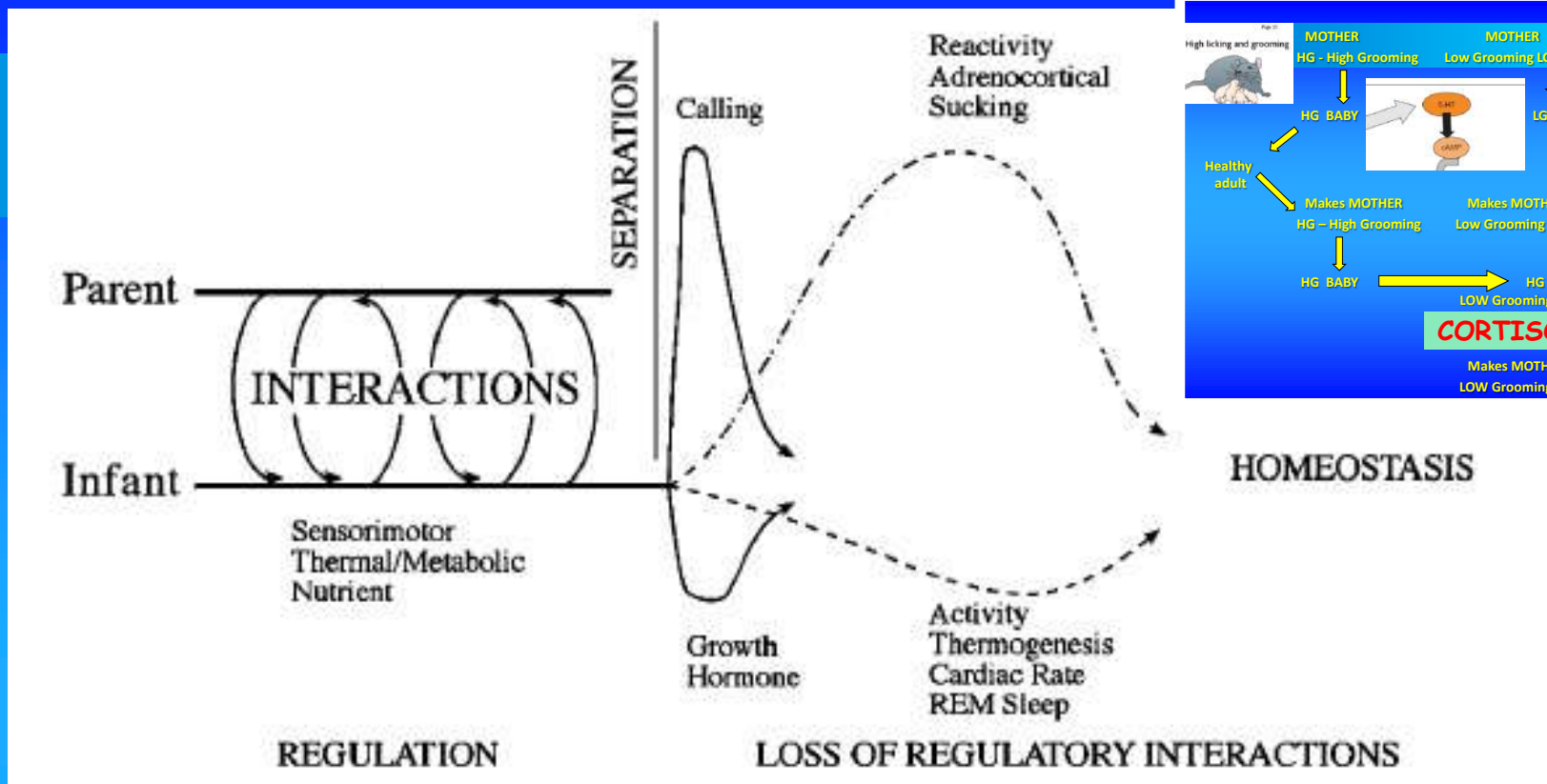
...ntation of the dynamics of ear  
...he loss of regulatory interactio  
...mother-infant relationship.



# Toxic Stress

- **Strong and prolonged activation of the body's stress management systems in the absence of the buffering protection of adult support.**

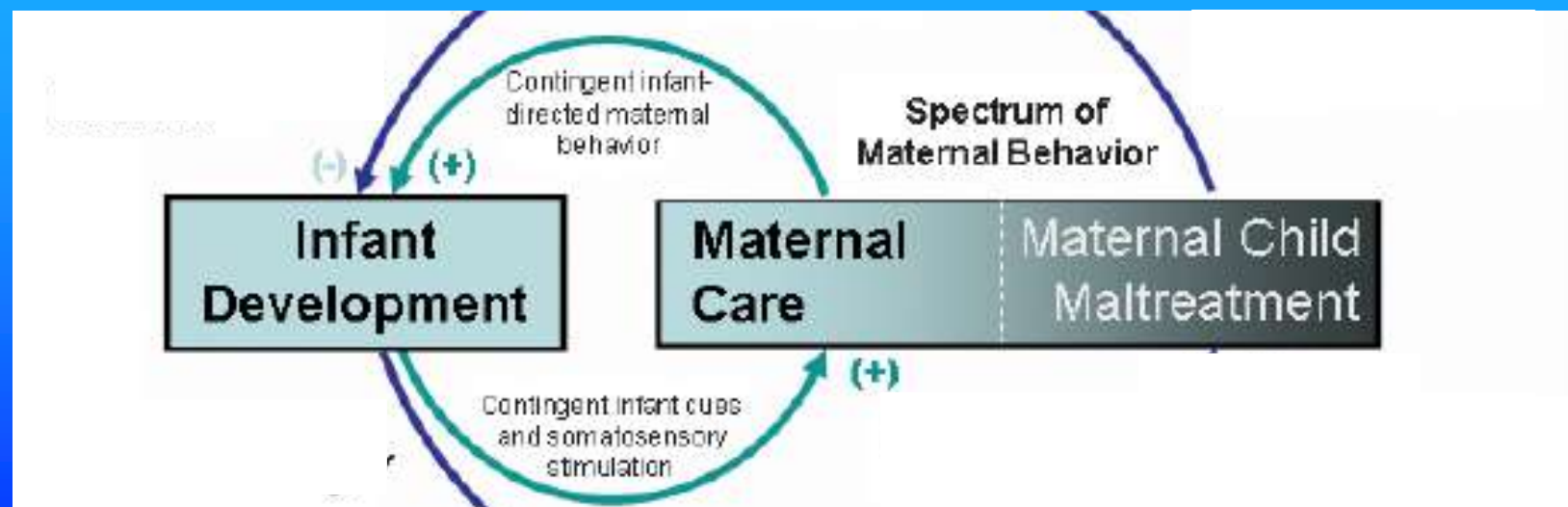
**Disrupts brain architecture and leads to stress management systems that respond at relatively lower thresholds, thereby increasing the risk of stress-related physical and mental illness.**



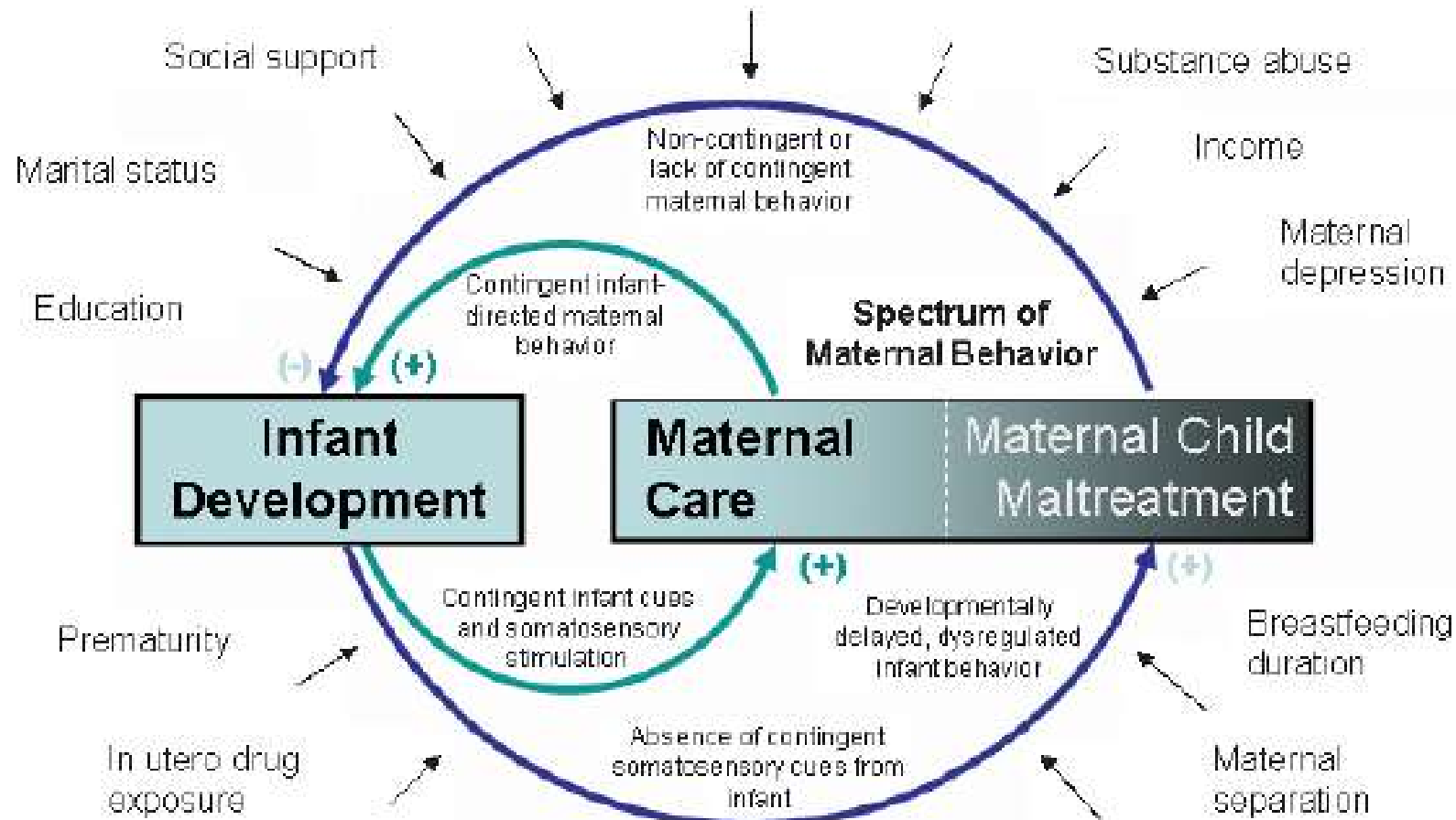
# Brain basis of early parent–infant interactions: psychology, physiology, and *in vivo* functional neuroimaging studies

James E. Swain,<sup>1</sup> Jeffrey P. Lorberbaum,<sup>2,3</sup> Samet Kose,<sup>3</sup> and Lane Strathearn<sup>4,5</sup>

<sup>1</sup>Child Study Center, Yale University, New Haven, CT, USA; <sup>2</sup>Psychiatry Department, Penn State University – Hershey Medical Center, Hershey, PA, USA; <sup>3</sup>Brain Stimulation Laboratory, Medical University of South Carolina, Charleston, SC, USA; <sup>4</sup>Meyer Center for Developmental Pediatrics, Baylor College of Medicine, Houston, TX, USA; <sup>5</sup>Human Neuroimaging Laboratory, Baylor College of Medicine, Houston, TX, USA



## Environmental Factors Impacting on Mother-Infant Interactions

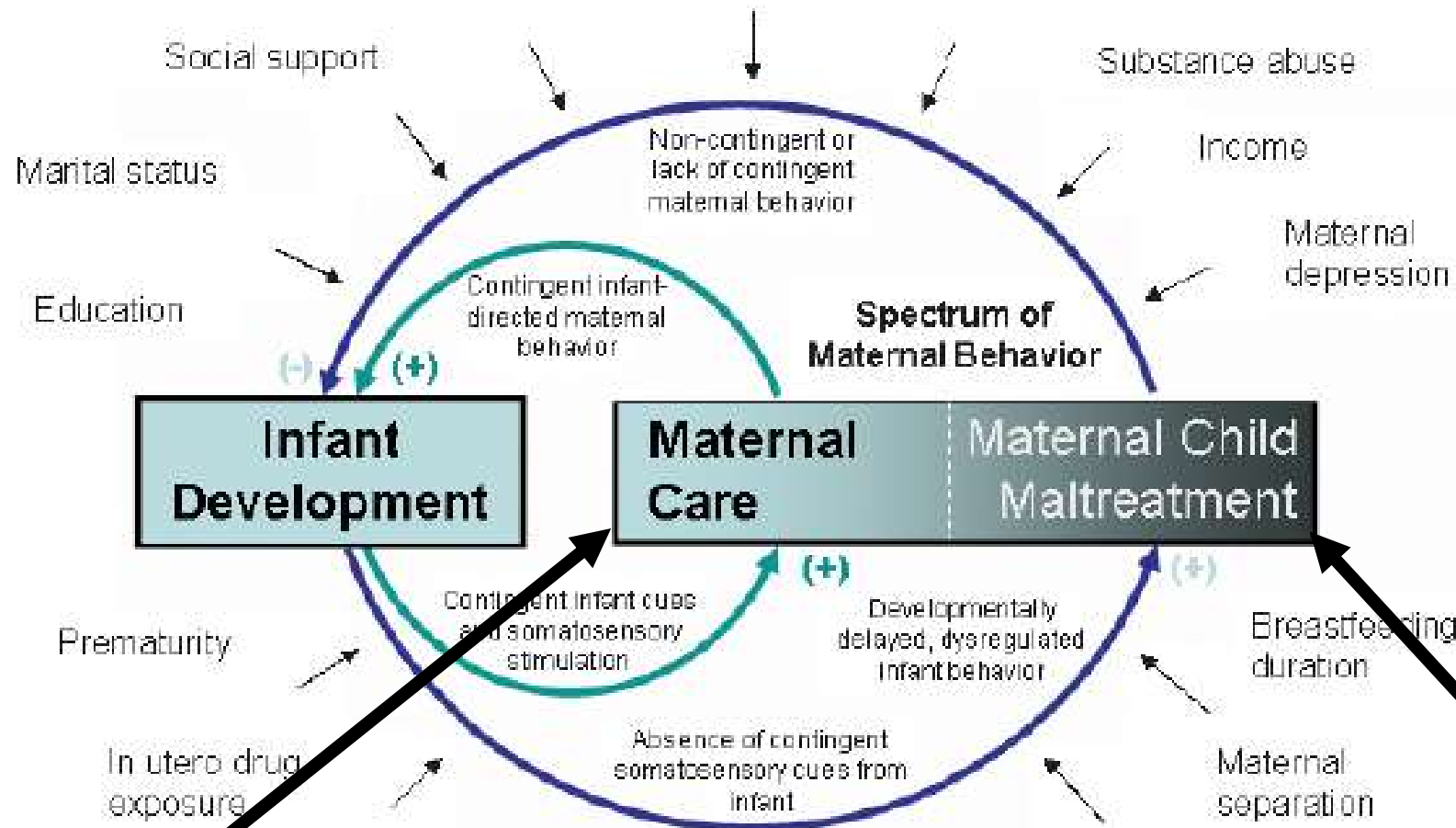


**Table 2** Comparison of prominent features of early parent–infant bonding in humans (adapted from Leckman et al., 2006). Early parental love was rated by 21 experts as similar to infant responsiveness except where indicated by an asterisk

Feature of love	Early parental love	Infant responsiveness
Selective recognition – focus exclusivity	+++ / ++++	+++
Altered mental state – altered autonomic and behavioral responsivity	+++ / ++++	+++ <sup>a</sup>



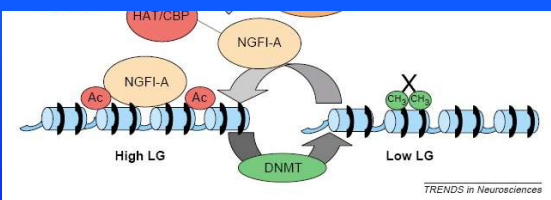
# Environmental Factors Impacting on Mother-Infant Interactions



**HEALTH**

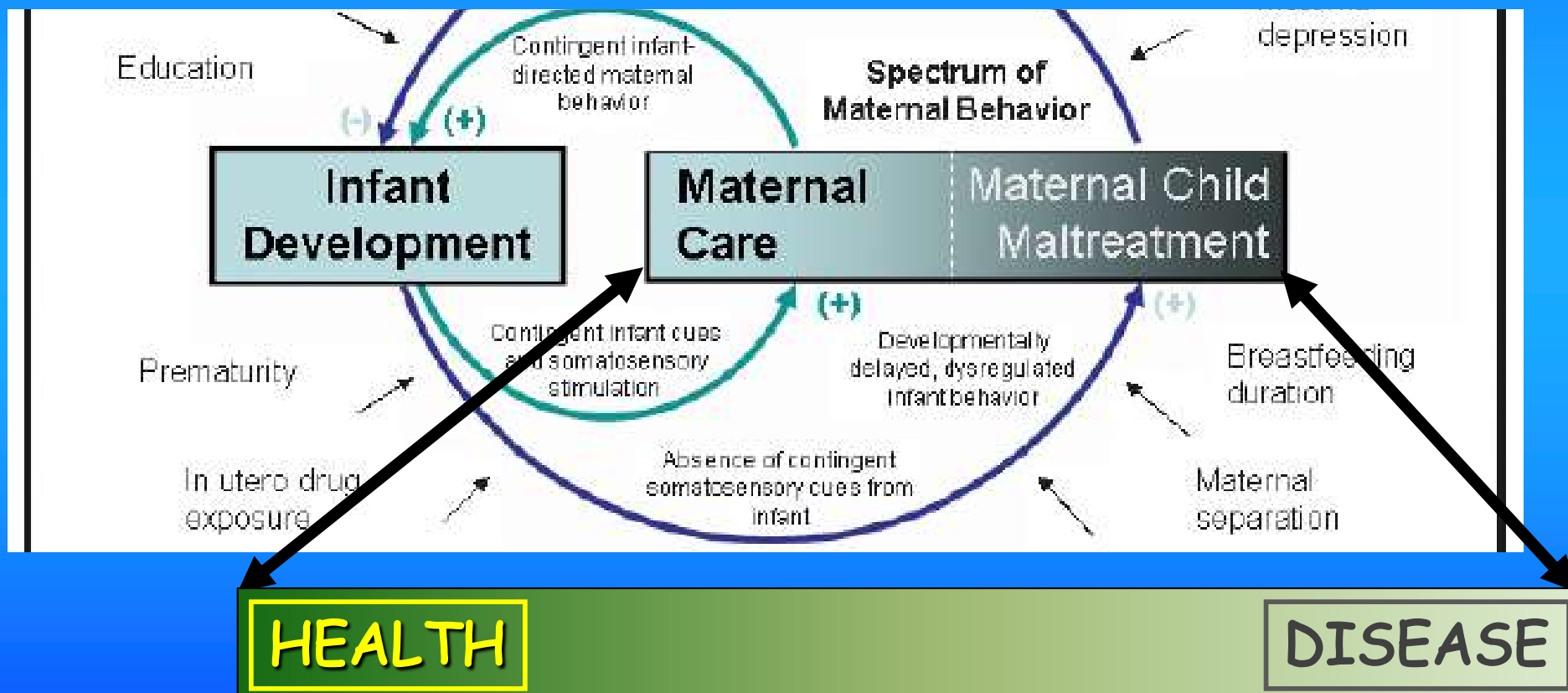
**DISEASE**

**OXYTOCIN**

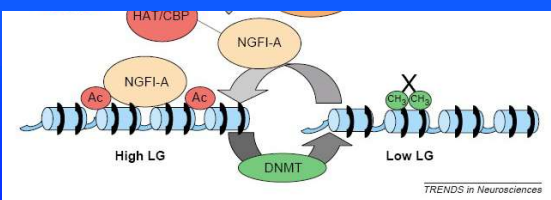


**CORTISOL**

# "Womb ecology becomes world ecology."



**OXYTOCIN**



**CORTISOL**

**SOCIAL  
CONTROL  
CENTRE**



**REWARD  
CONTROL  
CENTRE**



**OXYTOCIN**

**DOPAMINE**

Medial prefrontal cortex

Sensory cortex

Caudate nucleus

Glutamate

Oxytocin

Vasopressin

N-Methyl-D-aspartate receptor

N-Methyl-D-aspartate receptor

Amygdala

Nucleus accumbens

Glutamate

Oxytocin

Vasopressin

Hippocampus

Cortisol

N-Methyl-D-aspartate receptor

Glucocorticoid receptor

Corticotropin-releasing hormone

Corticotropin-releasing hormone

$\beta$ -Adrenergic receptor

Corticotropin-releasing hormone

Norepinephrine

Dopamine

Norepinephrine

Dopamine

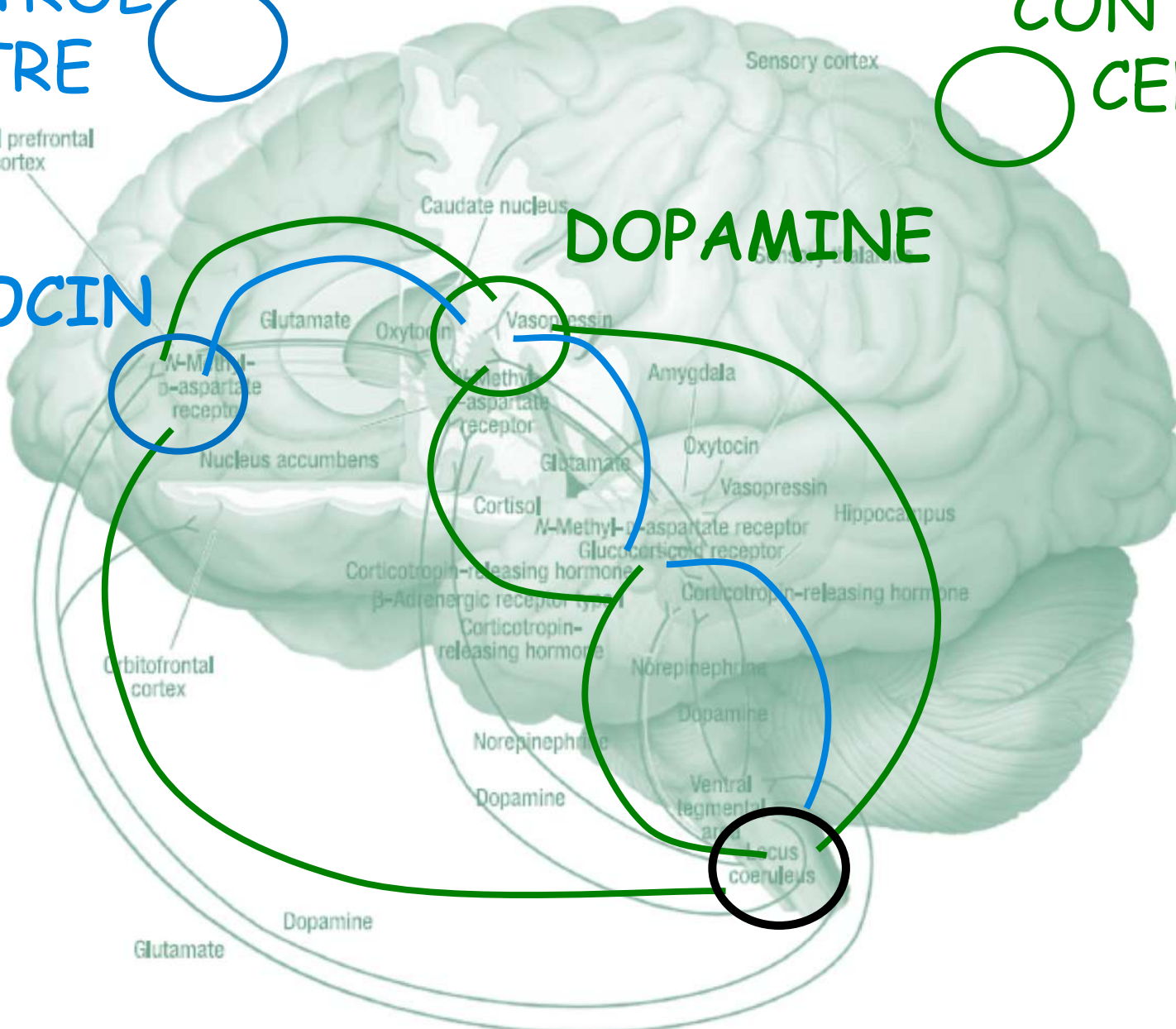
Ventral tegmental area

Locus coeruleus

Orbitofrontal cortex

Glutamate

Dopamine



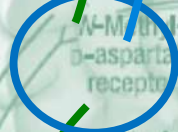
**SOCIAL  
CONTROL  
CENTRE**



**REWARD  
CONTROL  
CENTRE**



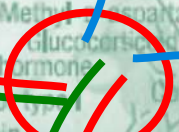
**OXYTOCIN**



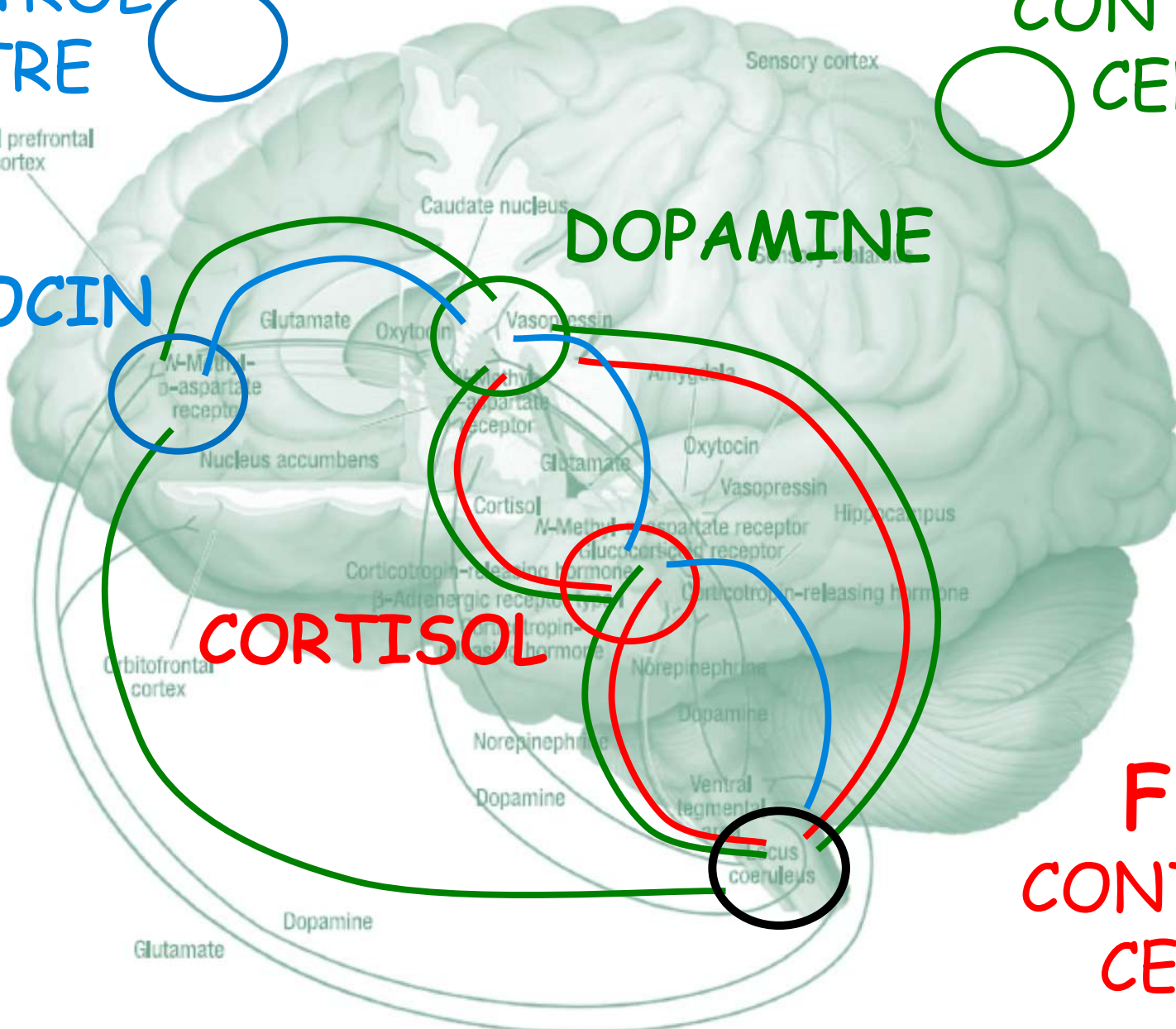
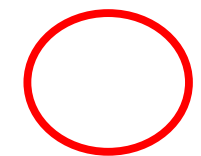
**DOPAMINE**



**CORTISOL**



**FEAR  
CONTROL  
CENTRE**



Medial prefrontal cortex

Sensory cortex

Caudate nucleus

Glutamate

Oxytocin

Vasopressin

N-Methyl-D-aspartate receptor

N-Methyl-D-aspartate receptor

Angiotensin

Nucleus accumbens

Glutamate

Oxytocin

Vasopressin

Hippocampus

Cortisol

N-Methyl-D-aspartate receptor

Glucocorticoid receptor

Corticotropin-releasing hormone

Corticotropin-releasing hormone

B-Adrenergic receptor

Corticotropin-releasing hormone

Orbitofrontal cortex

Norepinephrine

Dopamine

Norepinephrine

Dopamine

Dopamine

Ventral tegmental area

Locus coeruleus

Glutamate

Dopamine

**SOCIAL CONTROL CENTRE**

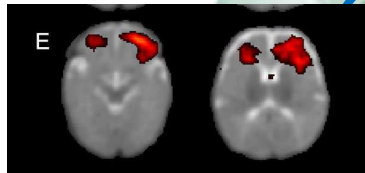


**REWARD CONTROL CENTRE**



**DOPAMINE**

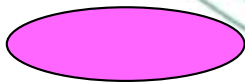
**OXYTOCIN**



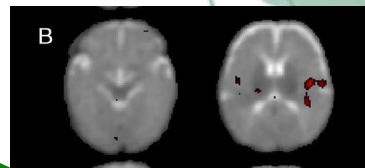
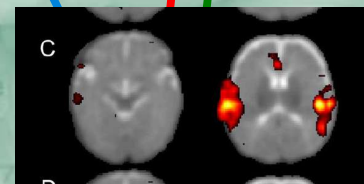
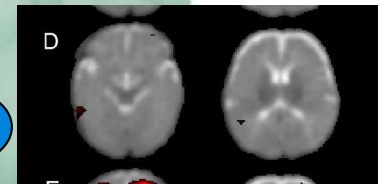
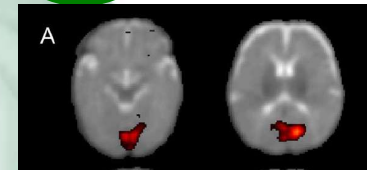
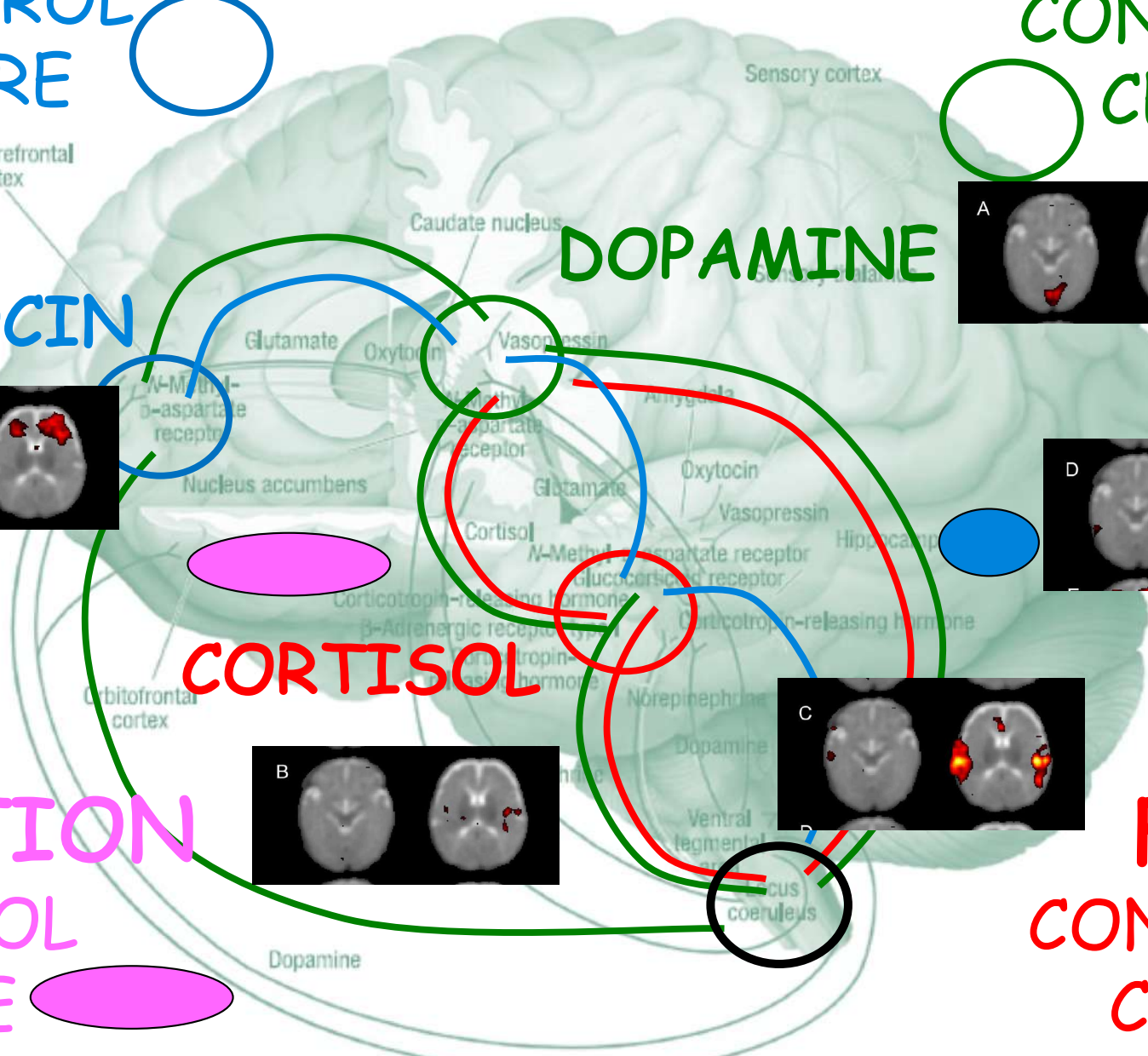
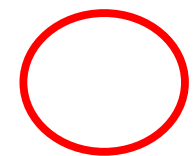
**CORTISOL**



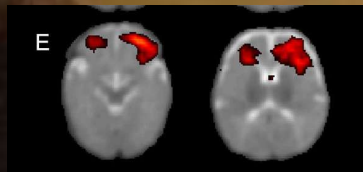
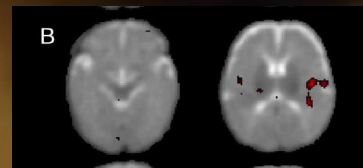
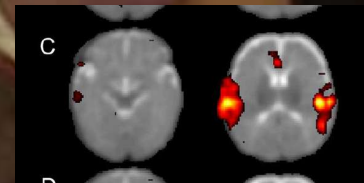
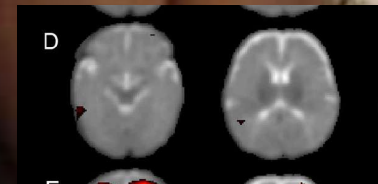
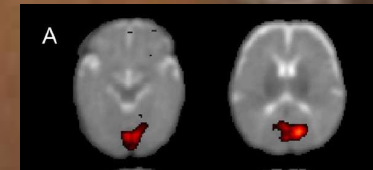
**EMOTION CONTROL CENTRE**



**FEAR CONTROL CENTRE**



# HIGHLY CONSERVED NEURO-ENDOCRINE BEHAVIOR



EMOTION  
CONTROL  
CENTRE

**SOCIAL CONTROL CENTRE**

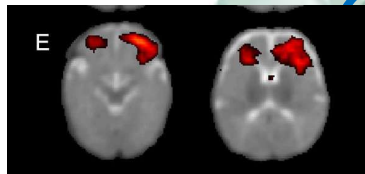


**REWARD CONTROL CENTRE**



**DOPAMINE**

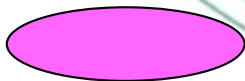
**OXYTOCIN**



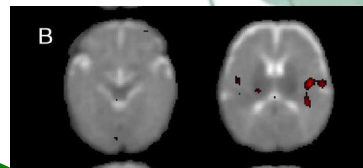
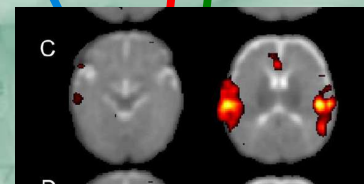
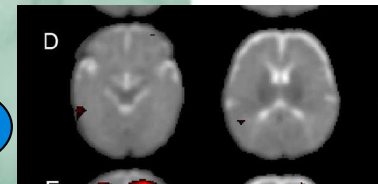
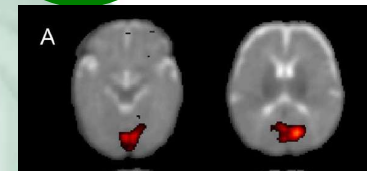
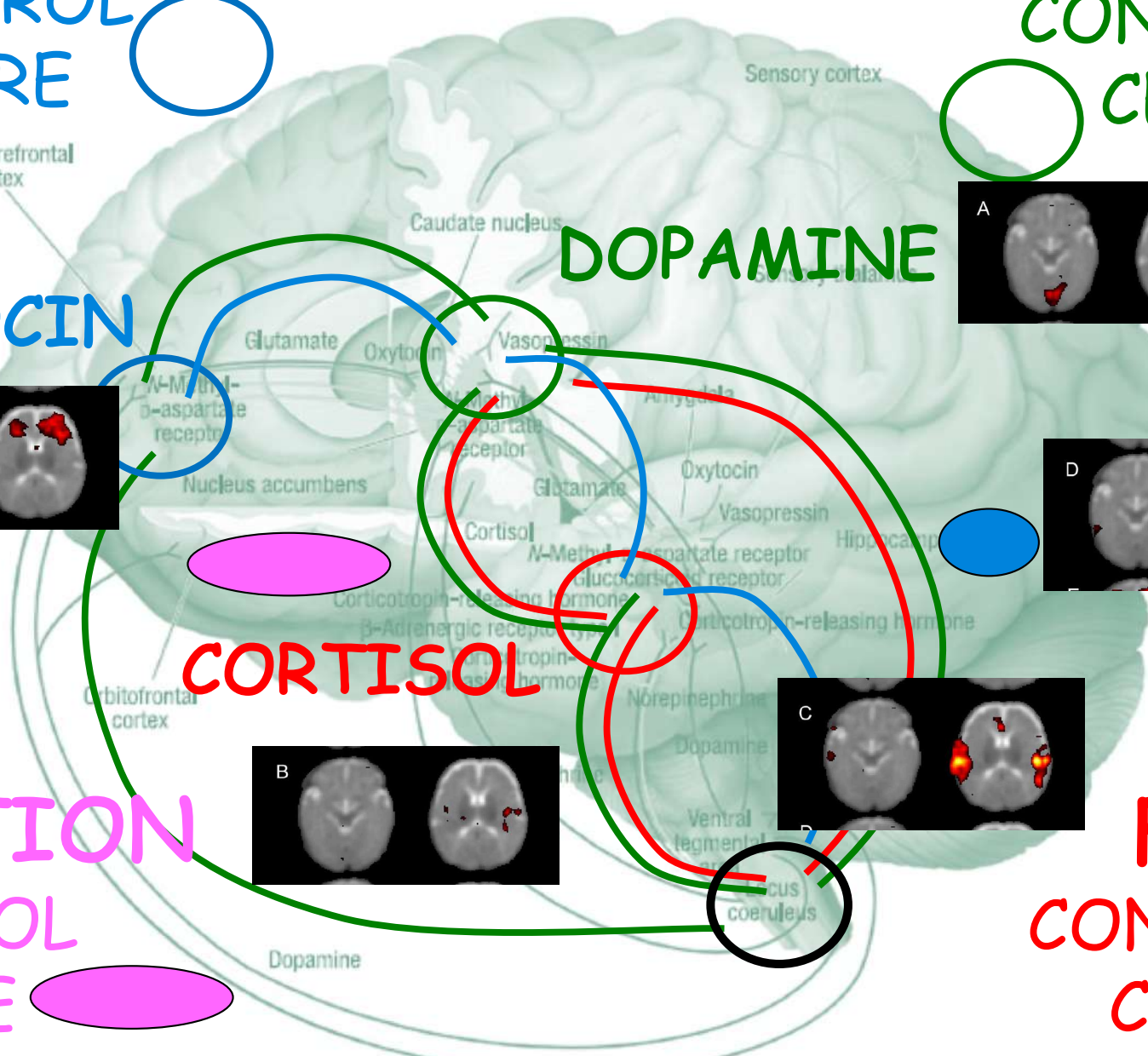
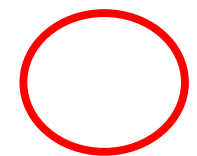
**CORTISOL**



**EMOTION CONTROL CENTRE**

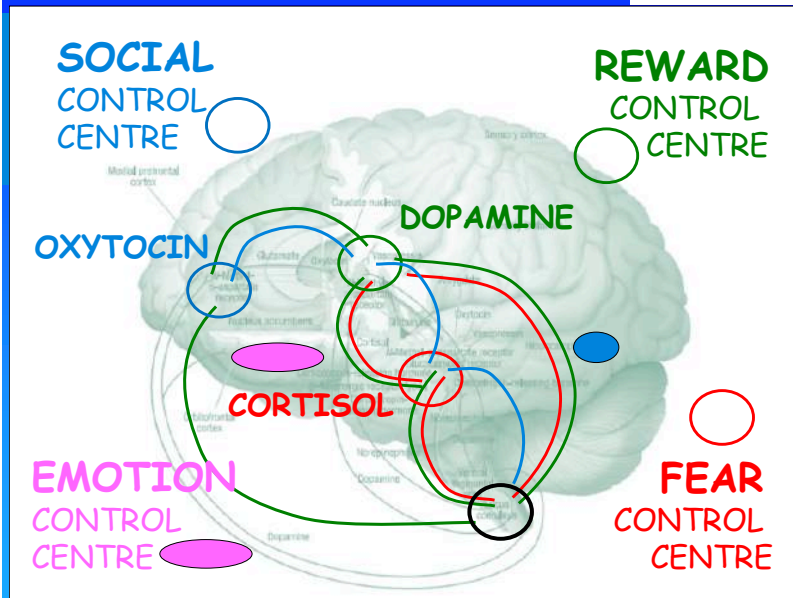


**FEAR CONTROL CENTRE**



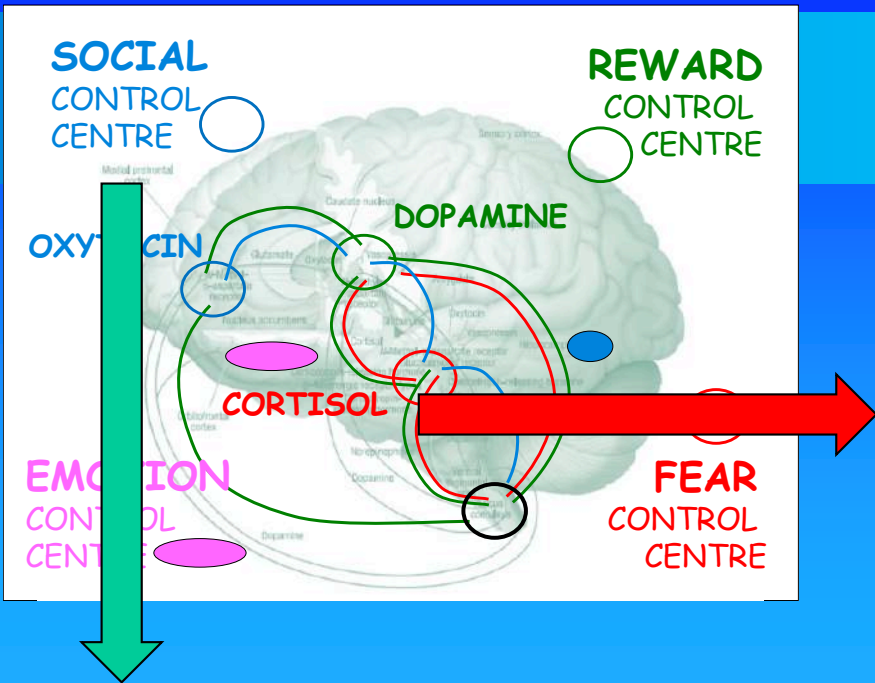
# Psychobiological Mechanisms of Resilience and Vulnerability:

## Implications for Successful Adaptation to Extreme Stress



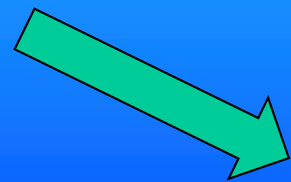
... there is considerable overlap in the brain structures associated with these neural mechanisms ... functional interactions among the circuits.





An overly responsive FEAR circuit ... may negatively influence functioning of the reward system.

... a properly functioning REWARD circuit may be necessary for positive social behaviors.



REWARD

Resilience

HEALTH



FEAR

Vulnerability

DISEASE

# RESILIENCE

(= STRESS RESISTANCE)

"capacity to maintain healthy emotional functioning in the aftermath of stressful experiences"

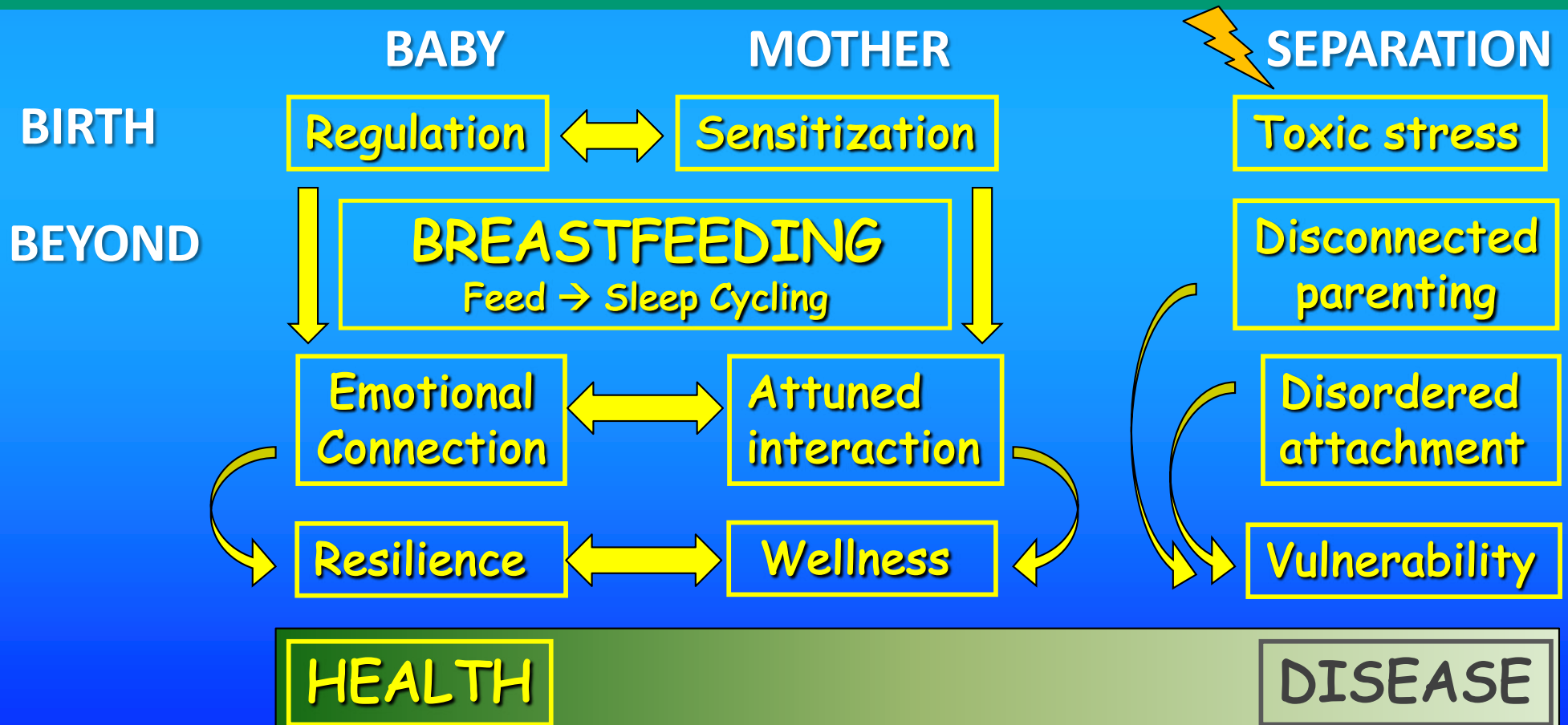
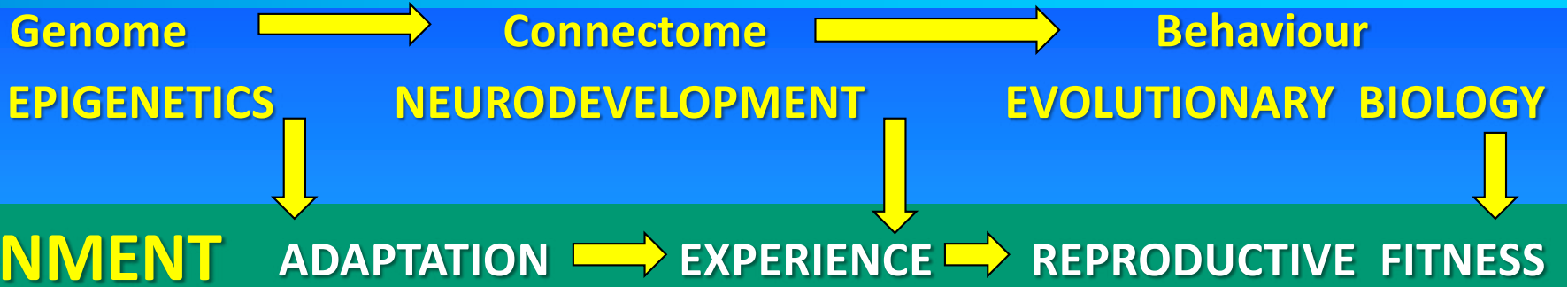
Resilience

Vulnerability

HEALTH

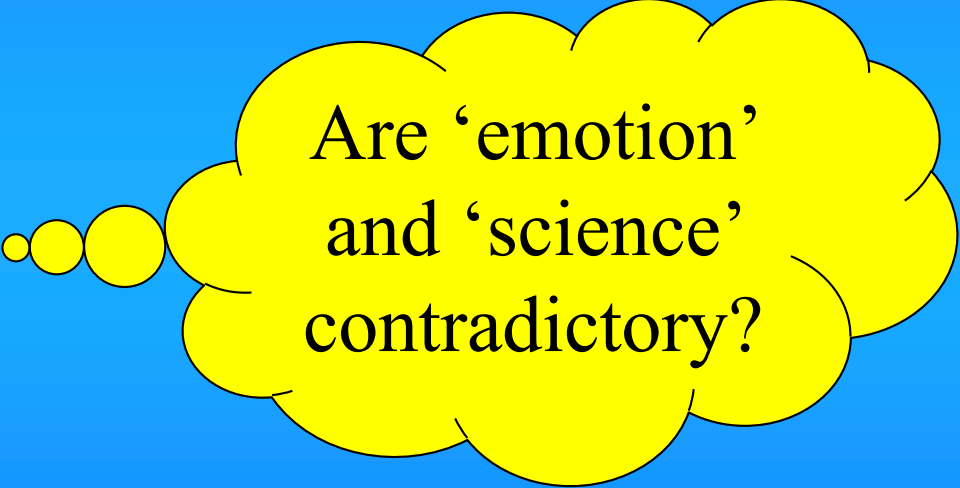
DISEASE

# NURTURESCIENCE



# INTRODUCING NURTURESCIENCE

Jaak Panksepp  
dedicated his  
professional career  
to the study of  
mammalian  
emotions



Are 'emotion'  
and 'science'  
contradictory?

(TED talk)

[https://www.youtube.com/watch?v=65e2qScV\\_K8](https://www.youtube.com/watch?v=65e2qScV_K8)

# INTRODUCING NURTURESCIENCE

Jaak Panksepp  
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mammalian  
emotions

(TED talk)



AFFECTIVE  
NEUROSCIENCE

# Introducing NURTURESCIENCE a new model with ancient roots.



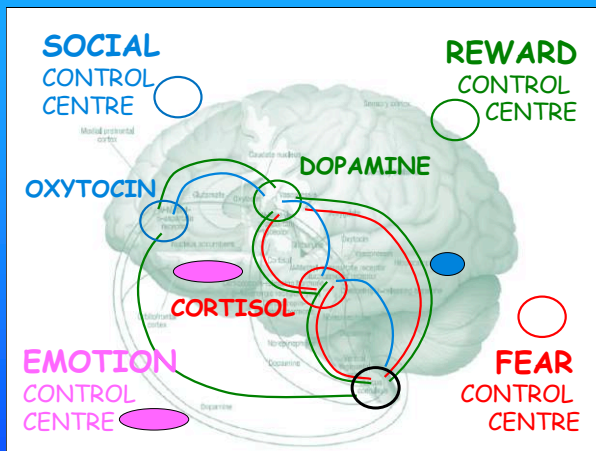
Instituto Europeo de  
Salud Mental Perinatal

... with focus on long  
term mental health  
benefits.

# Introducing NURTURESCIENCE a new model with ancient roots.



Instituto Europeo de  
Salud Mental Perinatal



... with focus on long term mental health benefits.

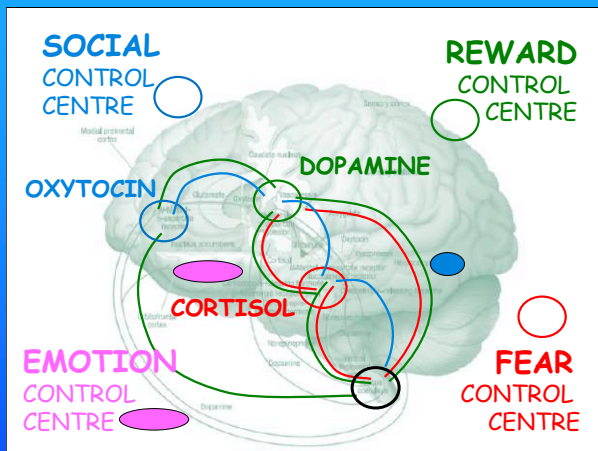
HEALTH

DISEASE

# AFFECTIVE NEUROSCIENCE

THE FOUNDATIONS  
OF HUMAN AND  
ANIMAL  
EMOTIONS

Jaak Panksepp



**HEALTH**

**HEALTH**

**DISEASE**

Levels of Analysis

Developmental Implication  
Behavioral Consequence  
Feeling State  
Sensory Controls  
Evolutionary Antecedent

competent sexual & maternal behavior

depression

social choice & approach

separation distress responses

somatosensory  
olfactory  
auditory

visual  
vestibular  
hunger/temp.

**Integrative Emotional System for Social Affect**

place attachment mechanisms

pain mechanisms

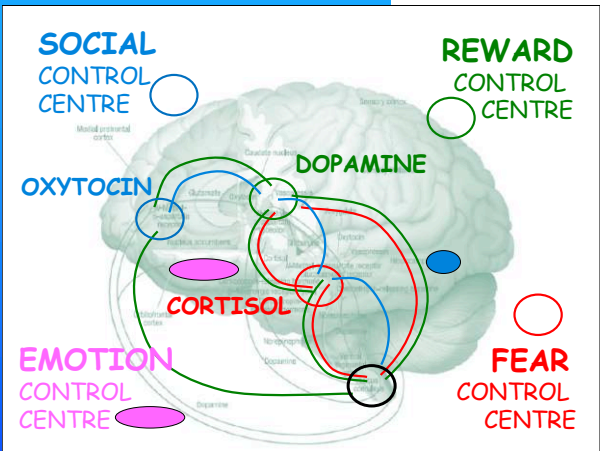
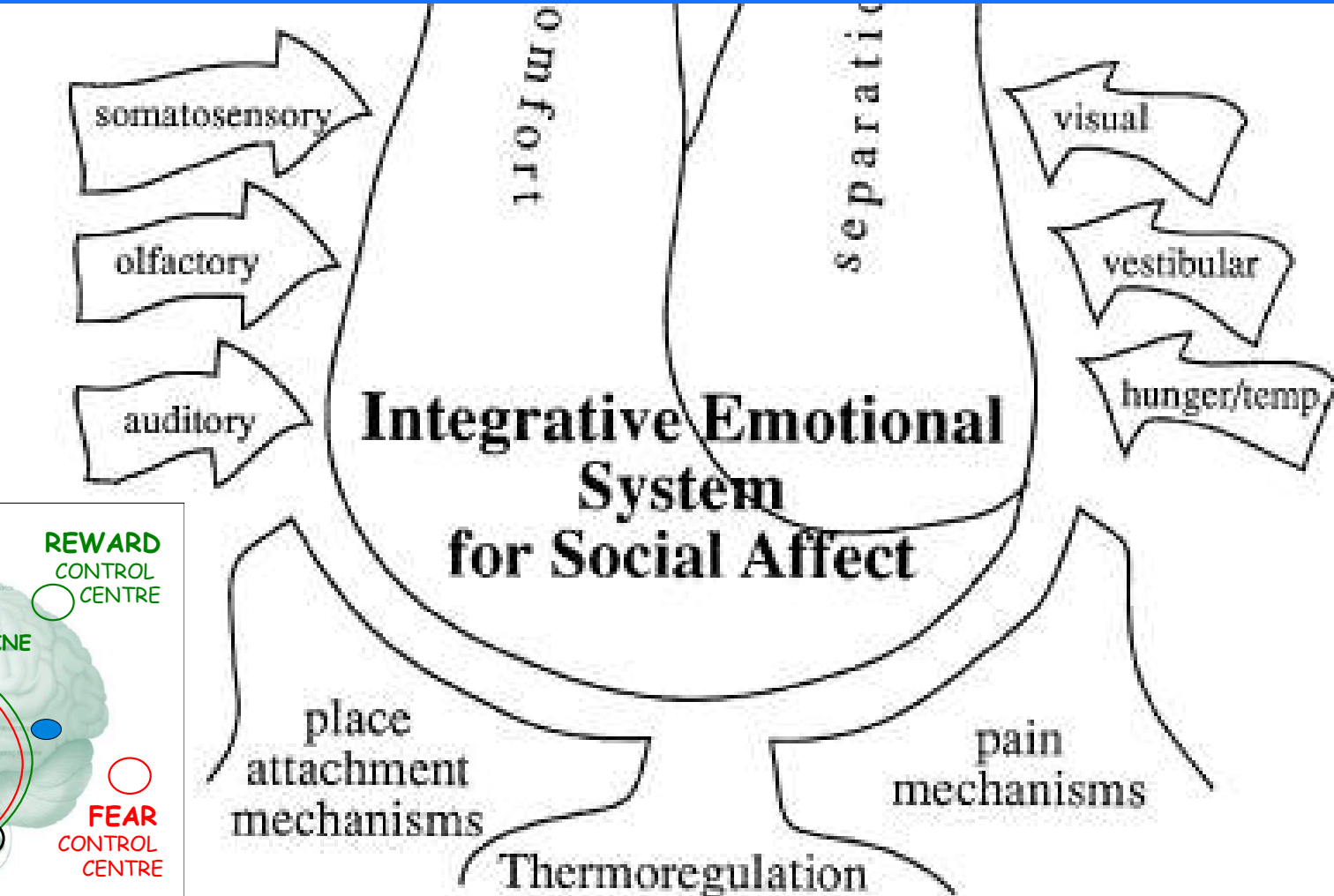
Thermoregulation

social comfort

separation distress

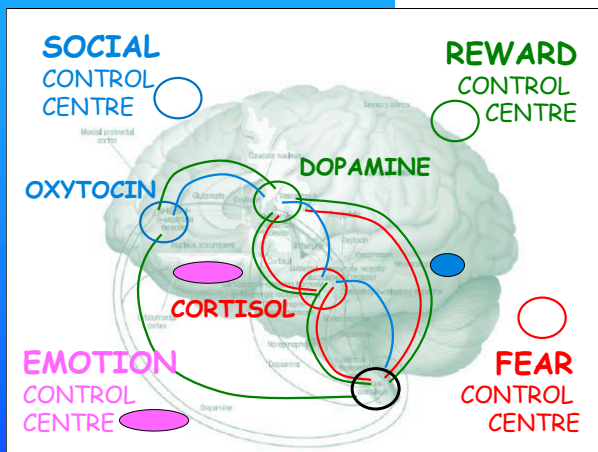
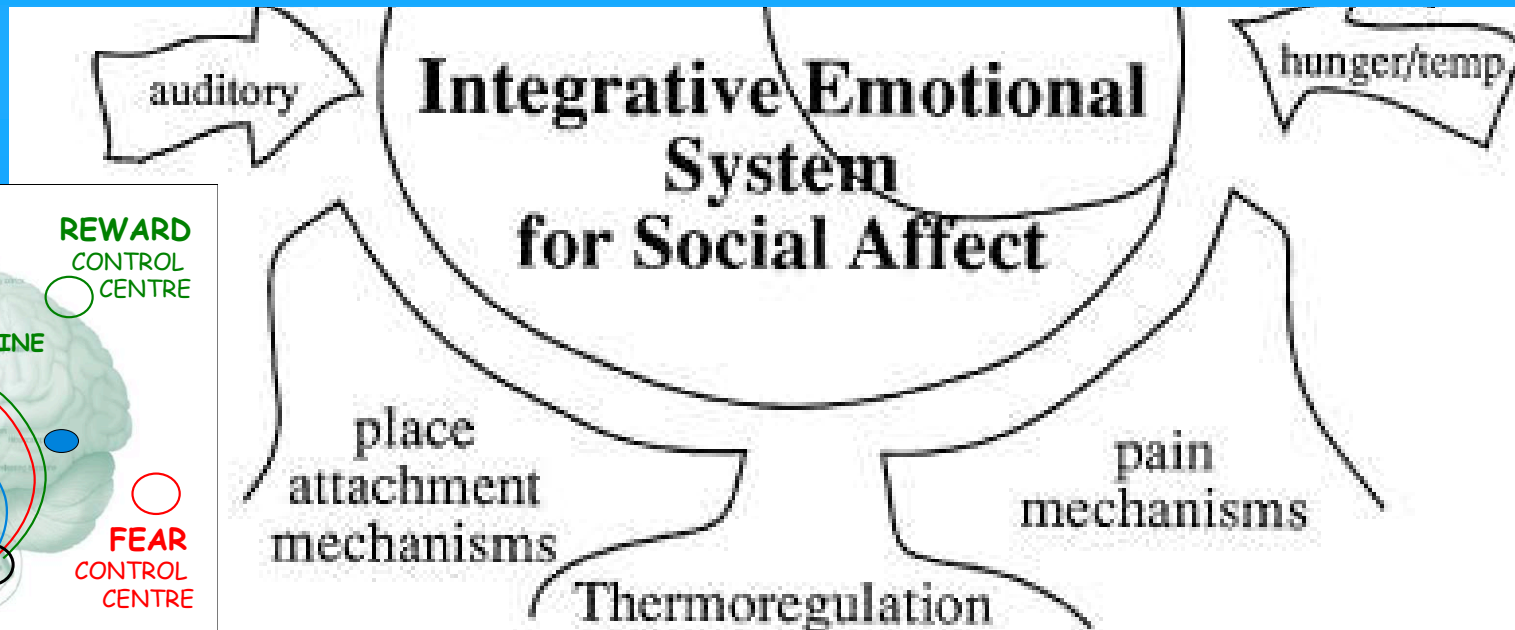
**DISEASE**





**HEALTH**

**DISEASE**

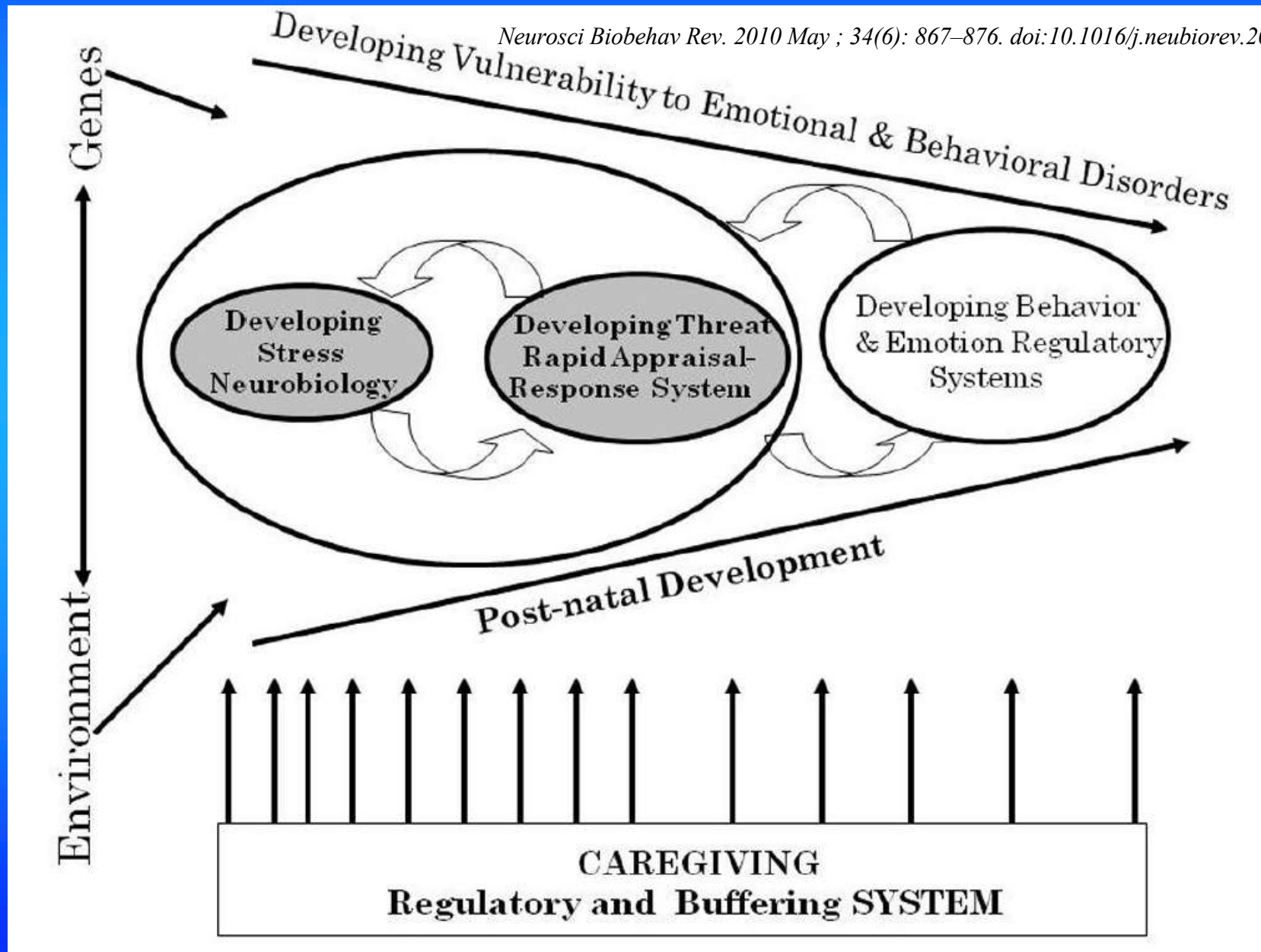


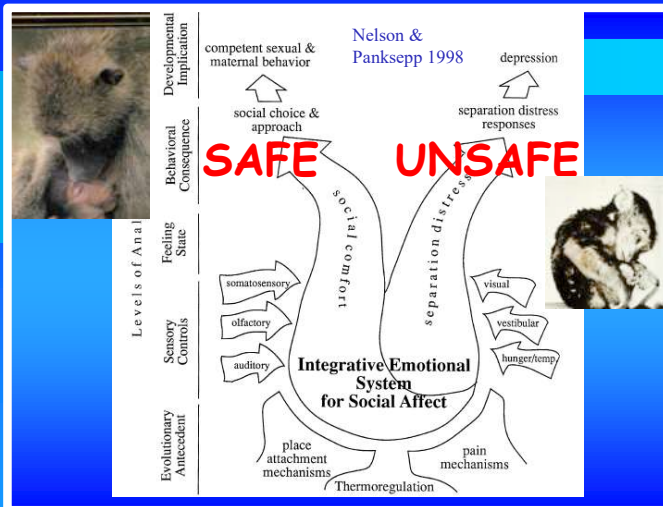
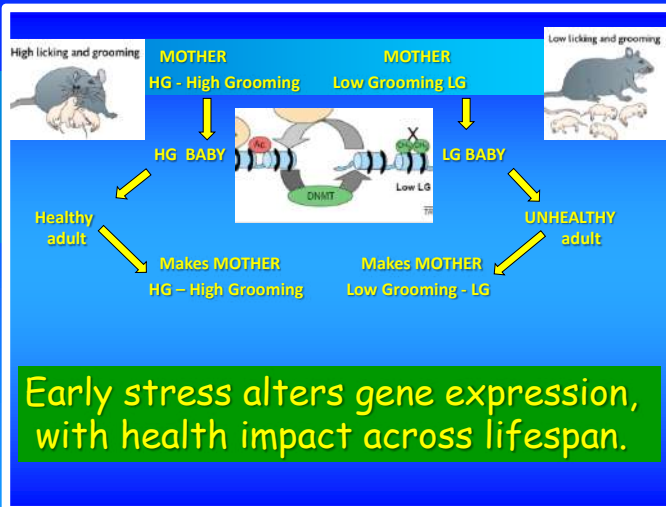
**HEALTH**

**DISEASE**

# Early Experience and the Development of Stress Reactivity and Regulation in Children (Gunnar 2010)

*Neurosci Biobehav Rev.* 2010 May ; 34(6): 867–876. doi:10.1016/j.neubiorev.2009.05.007.



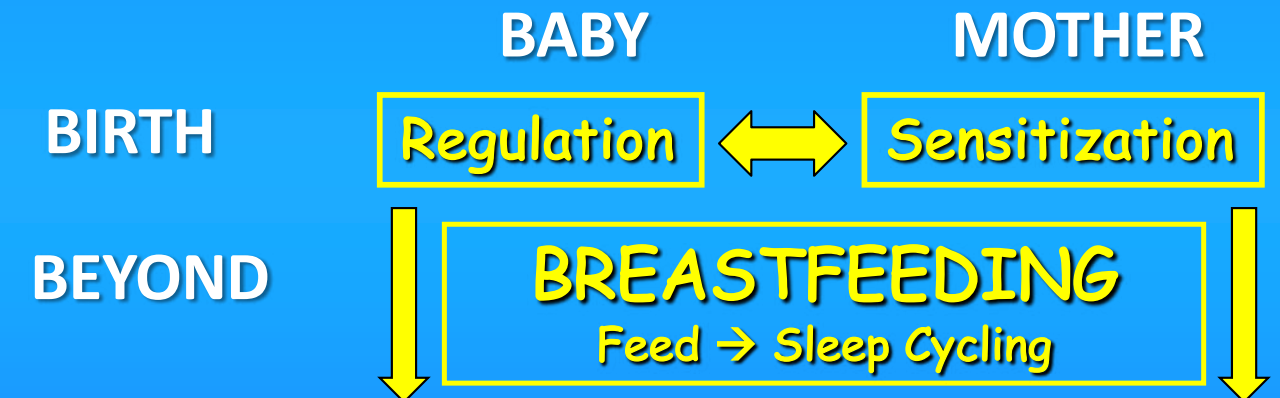
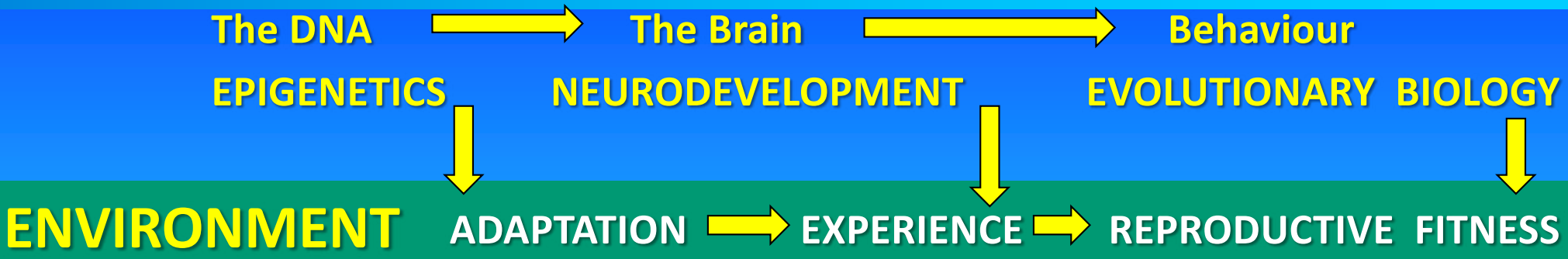


# NURTURESCIENCE

CAREGIVING

Regulatory and Buffering SYSTEM

# NURTURESCIENCE

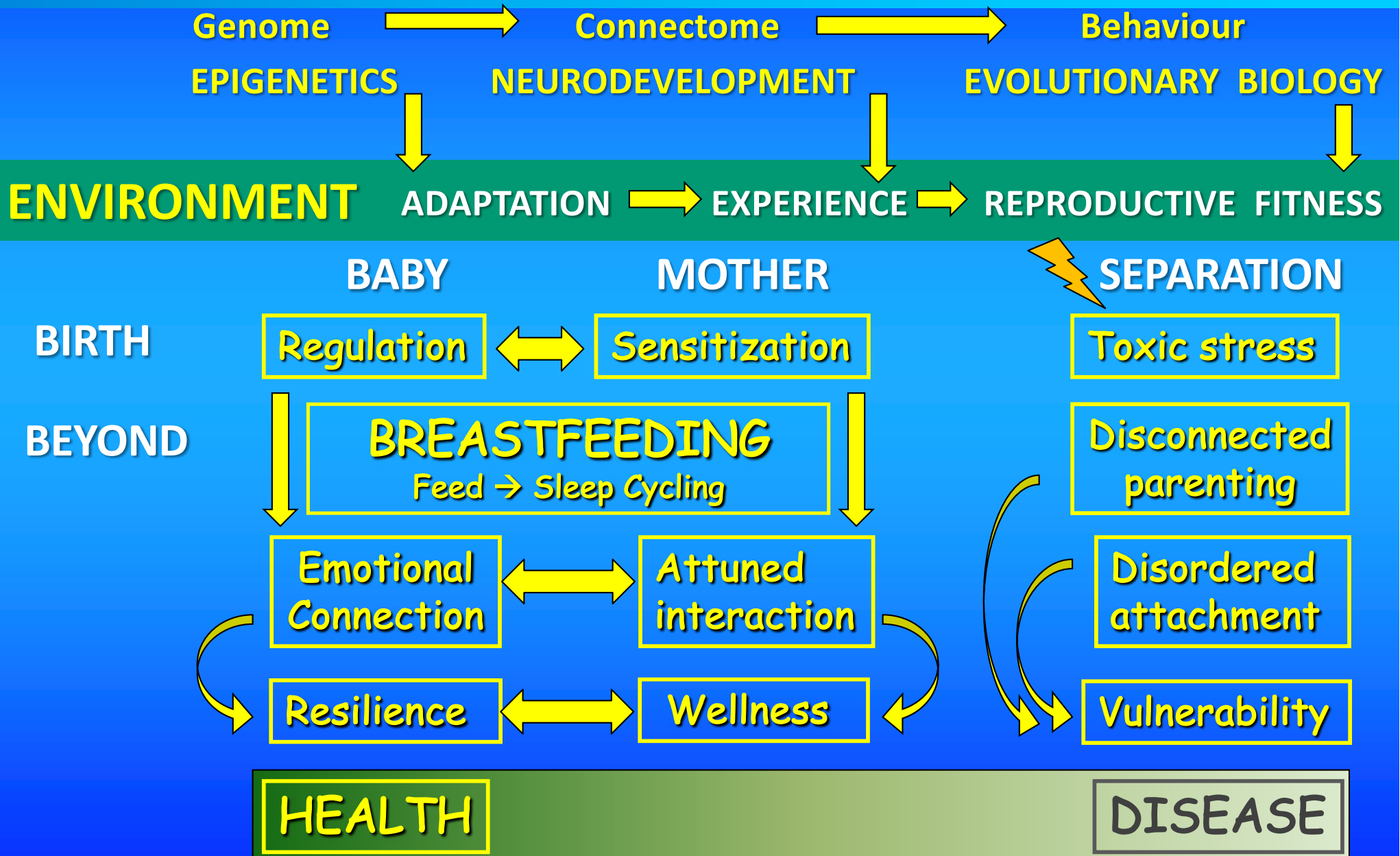


# NURTURESCIENCE

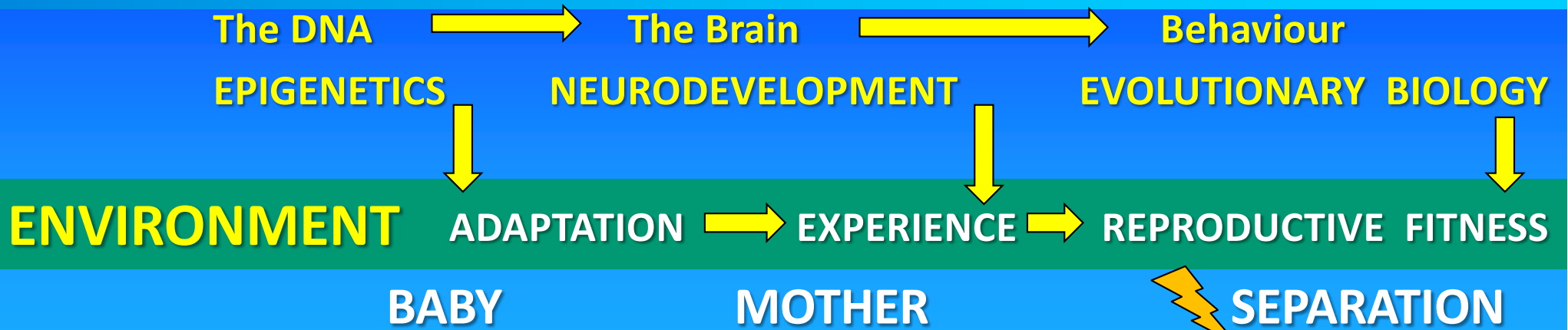
## CAREGIVING

## Regulatory and Buffering SYSTEM

# NURTURESCIENCE



# NURTURESCIENCE



February 19, 2018

## Cognitive Outcomes of Children Born Extremely or Very Preterm Since the 1990s and Associated Risk Factors

A Meta-analysis and Meta-regression

E. Sabrina Twilhaar, MSc<sup>1</sup>; Rebecca M. Wade, MSc<sup>1</sup>; Jorrit F. de Kieviet, MD, PhD<sup>1</sup>; et al

Toxic stress

Intrusive parenting

Disordered attachment

Vulnerability

HEALTH

DISEASE

## **Cognitive Outcomes of Children Born Extremely or Very Preterm Since the 1990s and Associated Risk Factors: A Meta-analysis and Meta-regression.**

Twilhaar ES<sup>1</sup>, Wade RM<sup>1</sup>, de Kieviet JF<sup>1</sup>, van Goudoever JB<sup>2,3</sup>, van Elburg RM<sup>2,4</sup>, Oosterlaan J<sup>1,2,3</sup>.

**Feb 19, 2018**

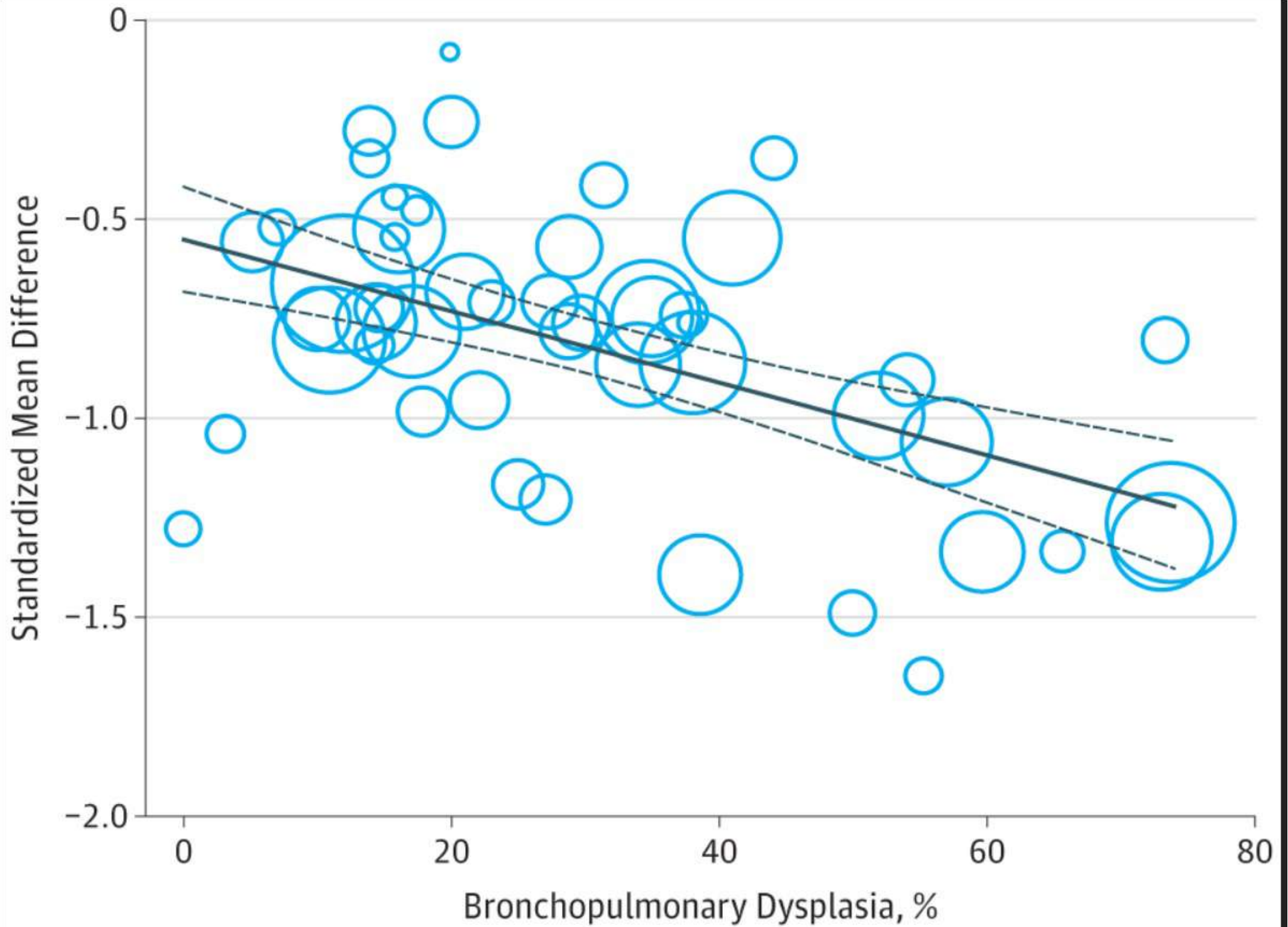
### **Conclusions and Relevance:**

Extremely or very preterm children born in the antenatal corticosteroids and surfactant era show large deficits in intelligence. No improvement in cognitive outcome was observed between 1990 and 2008.

...

Bronchopulmonary dysplasia was found to be a crucial factor for cognitive outcome. Lowering the high incidence of BPD may be key to improving long-term outcomes after EP/VP birth.





# The Stockholm Neonatal Family Centered Care Study: Effects on Length of Stay and Infant Morbidity



**WHAT'S KNOWN ON THIS SUBJECT:** Although advances in technology and medical treatment have allowed more infants to survive, morbidity remains high. The NICU environment and early parent-infant interaction have been associated with infant health and length of hospital stay.



**WHAT THIS STUDY ADDS:** Data from this study indicate that parents staying in the NICU from admission to discharge may reduce the total length of stay for infants born prematurely. An individual-room NICU design could have a direct effect on infant stability and morbidity.

**AUTHORS:** Annica Örtenstrand, RN, PhD,<sup>a</sup> Björn Westrup, MD, PhD,<sup>b,c</sup> Eva Berggren Broström, MD, PhD,<sup>a</sup> Susanne Åkerström, RN, PhD,<sup>a</sup> Susanna Brune, MD,<sup>c</sup> Lene Lindberg, PhD,<sup>d</sup> and Waldenström, RN, RM, BA, PhD<sup>e</sup>

<sup>a</sup>Department of Clinical Science and  
Sachs Children's Hospital, <sup>b</sup>Divisions  
<sup>c</sup>Reproductive and Perinatal Health  
and Child Health, and <sup>d</sup>Division of Applied  
Department of Public Health Science  
Stockholm, Sweden; and <sup>e</sup>Astrid Lind  
Danderyd, Karolinska University Hos



**n = 366**

**CONTROL GROUP: parents visit 6 - 10 hours per day**

**INTERVENTION : parents admitted ... present 24 h per day**

# The Stockholm Neonatal Family Centered Care Study: Effects on Length of Stay and Infant Morbidity



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<sup>a</sup>Department of Clinical Science and Education, Södersjukhuset, Sachs Children's Hospital, <sup>b</sup>Divisions of Neonatology and <sup>c</sup>Reproductive and Perinatal Health Care, Department of Woman and Child Health, and <sup>d</sup>Division of Applied Public Health, Department of Public Health Sciences, Karolinska Institutet, Stockholm, Sweden; and <sup>e</sup>Astrid Lindgren Children's Hospital, Danderyd, Karolinska University Hospital, Stockholm, Sweden

BPD<sup>f</sup>

Non-BPD to mild BPD

180 (98.4)

171 (94.0)

Moderate to severe BPD

3 (1.6)

11 (6.0)

Severe morbidity<sup>g</sup> or death

No severe morbidity

174 (95.1)

167 (91.3)

Severe morbidity

9 (4.9)

16 (8.7)

# The Stockholm Neonatal Family Centered Care Study: Effects on Length of Stay and Infant Morbidity

**CONCLUSIONS** This study demonstrated a reduction in total length of hospital stay for infants born prematurely by providing facilities for parents to stay in the NICU 24 hours/day from admission to discharge. Analyses of secondary outcomes also suggested a reduction in pulmonary morbidity, such as moderate-to-severe BPD.

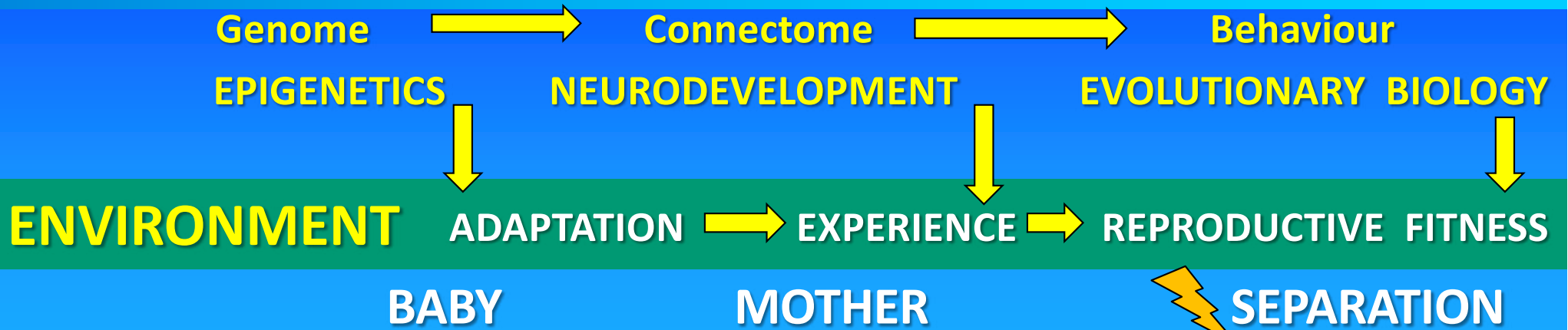


**INTERVENTION : parents admitted ... present 24 h**  
→ **BUFFERING PROTECTION OF ADULT SUPPORT**  
→ **ZERO SEPARATION REDUCES TOXIC STRESS**

**HEALTH**

**DISEASE**

# NURTURESCIENCE



February 19, 2018

## Cognitive Outcomes of Children Born Extremely or Very Preterm Since the 1990s and Associated Risk Factors

### A Meta-analysis and Meta-regression

E. Sabrina Twilhaar, MSc<sup>1</sup>; Rebecca M. Wade, MSc<sup>1</sup>; Jorrit F. de Kieviet, MD, PhD<sup>1</sup>; et al

Toxic stress

Disconnected parenting

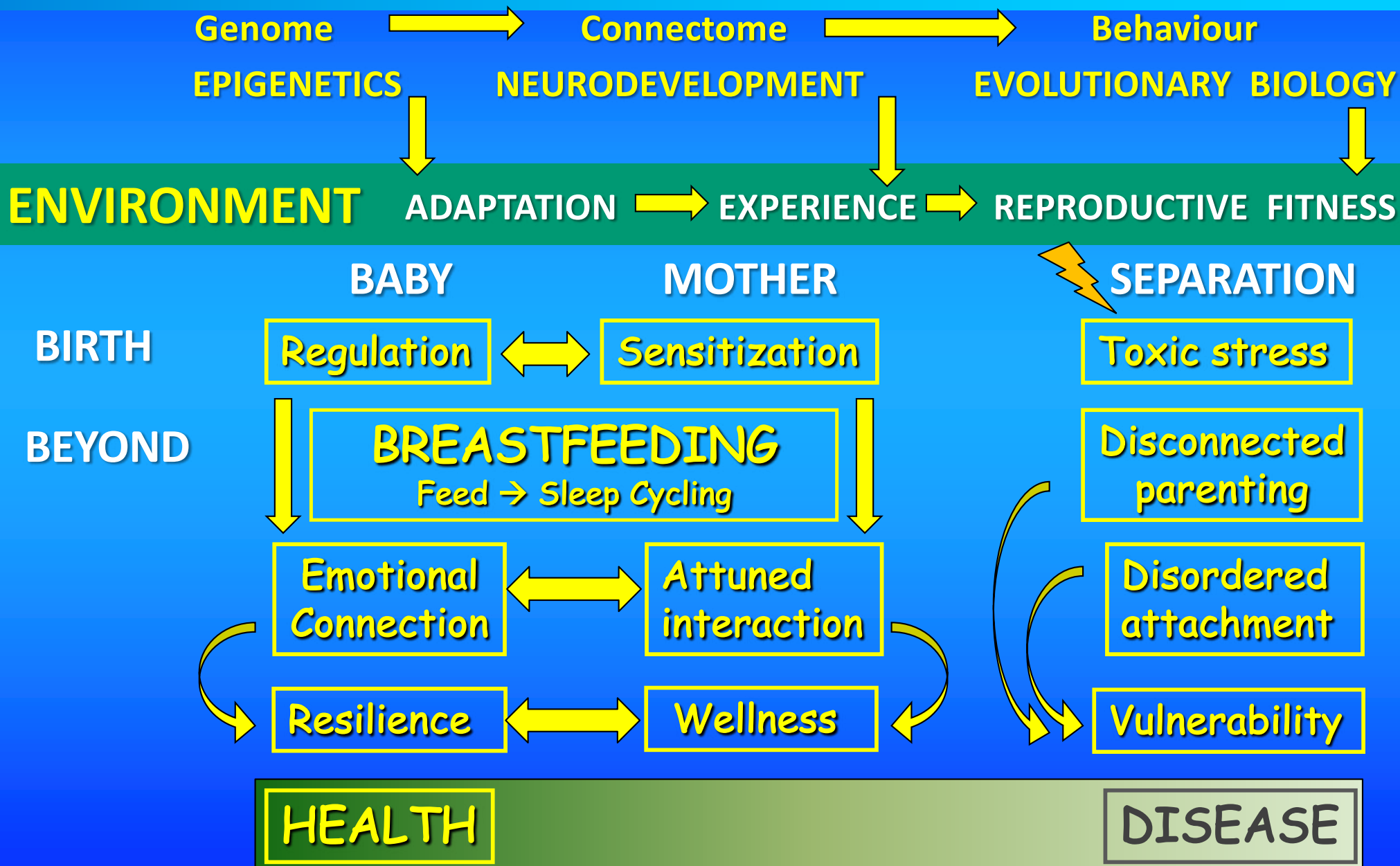
Disordered attachment

Vulnerability

HEALTH

DISEASE

# NURTURESCIENCE



# NURTURESCIENCE

Neuroscience developed  
in the old paradigm of  
maternal-infant separation.

a new model with ancient roots.

# NURTURESCIENCE

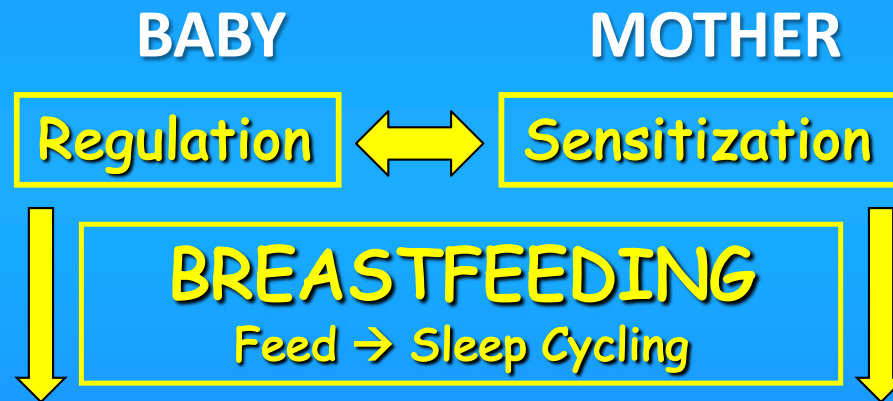
Nurturescience now engulfed or  
embedded in current neuroscience  
paradigms,

Needs dissecting out →



# NURTURESCIENCE

3 primary occupations:



CONNECTING  
BREASTFEEDING  
SLEEPING

# Comparison of nurturescience and neuroscience

	<b>NURTURESCIENCE</b>	<b>NEUROSCIENCE</b>
<b>Key time period</b>	Perinatal, conception to birth to 1 month	1 month – 3 years (ECD)

→ First 1000 days

Early Childhood  
Development

# Comparison of nurturescience and neuroscience

	NURTURESCIENCE	NEUROSCIENCE
Key time period	Perinatal, conception to birth to 1 month	1 month – 3 years (ECD)

**Immediate**

**AT BIRTH**

First 1000 seconds (1<sup>st</sup> hour)

→ First 1000 days

TRANSITION  
MICROBIOTA  
SENSITISATION  
Early Childhood  
Development

# Comparison of nurturescience and neuroscience

	NURTURESCIENCE	NEUROSCIENCE
Key time period	Perinatal, conception to birth to 1 month	1 month – 3 years (ECD)

## Immediate

## AT BIRTH

First 1000 seconds (1<sup>st</sup> hour)

First 1000 minutes (1<sup>st</sup> day)

First 1000 hours (6 weeks)

TRANSITION

REGULATION

CONNECTION

SUCKLING / BREAST

CONSOLIDATION

# Comparison of nurturescience and neuroscience

	NURTURESCIENCE	NEUROSCIENCE
Key time period	Perinatal, conception to birth to 1 month	1 month – 3 years (ECD)

**Immediate**

**AT BIRTH**

First 1000 seconds (1<sup>st</sup> hour)

First 1000 minutes (1<sup>st</sup> day)

First 1000 hours (6 weeks)

→ First 1000 days

TRANSITION

CONNECTION

CONSOLIDATION

Early Childhood

Development

# Comparison of nurturescience and neuroscience

	<b>NURTURESCIENCE</b>	<b>NEUROSCIENCE</b>
<b>Key time period</b>	Perinatal, conception to birth to 1 month	1 month – 3 years (ECD)
	First 1000 minutes	First 1000 days
<b>ANS purpose</b>	HOMEORHESIS	HOMEOSTASIS

# REGULATION vs STIMULATION

Expected vs Unexpected  
Ecologic salience vs Potential threat  
Resource growth vs threat readiness

OXYTOCIN vs CORTISOL  
HOMEORHESIS vs HOMEOSTASIS  
MOTHER vs OTHER

Resilience

HEALTH

DISEASE

# Comparison of nurturescience and neuroscience

	NURTURESCIENCE	NEUROSCIENCE
Key time period	Perinatal, conception to birth to 1 month	1 month – 3 years (ECD)
Emotions Regulatory mechanism	Viscera / ANS / limbic brain	Limbic brain / neocortex
	Maternal regulation then co-regulation	Self-regulation (within self)
	Open	self)

**REGULATION vs STIMULATION**

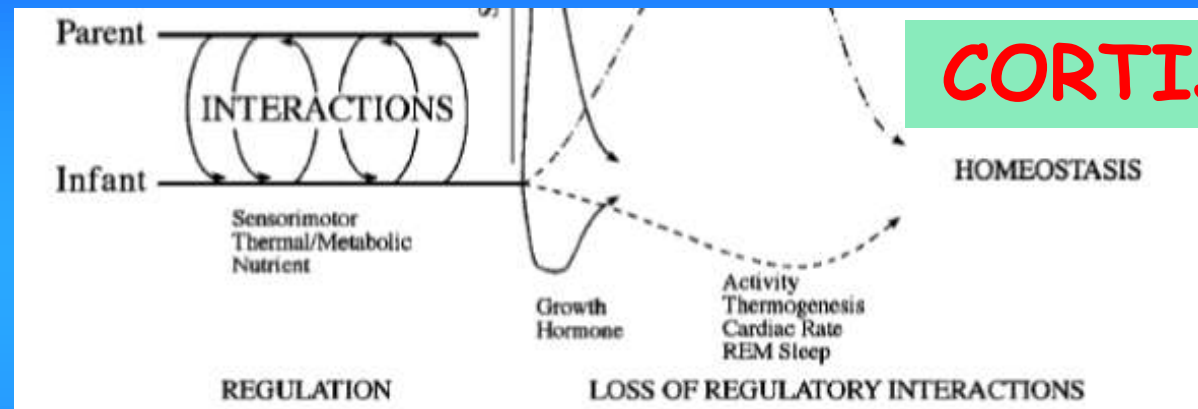
Expected vs Unexpected  
 Ecologic salience vs Potential threat  
 Resource growth vs threat readiness

OXYTOCIN vs CORTISOL  
 HOMEORHESIS vs HOMEOSTASIS  
 MOTHER vs OTHER



# Comparison of nurturescience and neuroscience

	NURTURESCIENCE	NEUROSCIENCE
Key time period	Perinatal, conception to birth to 1 month	1 month – 3 years (ECD)
Emotions Regulatory mechanism	Viscera / ANS / limbic brain	Limbic brain / neocortex
	Maternal regulation then co-regulation	Self-regulation (within self)
	Open feedback loop (with others)	Closed feed-back loop (within self)



# Comparison of nurturescience and neuroscience

	<b>NURTURESCIENCE</b>	<b>NEUROSCIENCE</b>
<b>Key time period</b>	Perinatal, conception to birth to 1 month	1 month – 3 years (ECD)
	First 1000 minutes	First 1000 days
<b>ANS purpose</b>	HOMEORHESIS	HOMEOSTASIS
	Dyadic / family (plural)	Individual (singular)
	Dynamic systems theory	Reductionistic logic

# Comparison of nurturescience and neuroscience

	NURTURESCIENCE	NEUROSCIENCE
	Dyadic / family (plural)	Individual (singular)
	Dynamic systems theory	Reductionistic logic

**Necessary,**

Randomized controlled trials (RCT)  
Evidence Based Medicine (EBM)

# Comparison of nurturescience and neuroscience

	NURTURESCIENCE	NEUROSCIENCE
	Dyadic / family (plural)	Individual (singular)
	Dynamic systems theory	Reductionistic logic

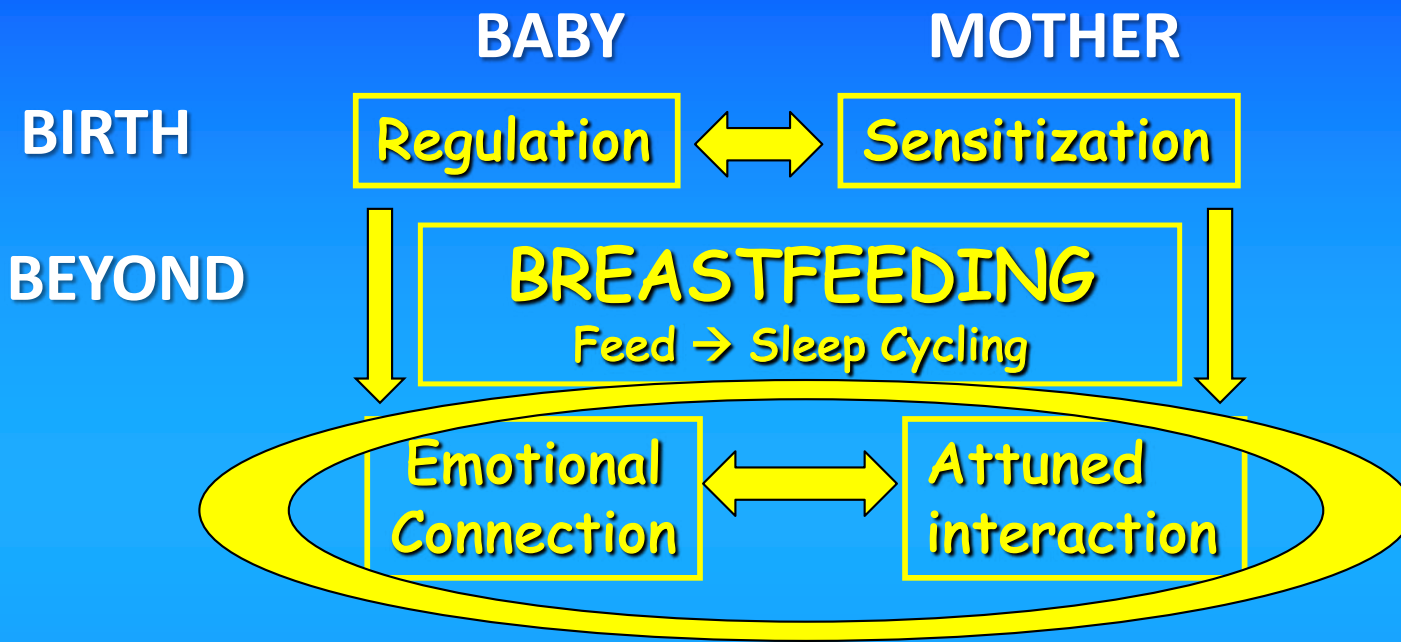
**Necessary,  
but  
not sufficient**

Randomized controlled trials (RCT)  
Evidence Based Medicine (EBM)

"Womb ecology becomes world ecology."

# Comparison of nurturescience and neuroscience

	<b>NURTURESCIENCE</b>	<b>NEUROSCIENCE</b>
<b>Key time period</b>	Perinatal, conception to birth to 1 month	1 month – 3 years (ECD)
	First 1000 minutes	First 1000 days
<b>ANS purpose</b>	HOMEORHESIS	HOMEOSTASIS
	Dyadic / family (plural)	Individual (singular)
	Dynamic systems theory	Reductionistic logic
<b>KEY OUT-COME</b>	<b>CONNECTION RESILIENCE</b>	<b>ATTACHMENT COGNITION</b>



<b>KEY OUT- COME</b>	<b>CONNECTION RESILIENCE</b>	<b>ATTACHMENT COGNITION</b>
------------------------------	----------------------------------	---------------------------------

**Table 1: Comparison of nurturescience and neuroscience**

❏	<i>Nurturescience</i> ❏	<i>Neuroscience</i> .....❏
<b>Relevant time period</b> ❏	Perinatal, conception to birth to 1 year❏ ...First 1000 minutes❏	1 month – 3 years (ECD)❏ ...First 1000 days❏
❏	Critical periods (brief)❏	Brain maturation, sensitive periods (long)❏
<b>Autonomic objective</b> ❏	Homeorhesis❏	Homeostasis; Allostasis❏
<b>Emotions regulatory mechanism</b> ❏	Viscera / ANS / Limbic❏	Limbic brain / neocortex...❏
	Fetus/neonate acutely aware of threat❏	Infant and toddler develop threat awareness❏
	Co-regulation, buffering of stress❏	Self-regulation of stress (within self)❏
<b>Emotional learning mechanism</b> ❏	ANS primary influence on behavior❏	CNS primary influence on behavior❏
	Autonomic learning or conditioning❏	CNS conditioning, operant❏
❏	Fetal & neonatal connectome❏	Prolonged infant brain maturation❏
❏	Maternal peripartum neuroplasticity❏	Maternal learning of competence❏
❏	Open feedback loop (with others)❏	Closed feed-back loop (within self)❏
❏	Dyadic / family (plural)❏	Individual (singular)❏

<b>Theoretical roots</b> ∞	Dynamic systems theory, ecology ∞	Reductionistic logic, isolationist ∞
∞	Biology, ethology, anthropology ∞	Sociology (Maslow, Dunbar) ∞
∞	Physiology, polyvagal theory ∞	Psychology, ∞
∞	Epigenetics ∞	Genetics-Epigenetics ∞
∞	Epigenetic adaptation / maladaptation ∞	Toxic stress, allostatic load ∞
<b>Intervention targets</b> ∞	Boost parasympathetic, calming ¶ ANS and emotional behavior ∞	Counter-sympathetic, excitability ¶ CNS and cognition ∞
<b>KEY OUTCOMES</b> ∞	EMOTIONAL CONNECTION ¶ RESILIENCE ∞	ATTACHMENT ¶ COGNITION ∞
<b>KEY OBJECTIVES</b> ∞	RELATIONAL HEALTH ¶ Sociality ¶ Interdependence ∞	SELF-ACTUALIZATION (Maslow) ¶ Individualistic ¶ Independence ∞

Ref: Bergman et al, 2019





**Karolinska  
Institutet**

**Nurturescience program  
now planned for  
KAROLINSKA, Stockholm**



**NILS BERGMAN**

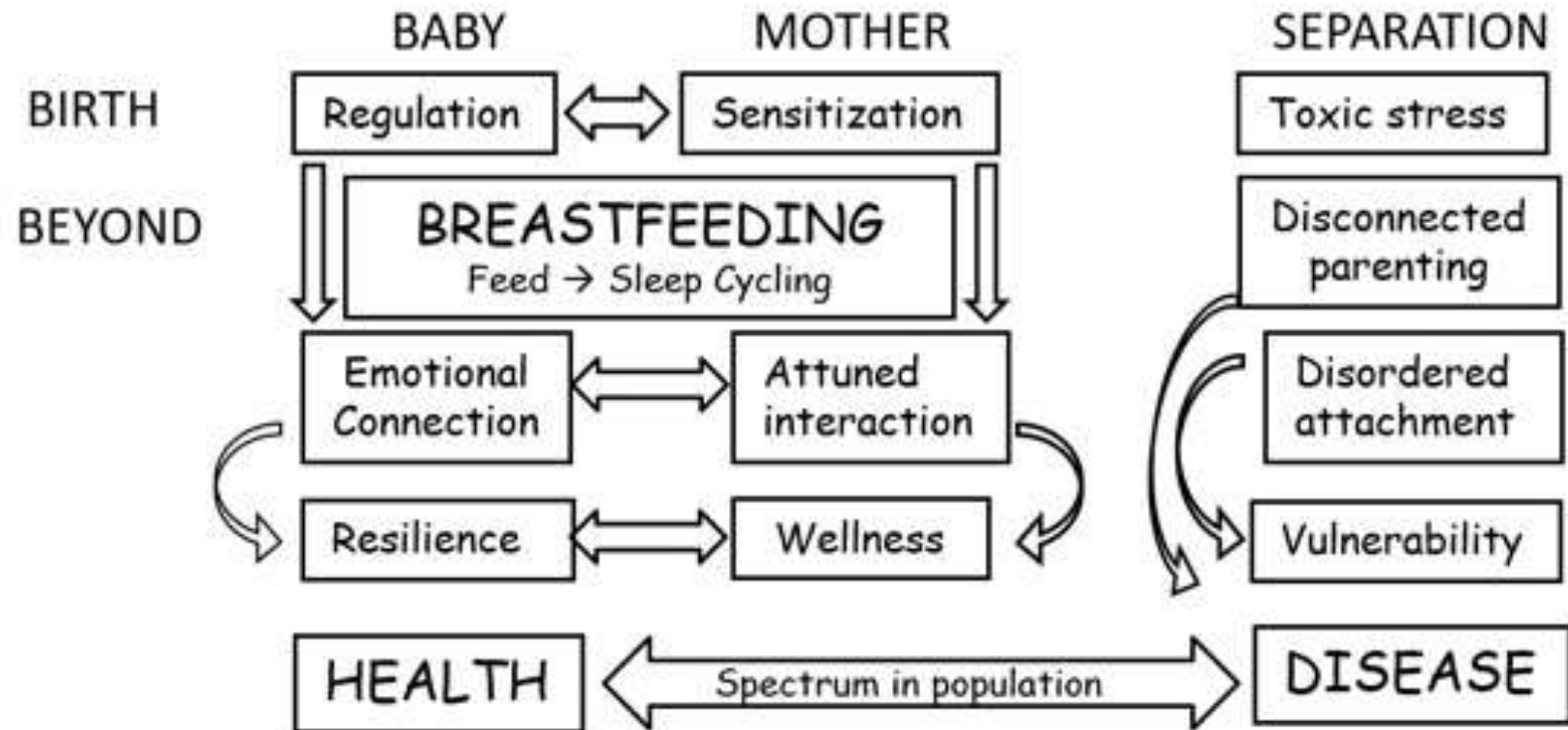


**ULRIKA ADEN**



**BJORN WESTRUP**

# NURTURESCIENCE



Ref: Bergman et al, 2019

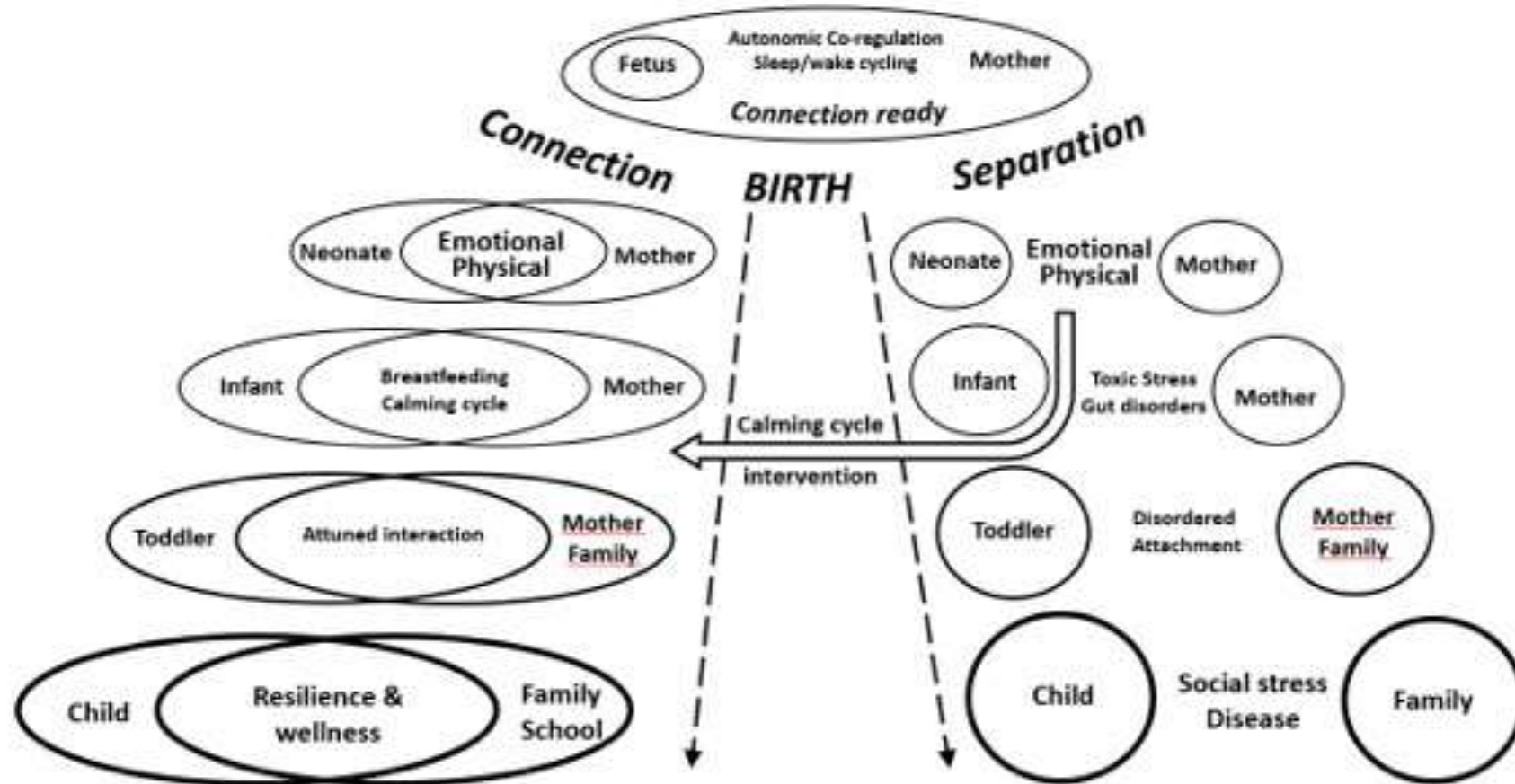


**MARTHA WELCH**



**Meyers, Hofer, Fifer, Ludwig etc**

# NURTURESCIENCE



Ref: Bergman et al, 2019

DOI: 10.1002/bdr2.1529

REVIEW ARTICLE

Birth Defects  
Research

THE TERATOLOGY  
SOCIETY  
1971, 1980

WILEY

# **Nurturescience versus neuroscience: A case for rethinking perinatal mother–infant behaviors and relationship**

**Nils J. Bergman<sup>1</sup> | Robert Ludwig<sup>2</sup> | Björn Westrup<sup>1</sup> | Martha Welch<sup>2,3,4</sup>**

DOI: 10.1002/bdr2.1530

REVIEW ARTICLE

Birth Defects  
Research

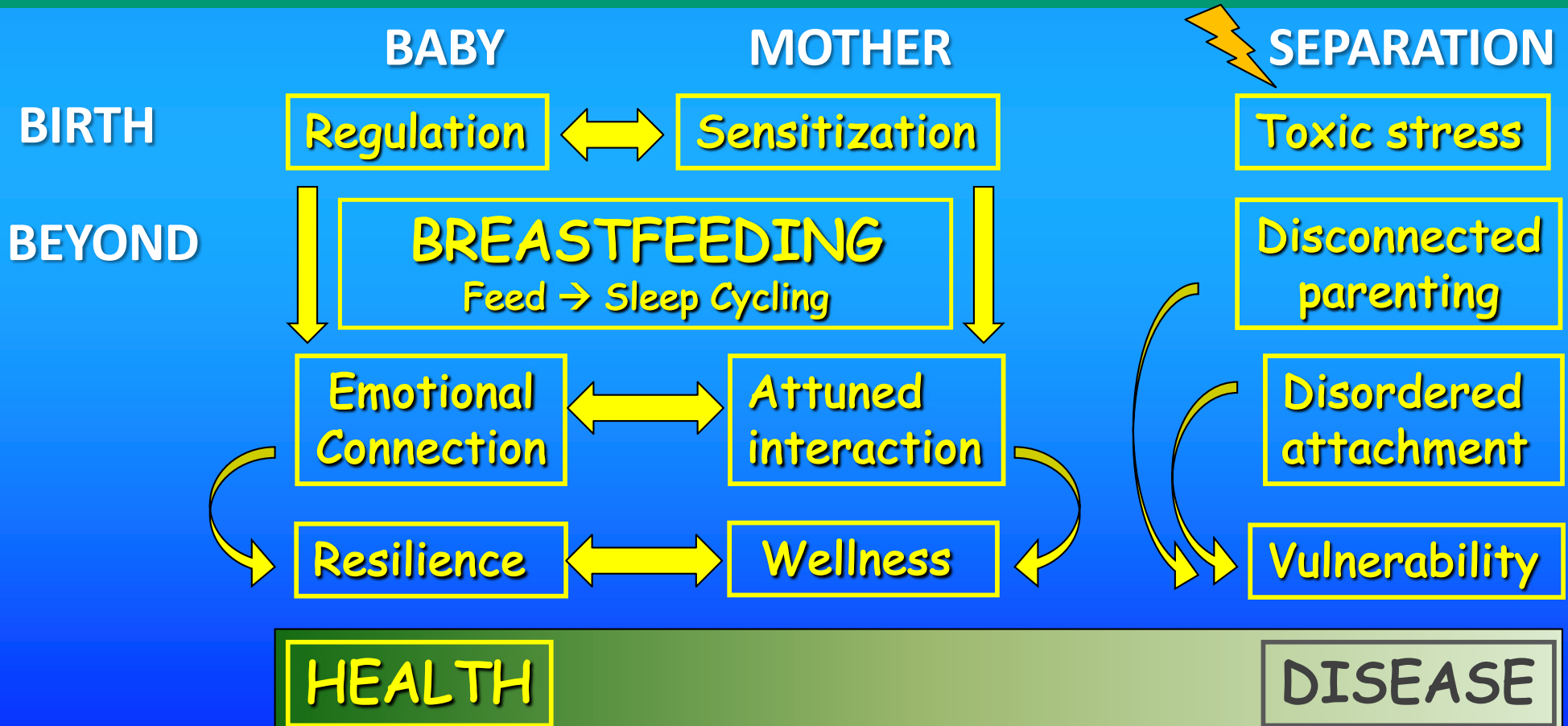
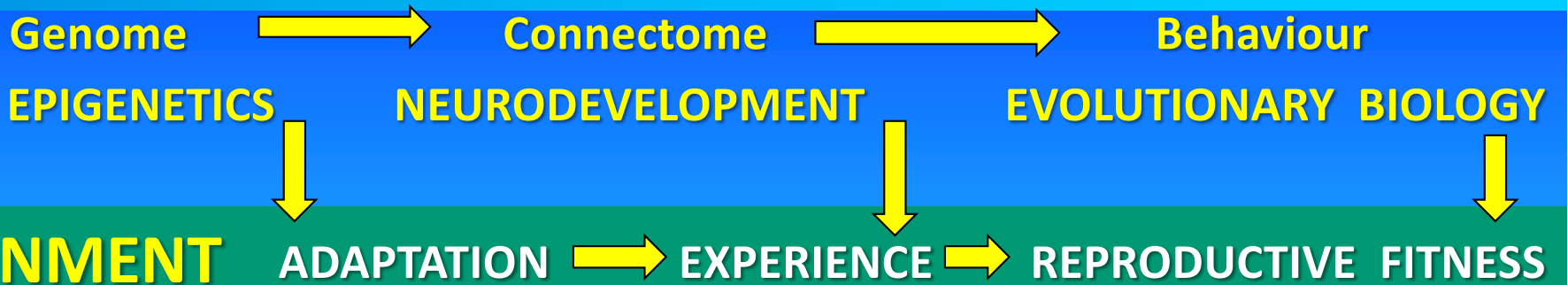
THE TERATOLOGY  
SOCIETY  
1971, 1980

WILEY

# **Birth practices: Maternal-neonate separation as a source of toxic stress**

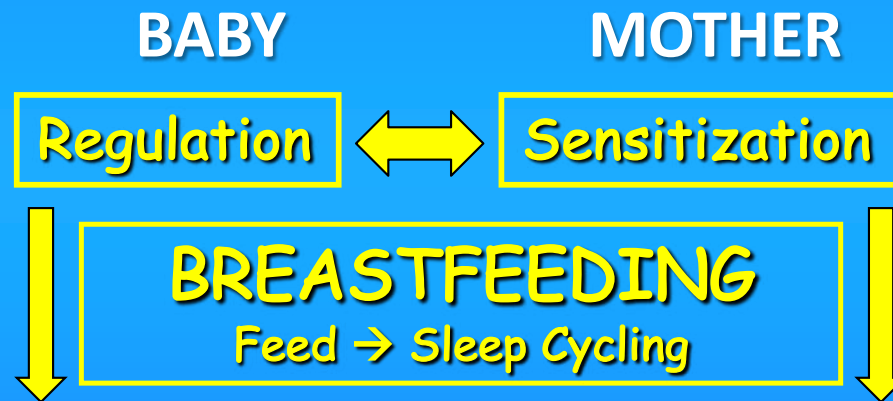
**Nils J Bergman**

# NURTURESCIENCE



# NURTURESCIENCE

3 primary occupations:



CONNECTING  
BREASTFEEDING  
SLEEPING

# 3 primary occupations:

BABY

MOTHER

Regulation

Sensitization



CONNECTING  
BREASTFEEDING  
SLEEPING



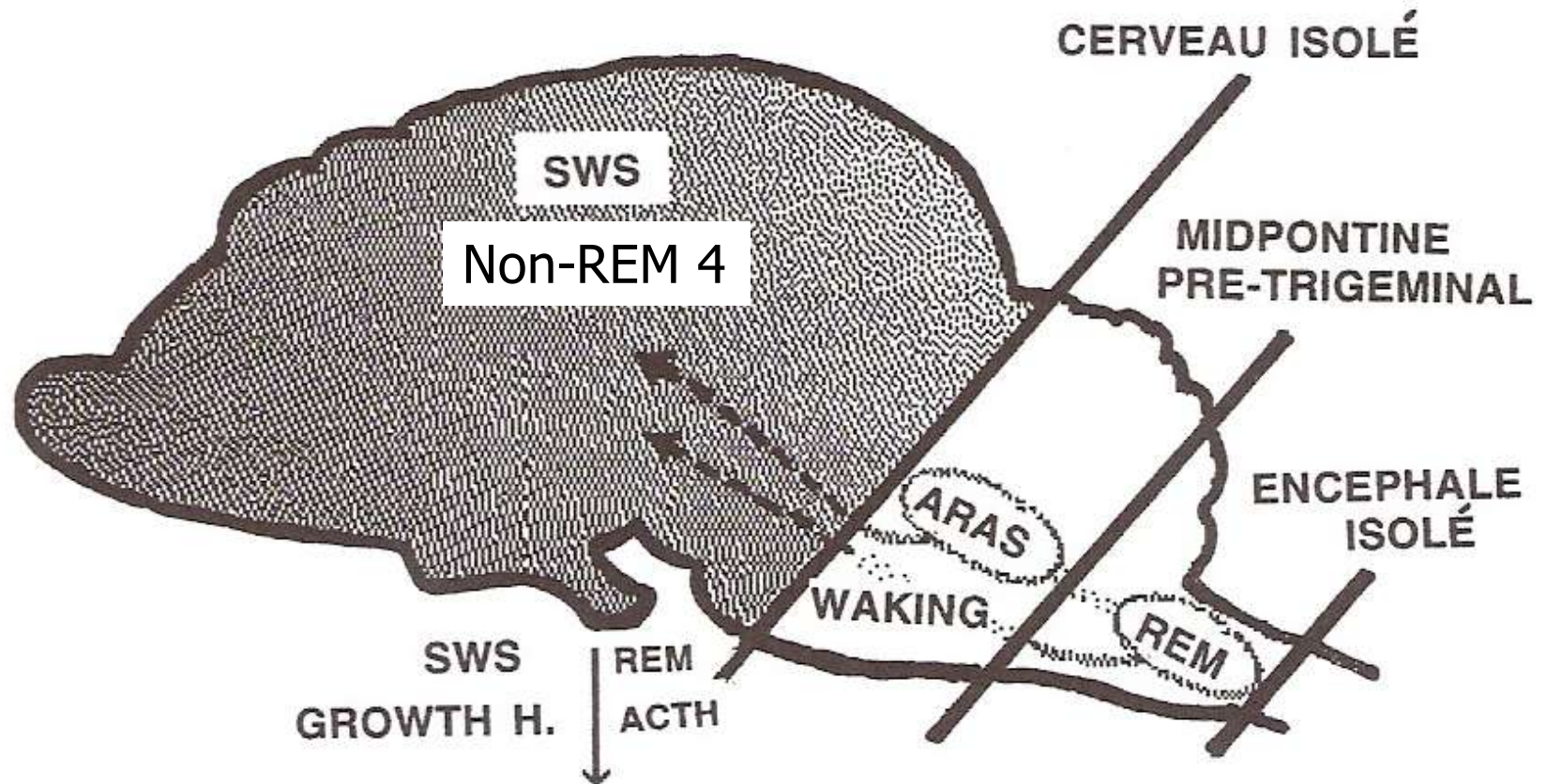
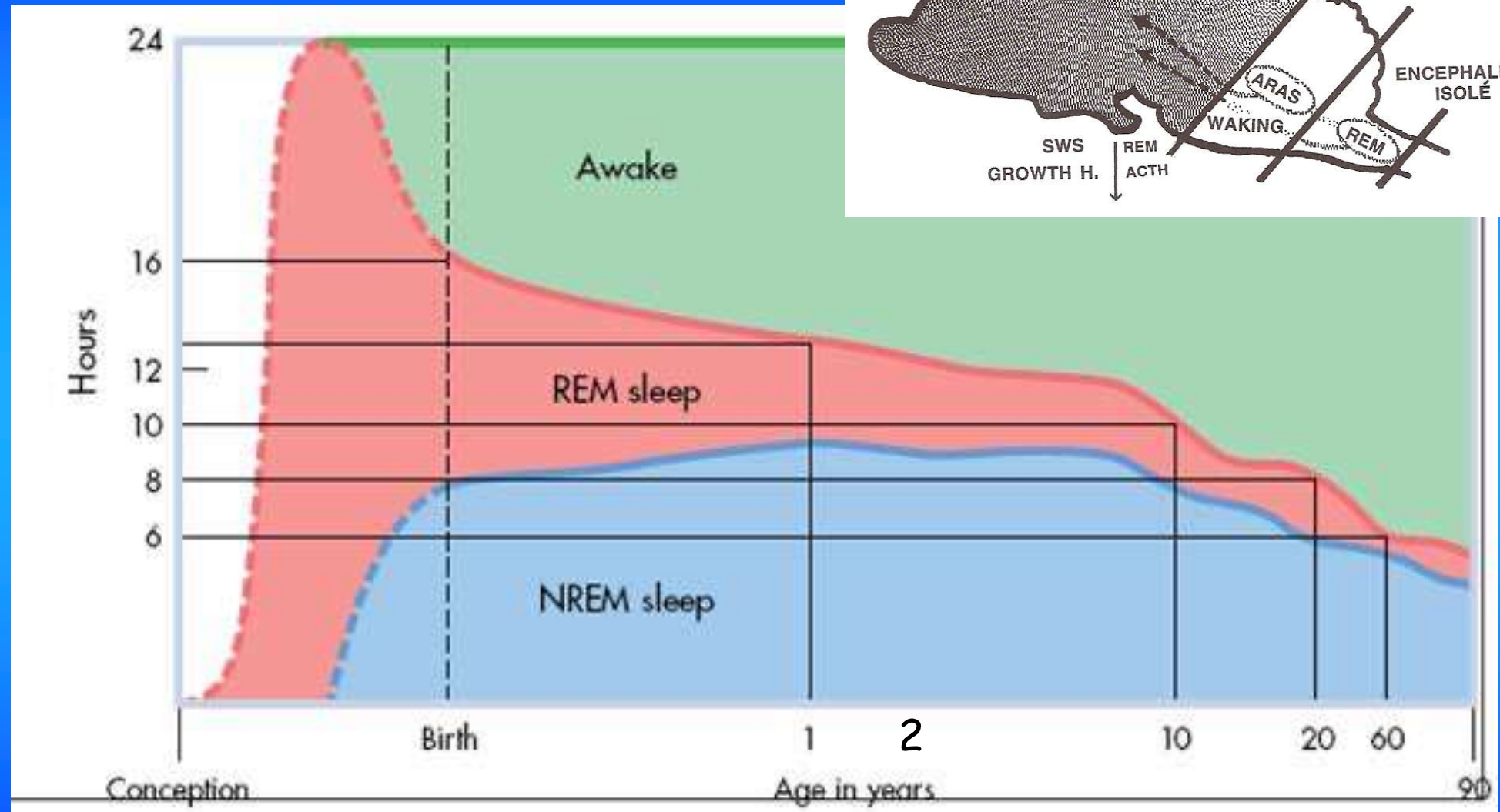
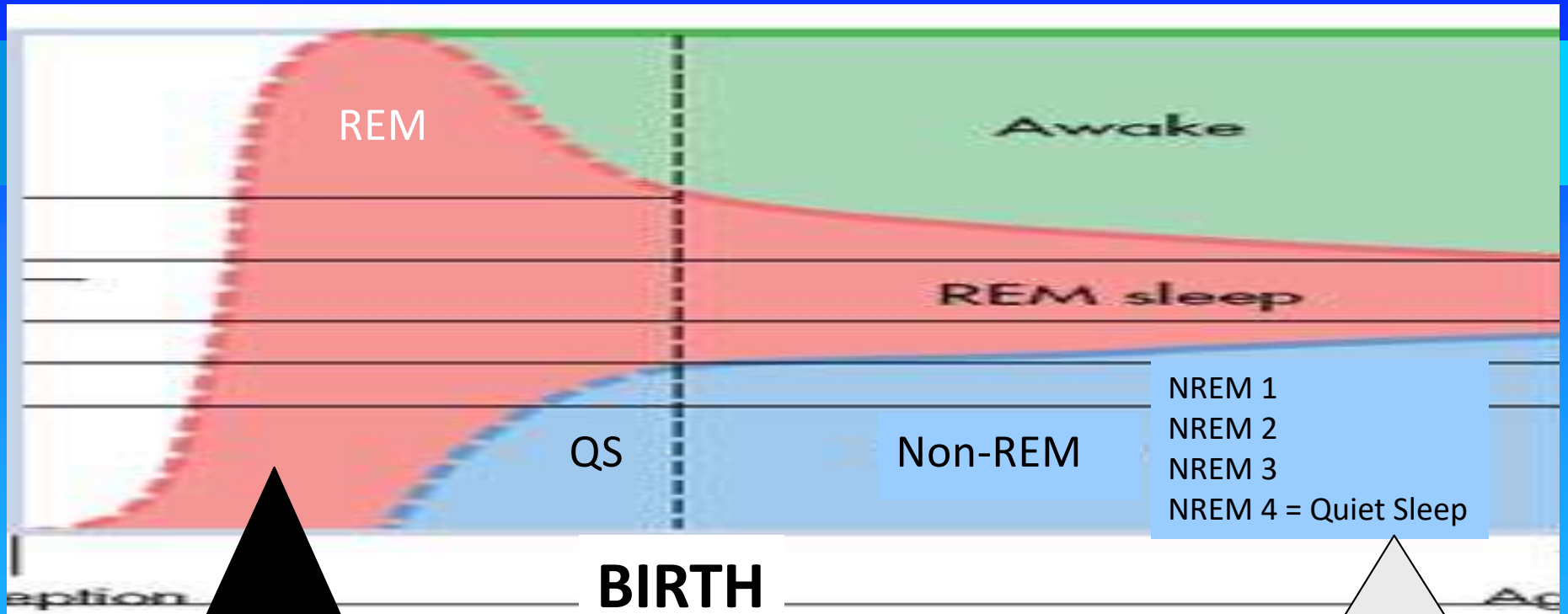


Figure 7.2. Overview of the types of brain transections that led to the general locations of major waking, SWS, and REM systems within the neuro-axis. For instance, with the midpontine pretrigeminal cut, waking and SWS were left in the forebrain, while the potential for REM was only manifested in neural and bodily systems below the cut. When the cut was slightly further rostral, through the midbrain (i.e., the *cerveau isolé* cut), the forebrain remained perpetually in the darkness of SWS, while tissue below the cut cycled between waking type arousal and activated sleep states. Also, note that growth hormone secretion from the pituitary occurs in conjunction to SWS episodes, while ACTH secretion is entrained to REM periods.

**Panksepp 1998**  
**Siegel 2005**



← 1<sup>st</sup> 1000 days →



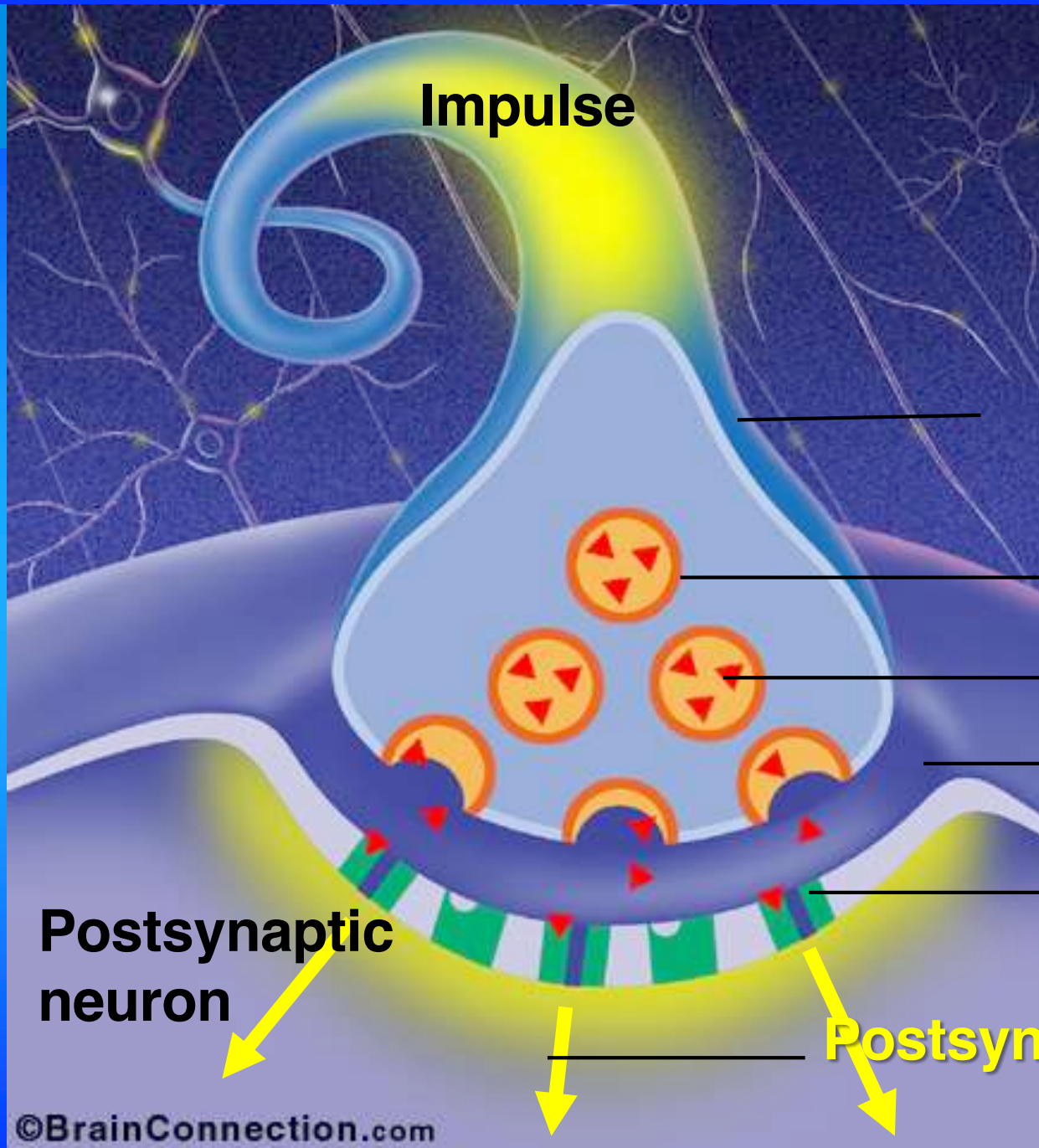
← 1<sup>st</sup> 270 days →

# fetal REM sleep

(or active sleep) seems to be particularly important to the developing organism



... spontaneous  
synchronous firing



**Impulse**

**Presynaptic neuron**

**Vesicle**

**Transmitters**

**Synaptic cleft**

**Receptors**

**Postsynaptic neuron**

**Postsynaptic activity**

SENSORY STIMULUS



synapse store chemical signal



chemical signal stronger



THRESHOLD →



EXEMPT from elimination  
(synapse stabilised)



PATHWAY

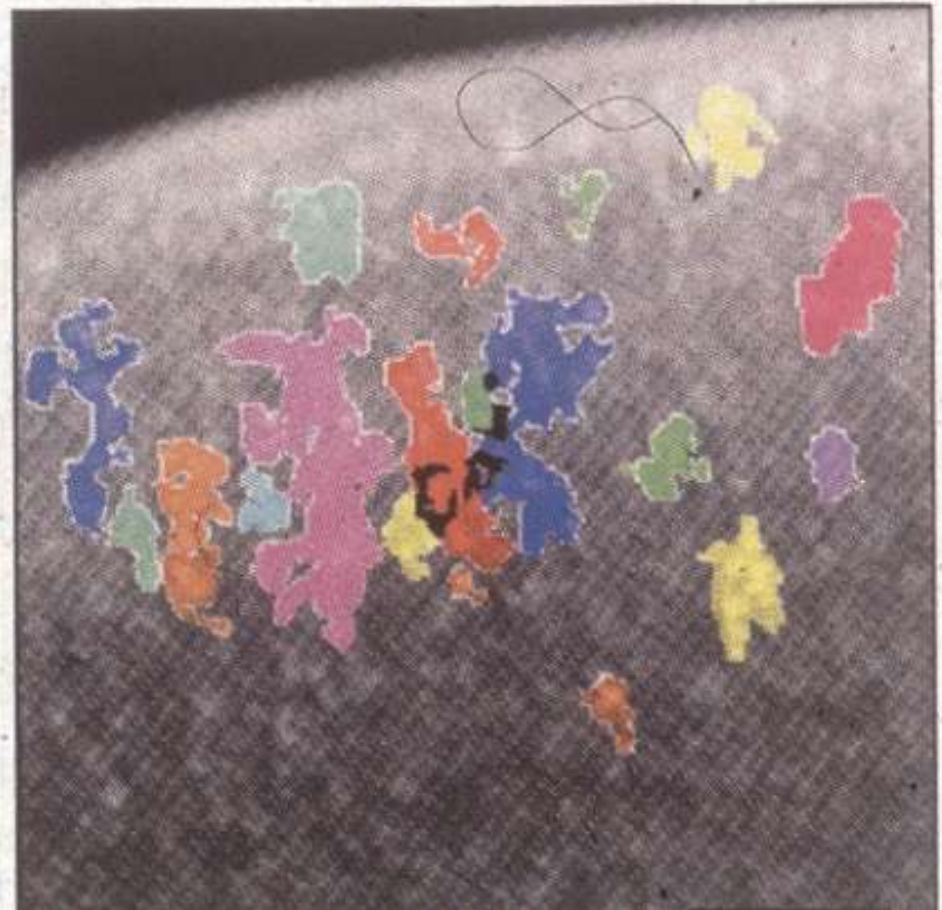
(Rima Shore 1997)

“Neurons that fire together wire together while those which don't, won't”  
*Hebb/Carla Shatz*

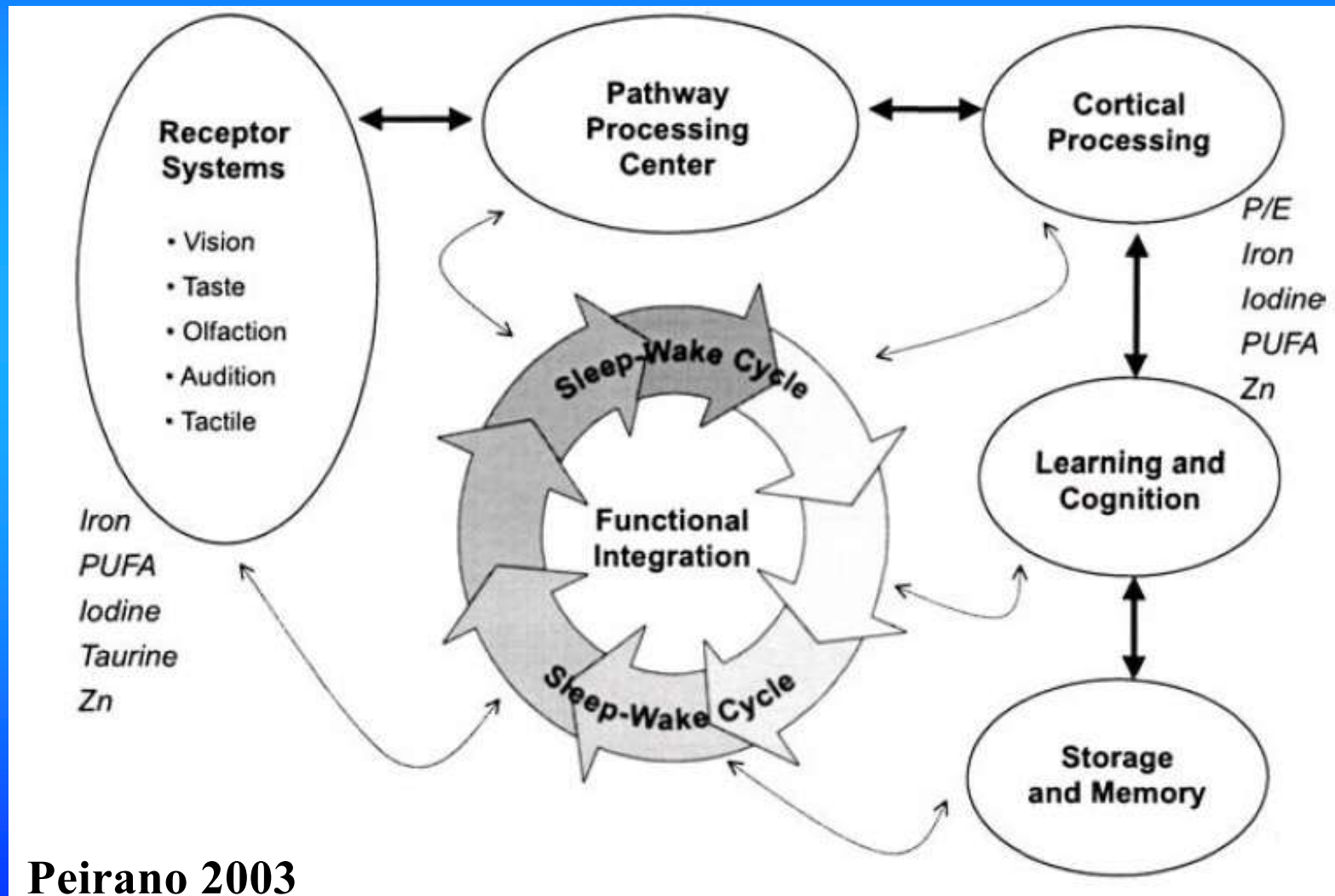
Retina



Cortex



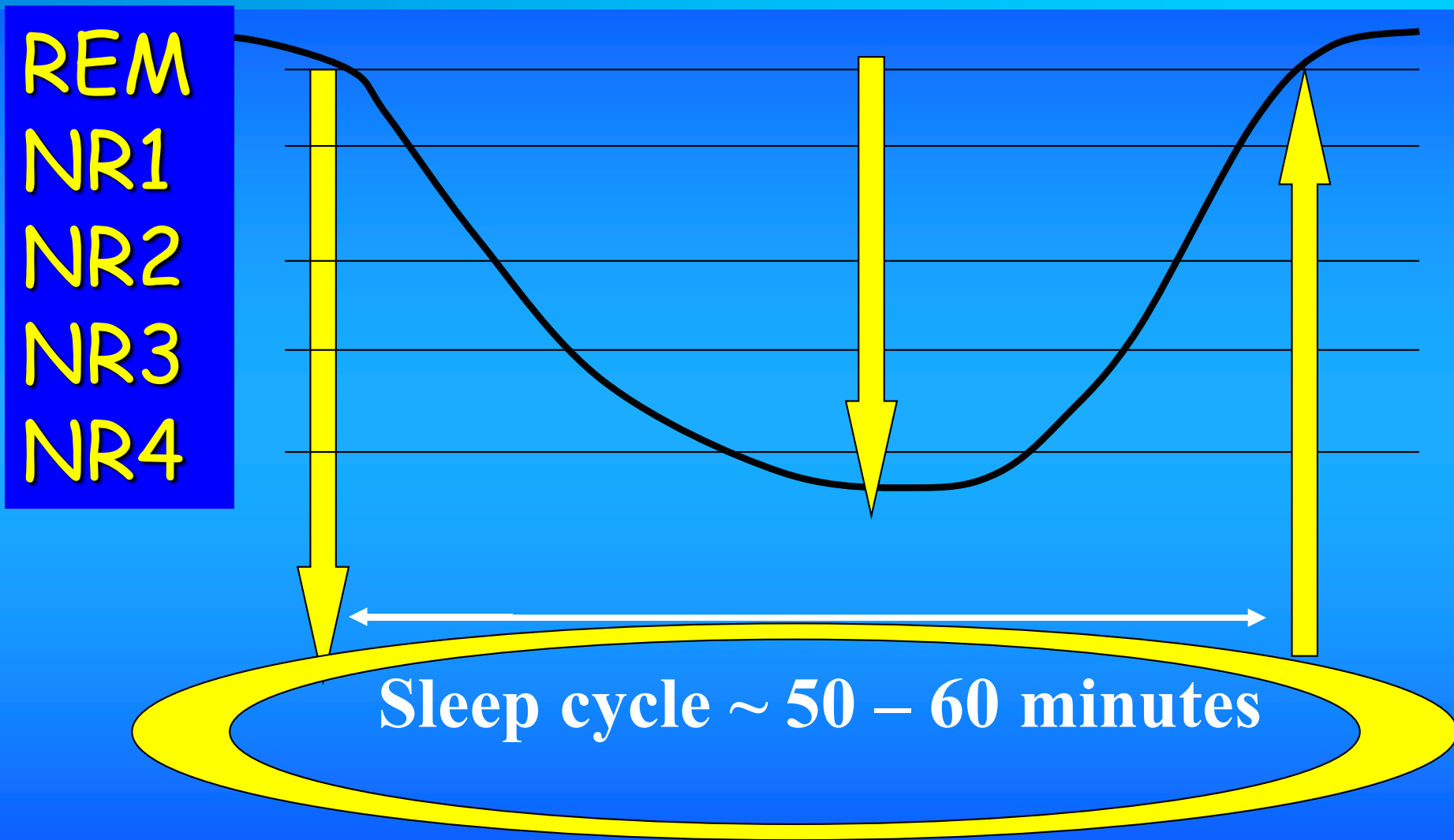
”Neurons that fire together wire together while those which don't, won't”  
*Hebb/Carla Shatz*



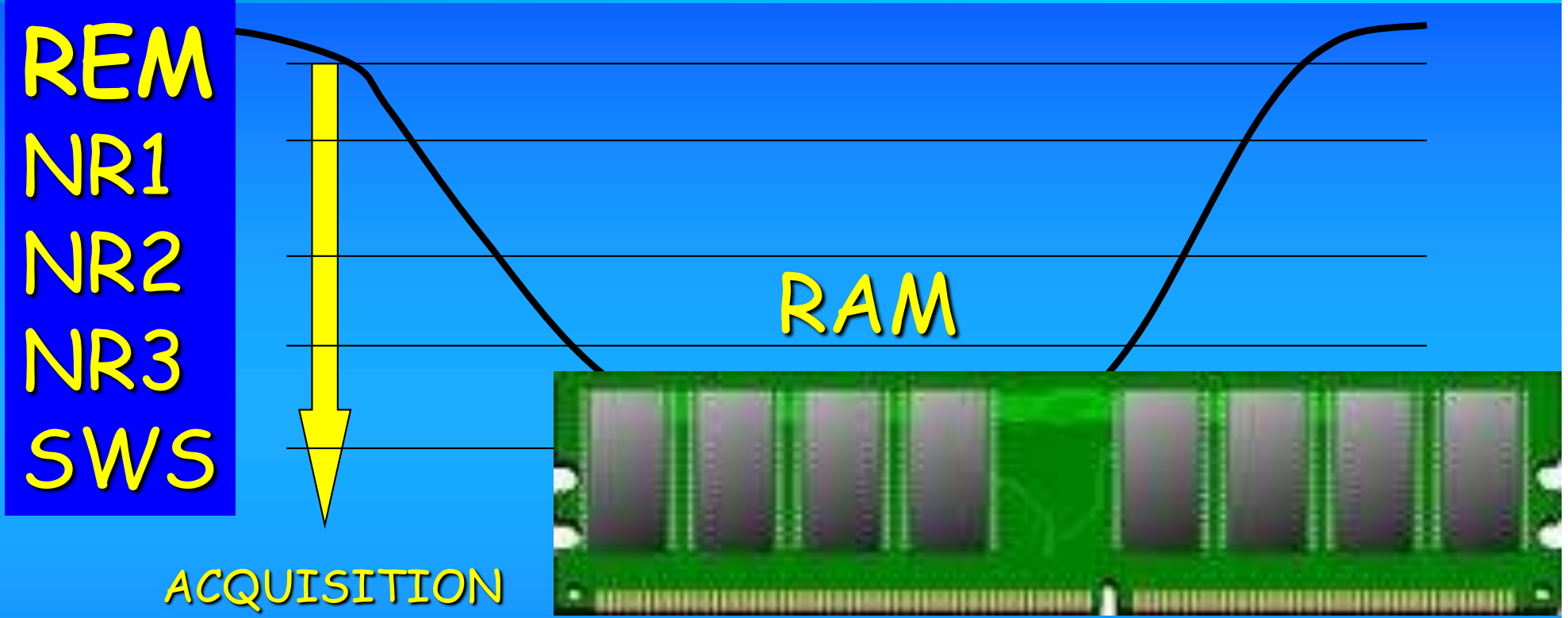
Peirano 2003



# BRAIN WIRING



# ACQUISITION



ACQUISITION

poly-sensory input  
short-term memory  
stored cortex

Awake and REM

Neocortex

consciousness

short term memory

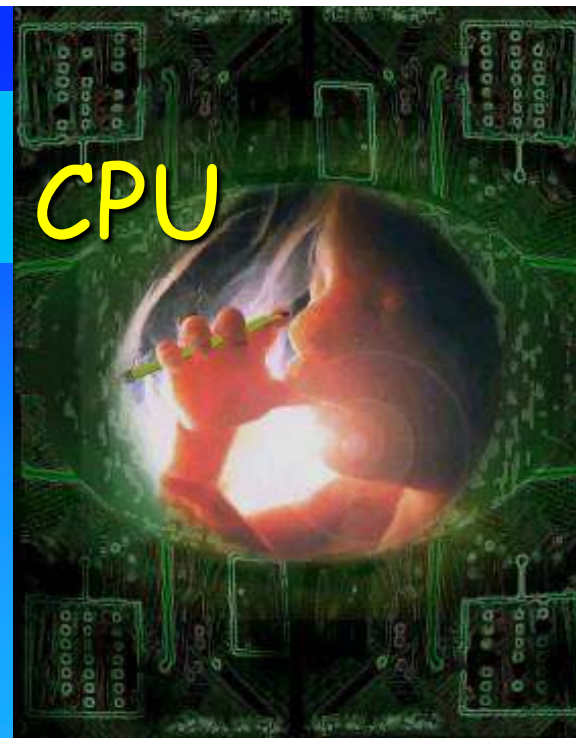
GPS



HIPPOCAMPUS

Memory function  
and spatial code

CPU



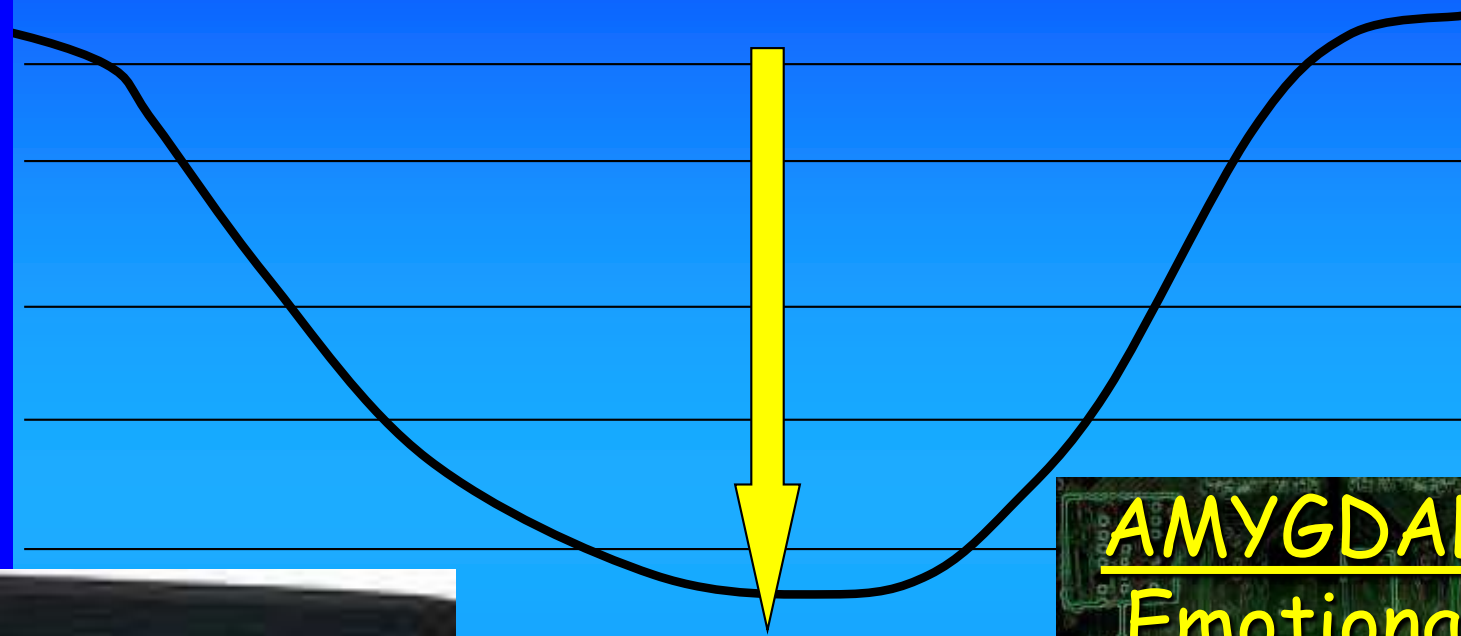
AMYGDALA:

Emotional  
Processing  
Unit

# CONSOLIDATION

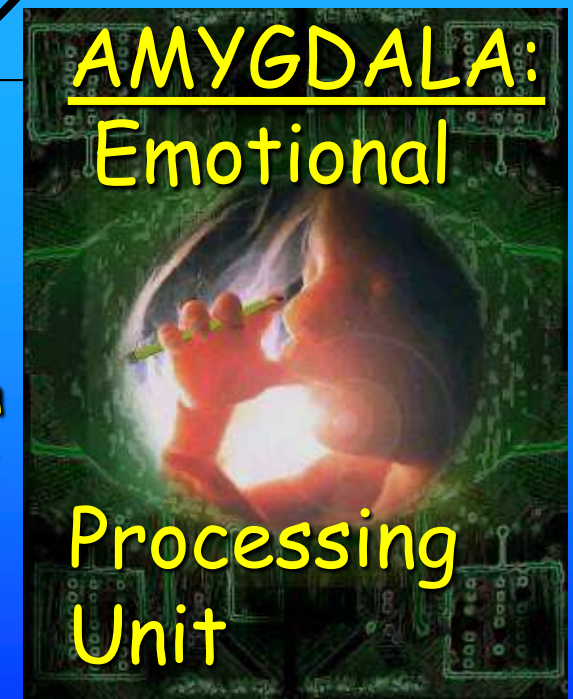
Amodio 2008

REM  
NR1  
NR2  
NR3  
SWS



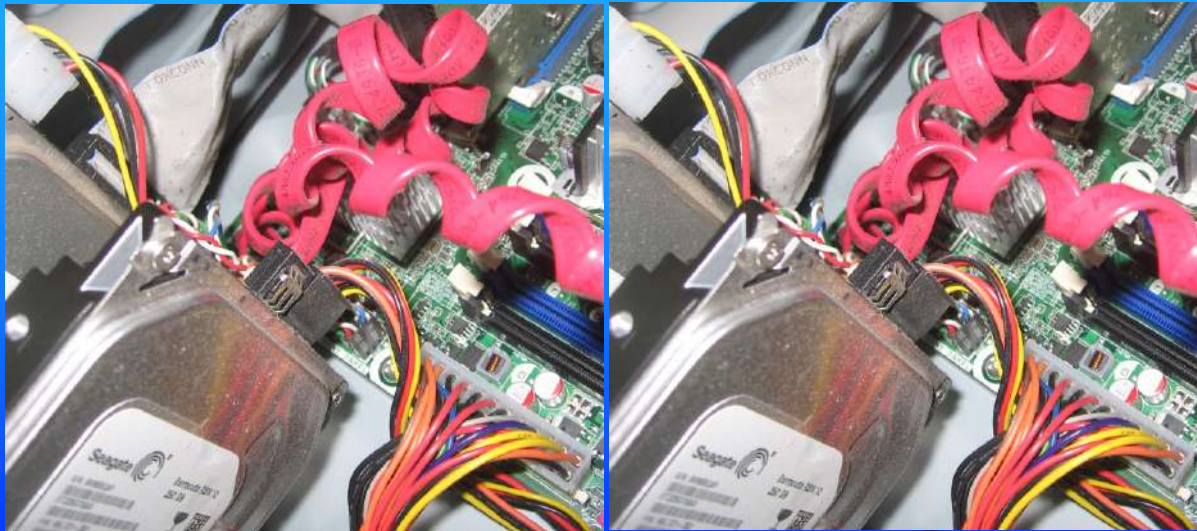
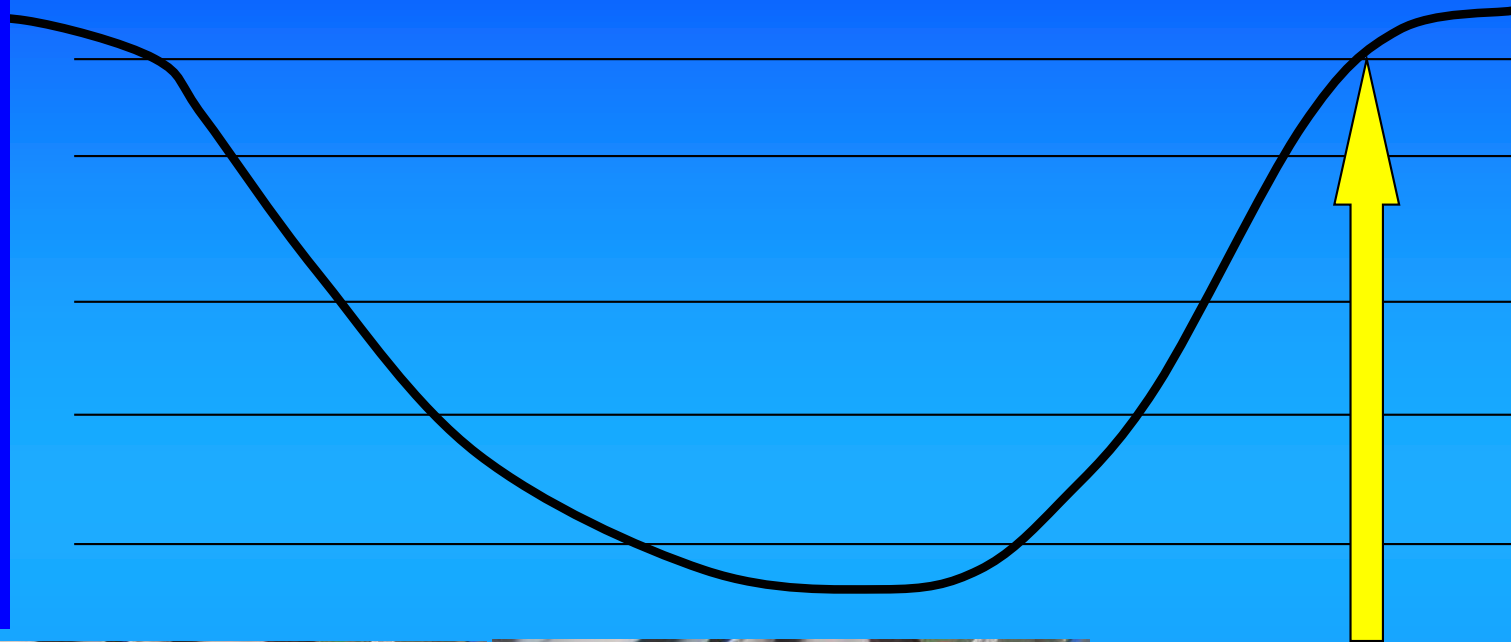
## CONSOLIDATION

transfer information  
"SNR" strong signals  
amygdala /  
hippocampus  
NREM stage 4



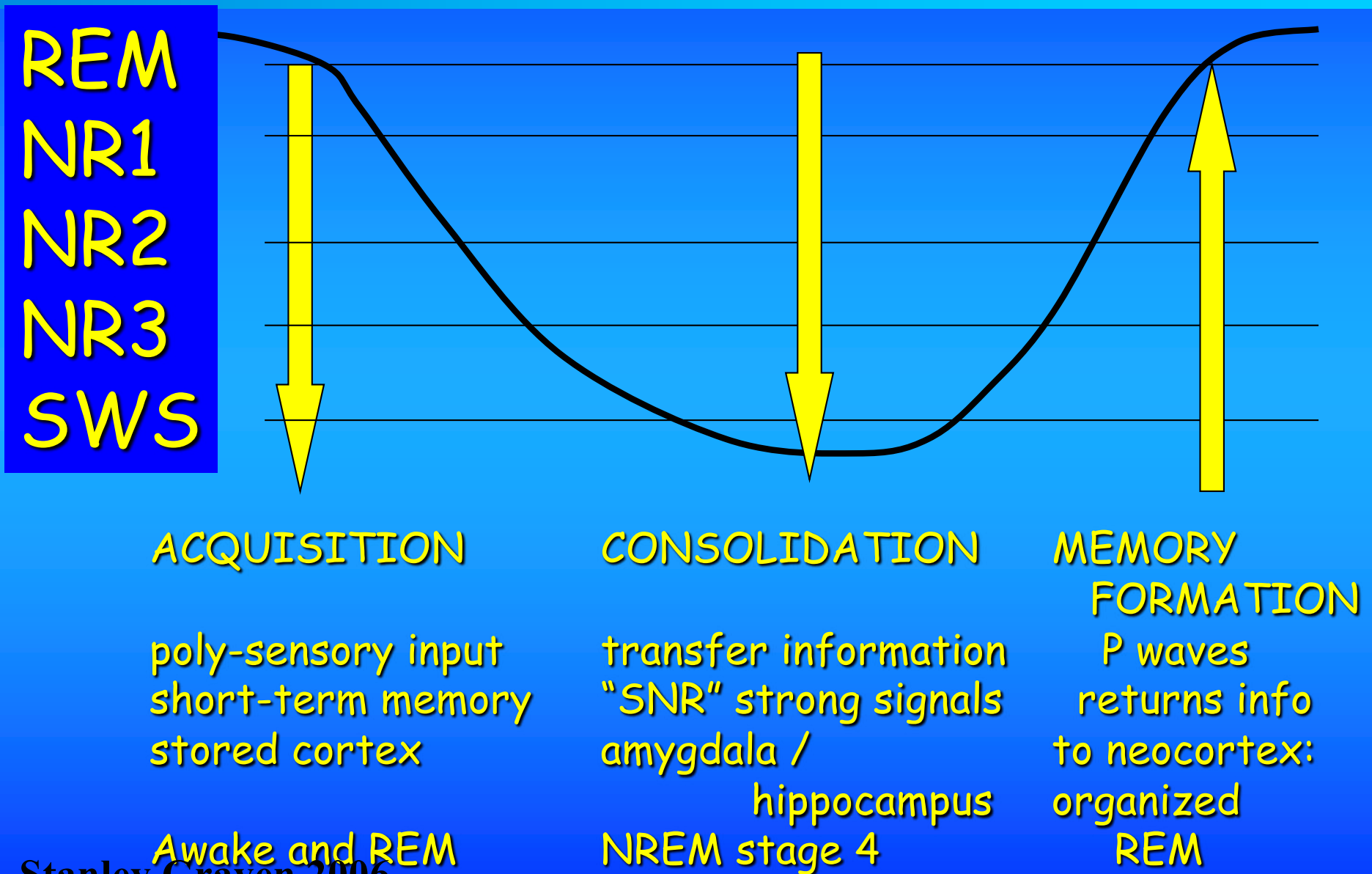
# MEMORY FORMATION

REM  
NR1  
NR2  
NR3  
SWS



MEMORY  
FORMATION  
P waves  
returns info  
to neocortex:  
organized  
REM

# BRAIN WIRING



Stanley Graven 2006

# Sleep, Hormones, and Memory

Jan Born, PhD<sup>a,\*</sup>, Ullrich Wagner, PhD<sup>b</sup>

Obstet Gynecol Clin N Am 36 (2009) 809–829



**Sleep**



This article follows the hypothesis that a primary function of sleep pertains to the consolidation of memory. In recent years, this view has received substantial support from a rapidly growing number of experiments performed in various species and at different levels of behavioral, cellular, and molecular analysis.<sup>2–7</sup>

In adult:  
sleep pertains  
to memory

# Sleep, Hormones, and Memory

Jan Born, PhD<sup>a,\*</sup>, Ullrich Wagner, PhD<sup>b</sup>

Obstet Gynecol Clin N Am 36 (2009) 809–829



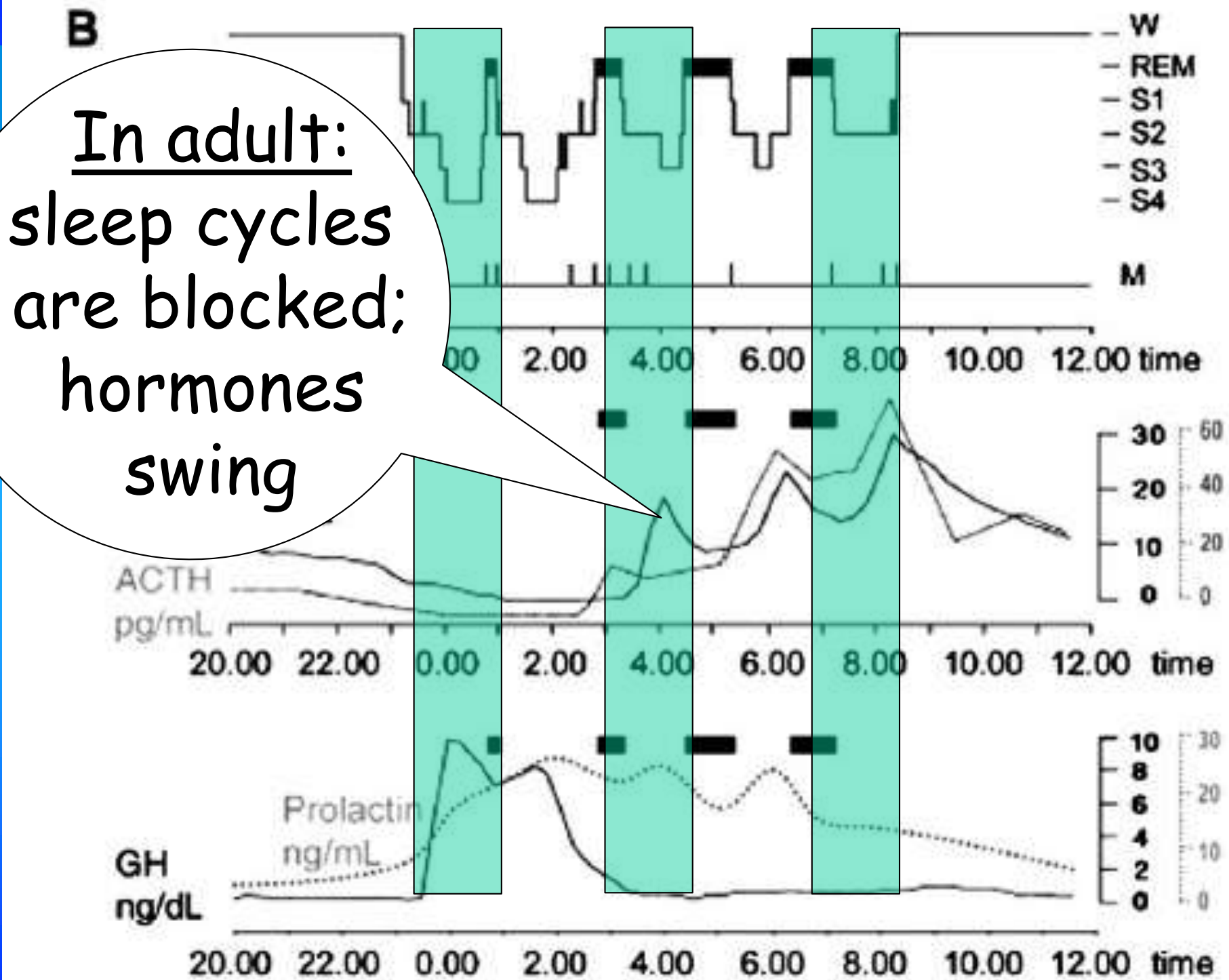
Sleep

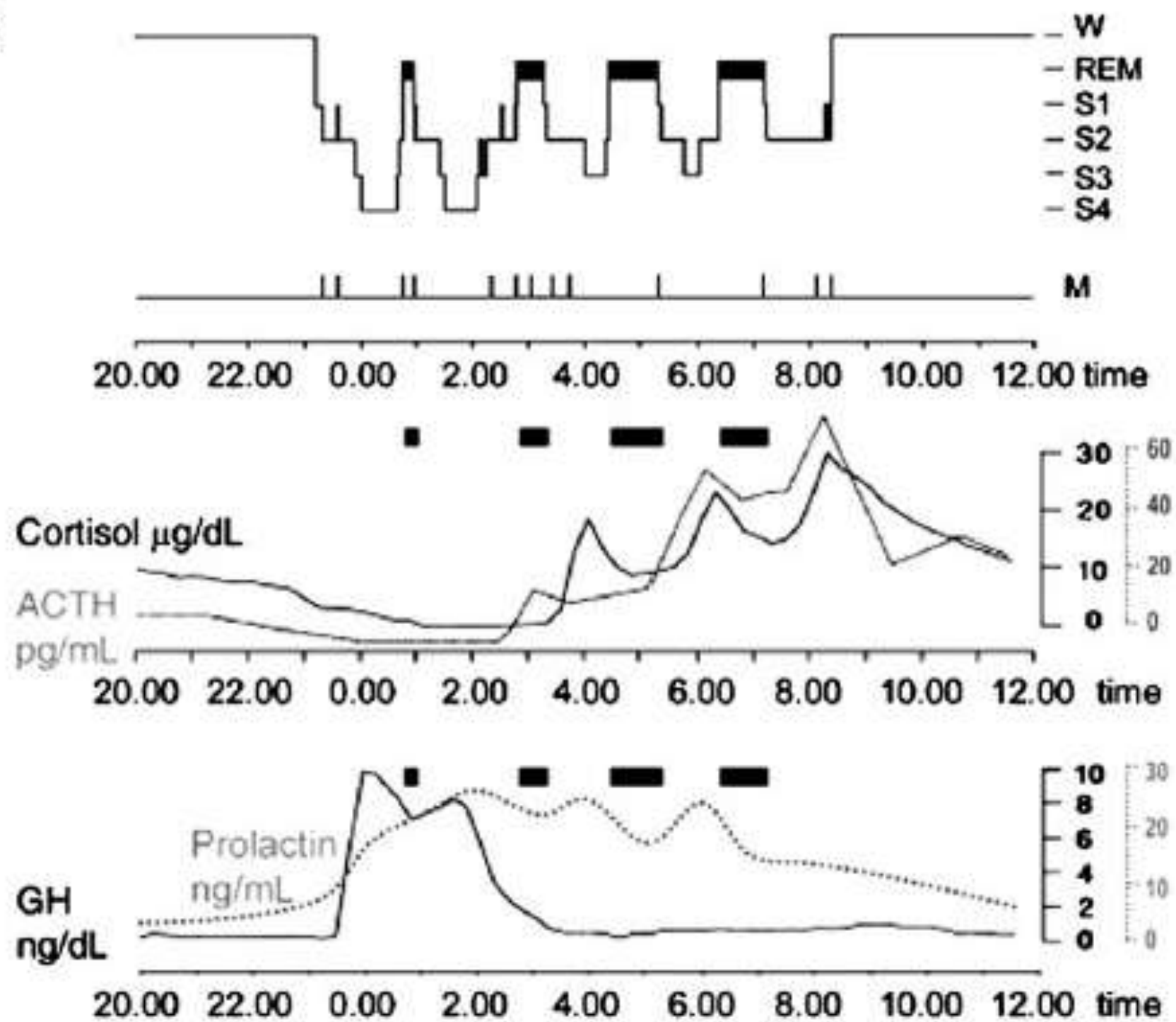
This article follows the hypothesis that a primary function of sleep pertains to the consolidation of memory. In recent years, this view has received substantial support from a rapidly growing number of experiments performed in various species and at different levels of behavioral, neural, cellular, and molecular analysis.<sup>2–7</sup>

In adult:  
sleep pertains  
to memory

In child:  
neurodevelopment  
(brain wiring)  
1<sup>st</sup> 1000 days





**B**

# Memory consolidation during sleep: Interactive effects of sleep stages and HPA regulation

*Stress*, January 2008; 11(1): 28–41

ULLRICH WAGNER & JAN BORN

SWS makes  
fact and  
episode  
(declarative)  
memory

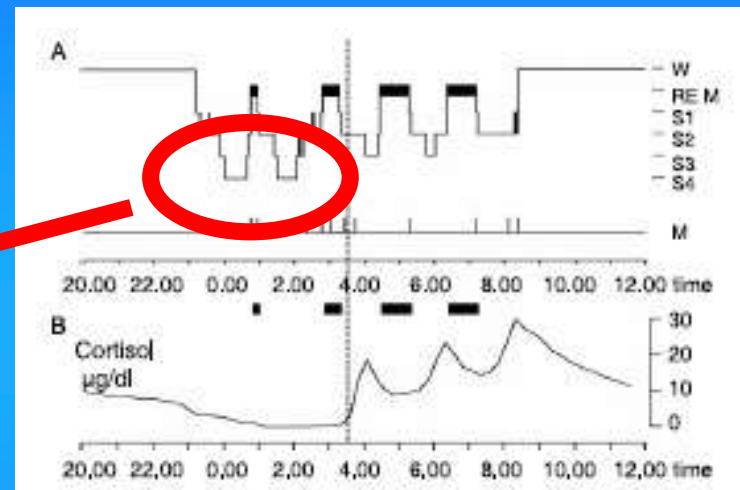


Figure 1. (A) Sleep profile (hypnogram) for a typical night of sleep, showing the nocturnal sequence of electrophysiologically defined sleep stages (REM sleep and Non-REM sleep stages S1–S4). The deepest sleep stages S3 and S4 indicate SWS, characterized by slowly oscillating activity (<4 Hz) in the EEG. SWS and REM sleep are not equally distributed across the night. While sleep in the first half of the night (left from vertical line) is dominated by SWS, sleep in the second half of the night (right from vertical line) contains high amounts of REM sleep. W, wake; M, movement activity. (B) Due to circadian and sleep-dependent regulation (see text), cortisol release is strongly suppressed during early sleep, but increases distinctly during late sleep, reaching a maximum in the early morning hours. Accordingly, SWS-dominated early sleep is accompanied by minimal levels of circulating cortisol, while basal cortisol levels are high during REM sleep-dominated late sleep. These changing patterns of electrophysiological and endocrine activity across nocturnal sleep interactively affect memory consolidation.

# Memory consolidation during sleep: Interactive effects of sleep stages and HPA regulation

*Stress*, January 2008; 11(1): 28–41

ULLRICH WAGNER & JAN BORN

CORTISOL

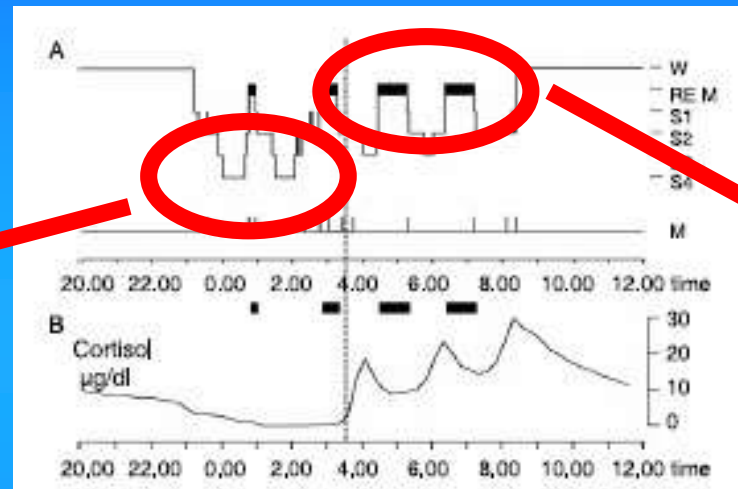


Figure 1. (A) Sleep profile (hypnogram) for a typical night of sleep, showing the nocturnal sequence of electrophysiologically defined sleep stages (REM sleep and Non-REM sleep stages S1–S4). The deepest sleep stages S3 and S4 indicate SWS, characterized by slowly oscillating activity (<4 Hz) in the EEG. SWS and REM sleep are not equally distributed across the night. While sleep in the first half of the night (left from vertical line) is dominated by SWS, sleep in the second half of the night (right from vertical line) contains high amounts of REM sleep. W, wake; M, movement activity. (B) Due to circadian and sleep-dependent regulation (see text), cortisol release is strongly suppressed during early sleep, but increases distinctly during late sleep, reaching a maximum in the early morning hours. Accordingly, SWS-dominated early is accompanied by minimal levels of circulating cortisol, while basal cortisol levels are high during REM sleep-dominated late sleep. These changing patterns of electrophysiological and endocrine activity across nocturnal sleep interactively affect memory consolidation.

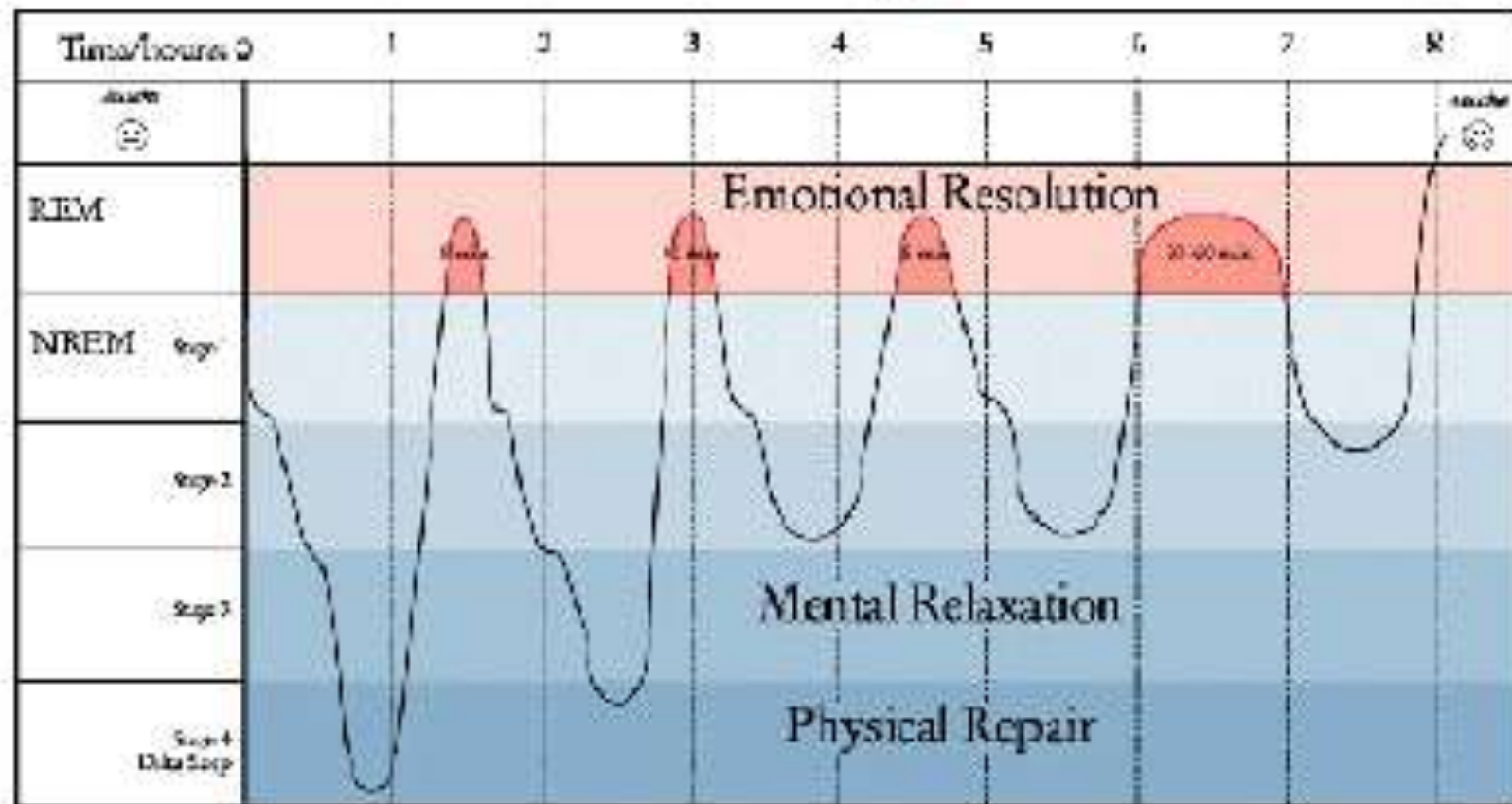
SWS makes fact and episode (declarative) memory

REM sleep makes emotional memory

Also skills

CORTISOL protects from negative embedding in REM

# The Natural Sleep Process

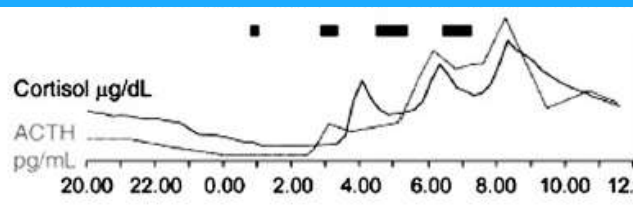


© 2004 by the author. All rights reserved.

# Joseph 2014

Arch Dis Child Fetal Neonatal Ed. 2014 Sep 22. pii: fetalneonatal-2014-306104.  
doi: 10.1136/archdischild-2014-306104. [Epub ahead of print]

## Getting rhythm: how do babies do it?



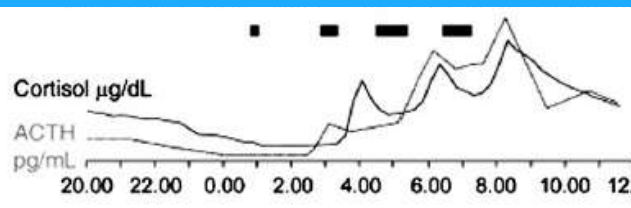
**CORTISOL**  
day-night  
rhythm

Birth ~ / ~ 8w 9w 10w 11w  
dates averaged → “between 6 and 18 weeks”

# Joseph 2014

Arch Dis Child Fetal Neonatal Ed. 2014 Sep 22. pii: fetalneonatal-2014-306104.  
doi: 10.1136/archdischild-2014-306104. [Epub ahead of print]

## Getting rhythm: how do babies do it?



**MELATONIN**  
day-night rhythm

**CORTISOL**  
day-night  
rhythm

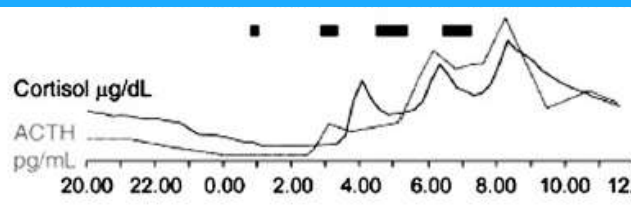
Birth ~ / ~ 8w 9w 10w 11w

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doi: 10.1136/archdischild-2014-306104. [Epub ahead of print]

## Getting rhythm: how do babies do it?



**MELATONIN**  
day-night rhythm

**CORTISOL**  
day-night  
rhythm

**TEMPERATURE**  
day-night  
rhythm

Birth ~ / ~ 8w 9w 10w 11w

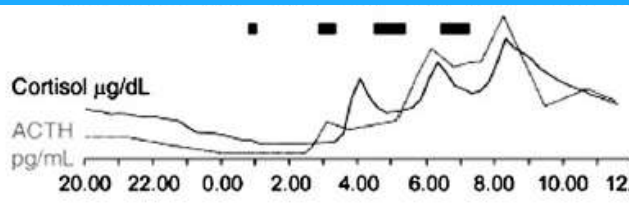
dates averaged → “between 6 and 18 weeks”



# Joseph 2014

Arch Dis Child Fetal Neonatal Ed. 2014 Sep 22. pii: fetalneonatal-2014-306104.  
doi: 10.1136/archdischild-2014-306104. [Epub ahead of print]

## Getting rhythm: how do babies do it?



**MELATONIN**  
day-night rhythm

**H3f3b gene**  
detected

**CORTISOL**  
day-night  
rhythm

**TEMPERATURE**  
day-night  
rhythm

Birth ~ / ~ 8w                      9w                      10w                      11w

dates averaged → “between 6 and 18 weeks”

Infant:  
sleep cycles  
begin to block  
on diurnal  
rhythms

## Mother-infant synchrony

... at 12 weeks  
(circadian)

Thomas 2014

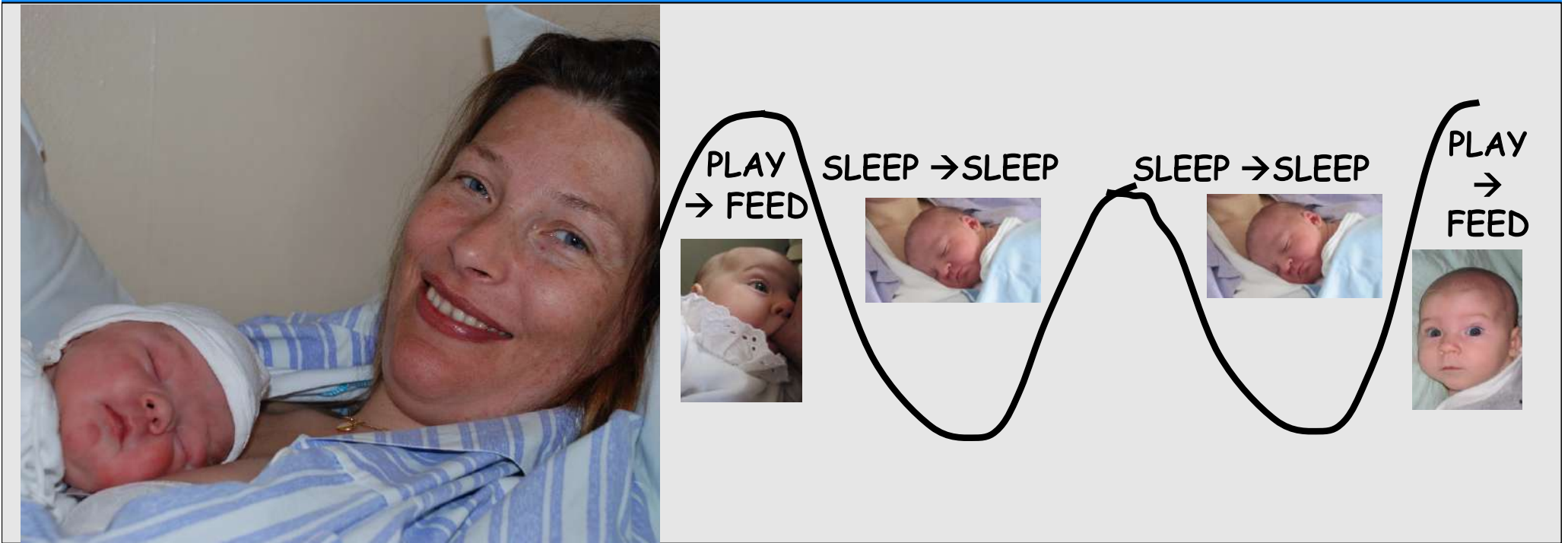
START at 3 months

Can be “adult-like”  
at 6 months.

Infant:  
sleep cycles  
begin to block  
on diurnal  
rhythms



Infant sleep cycling and synchronicity with  
maternal sleep ensure development.



Infant sleep cycling and synchronicity with maternal sleep ensure development.



Infant sleep cycling and synchronicity with maternal sleep ensure development.

137

Infant sleep cycling  
→ critical for brain  
development,

BUT is also determined by brain requirements:

TEMPERAMENT

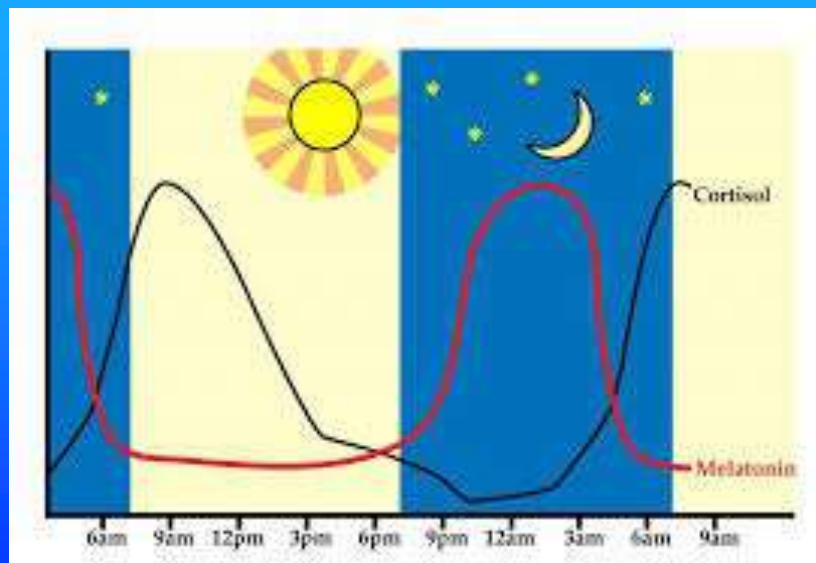
PERSONALITY

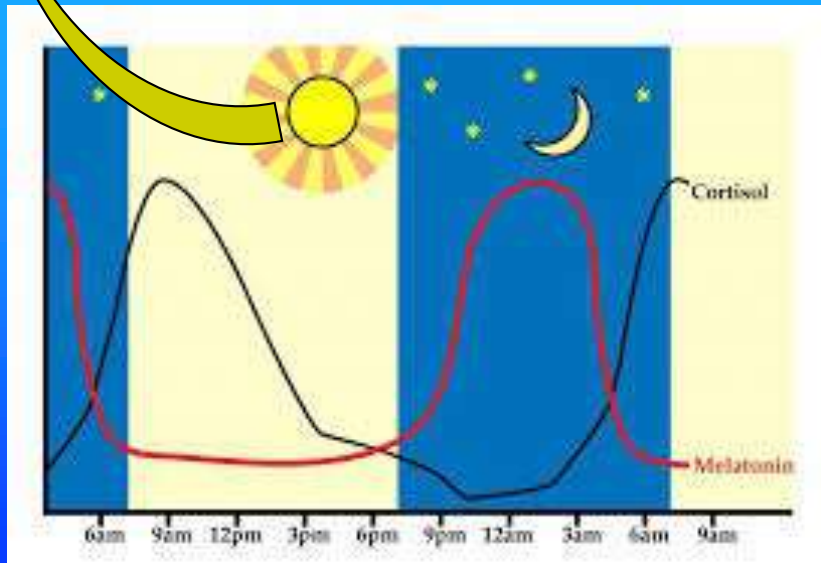
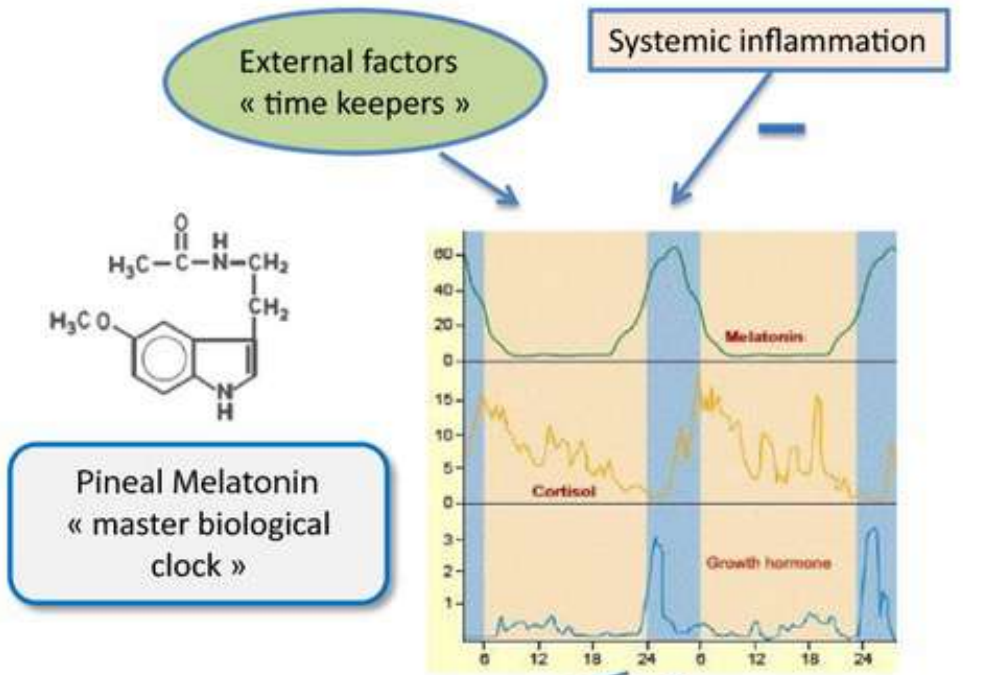
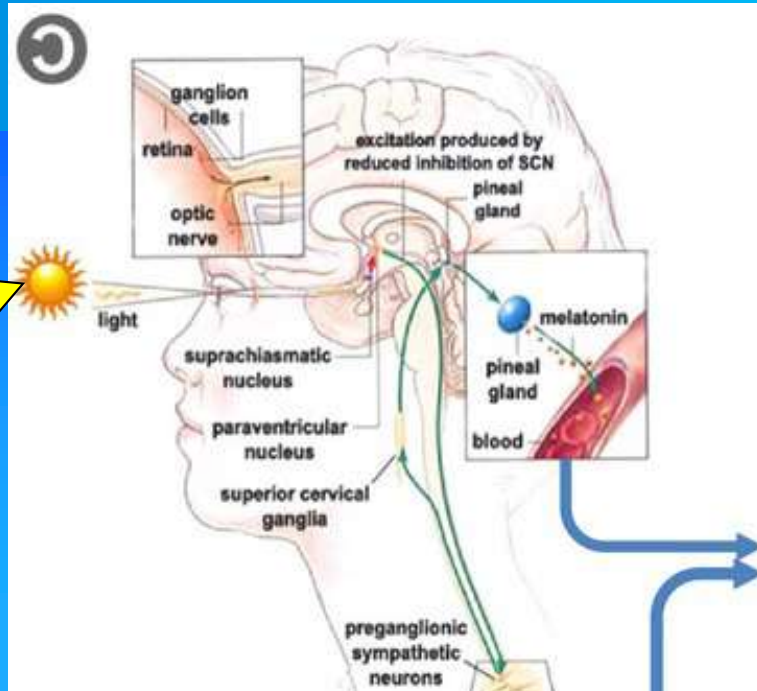
OREXIN METABOLISM

“MORE SLEEP → MORE WIRING”

Infant sleep cycling  
→ critical for brain  
development,

BUT is also determined by brain requirements:

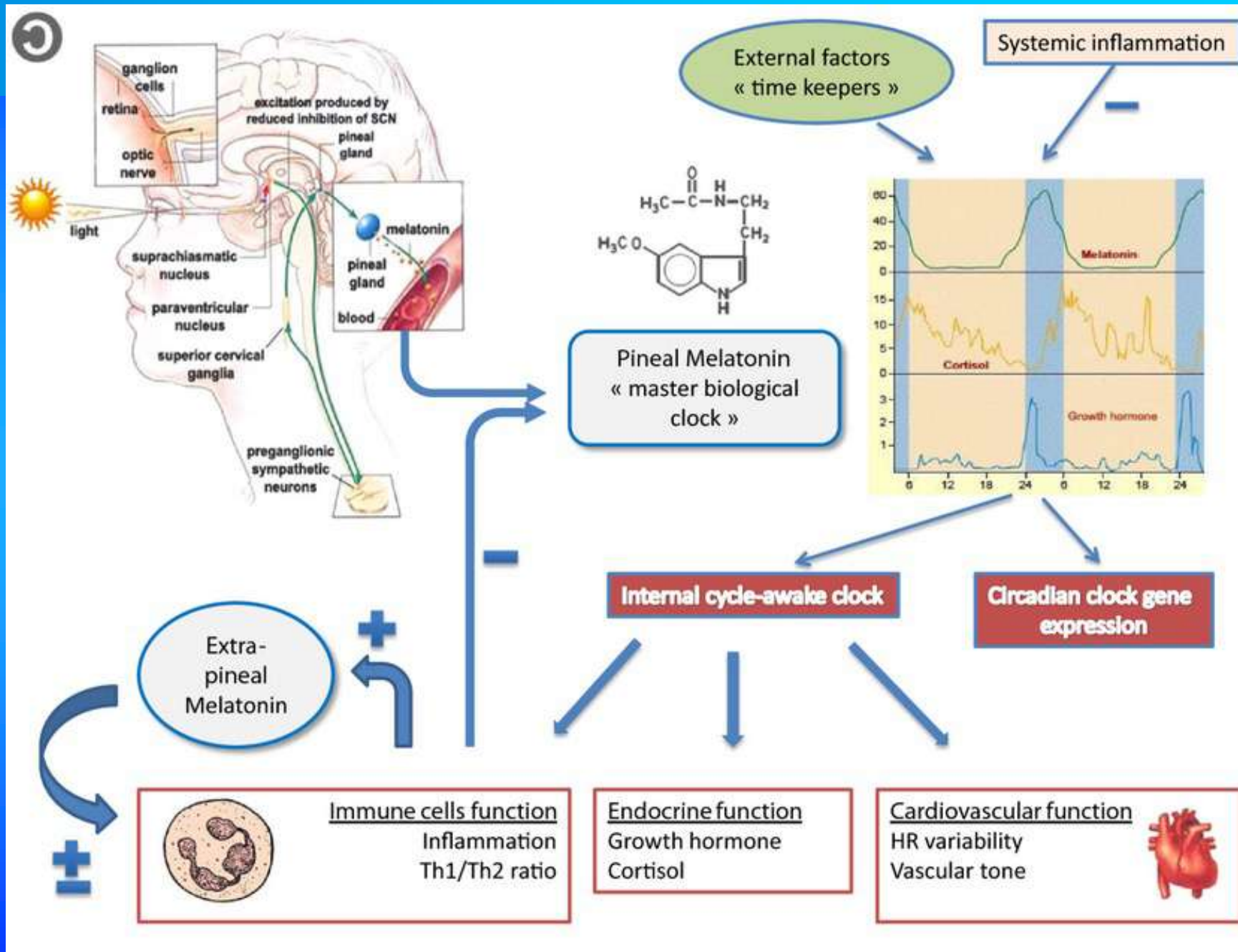




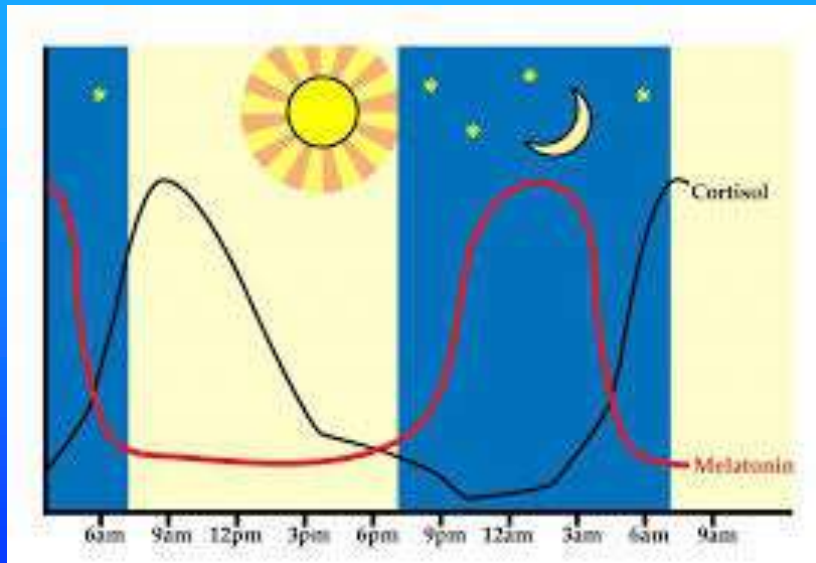
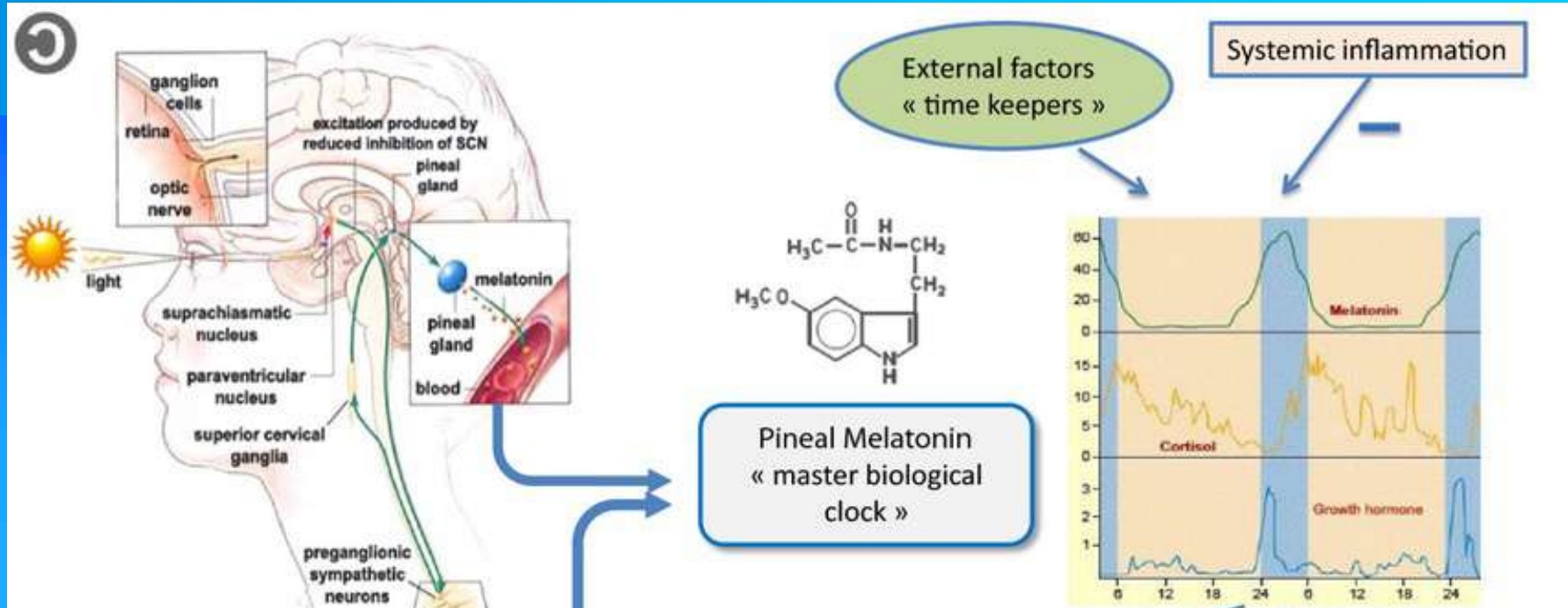
# CIRCADIAN RHYTHM

## SCN

Suprachiasmatic nucleus,  
Pineal gland, melatonin





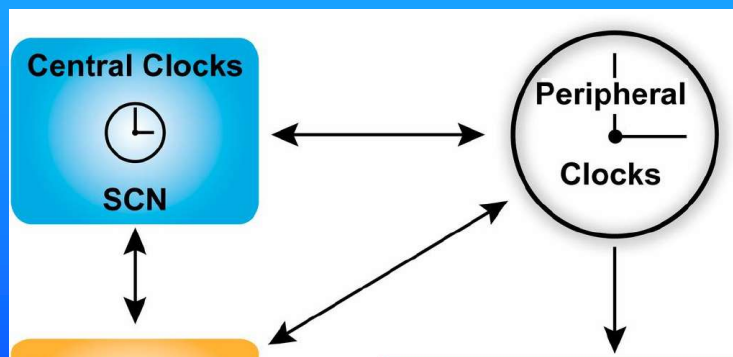


# CIRCADIAN RHYTHM

Master clock,  
sets other clocks  
**'zeitgeber'**

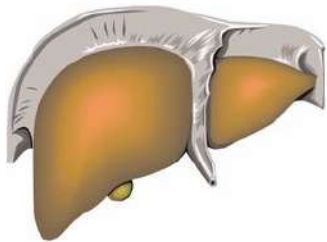
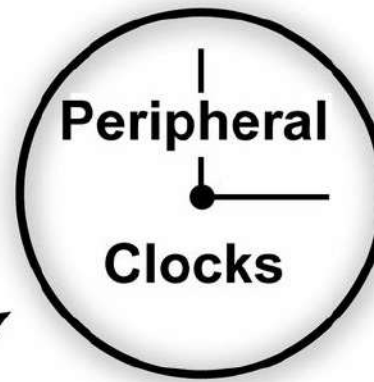
# Human clock genes.

Rhythmic variations in physiological and behavioural processes are mediated by both endogenous and exogenous factors. Endogenous factors include self-sustaining biological pacemakers or clocks which in the absence of strong external influences ...



## CIRCADIAN RHYTHM

Master clock,  
sets other clocks  
**'zeitgeber'**



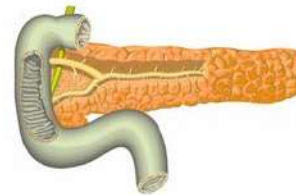
**Liver**

Gluconeogenesis  
Glucose export



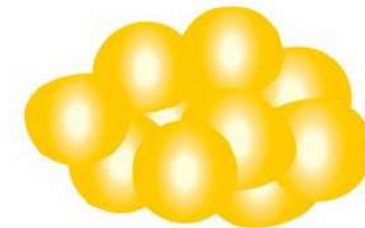
**Skeletal muscle**

Mitochondrial biogenesis  
Respiratory function



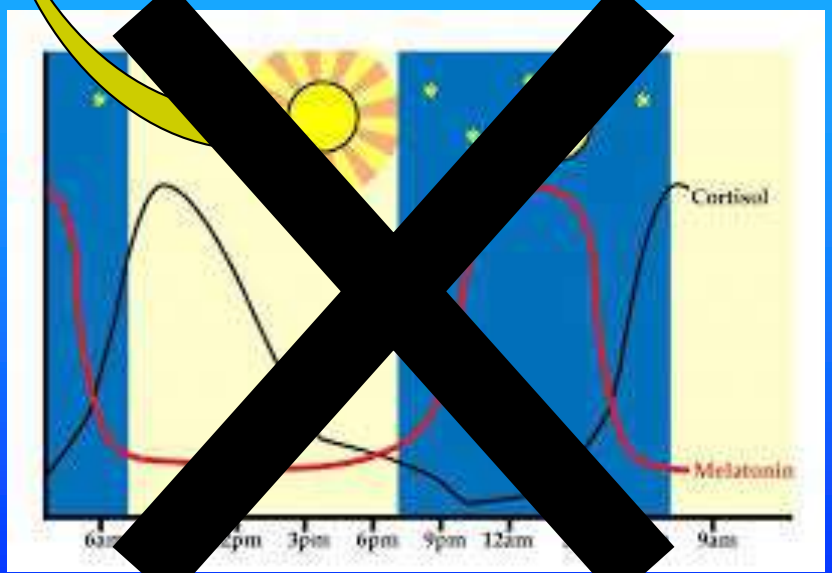
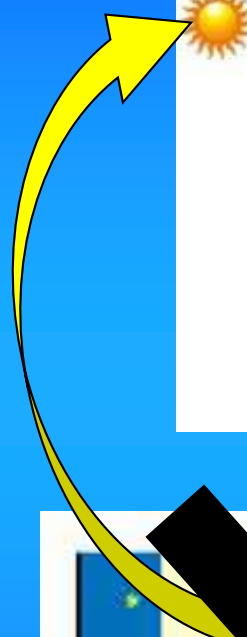
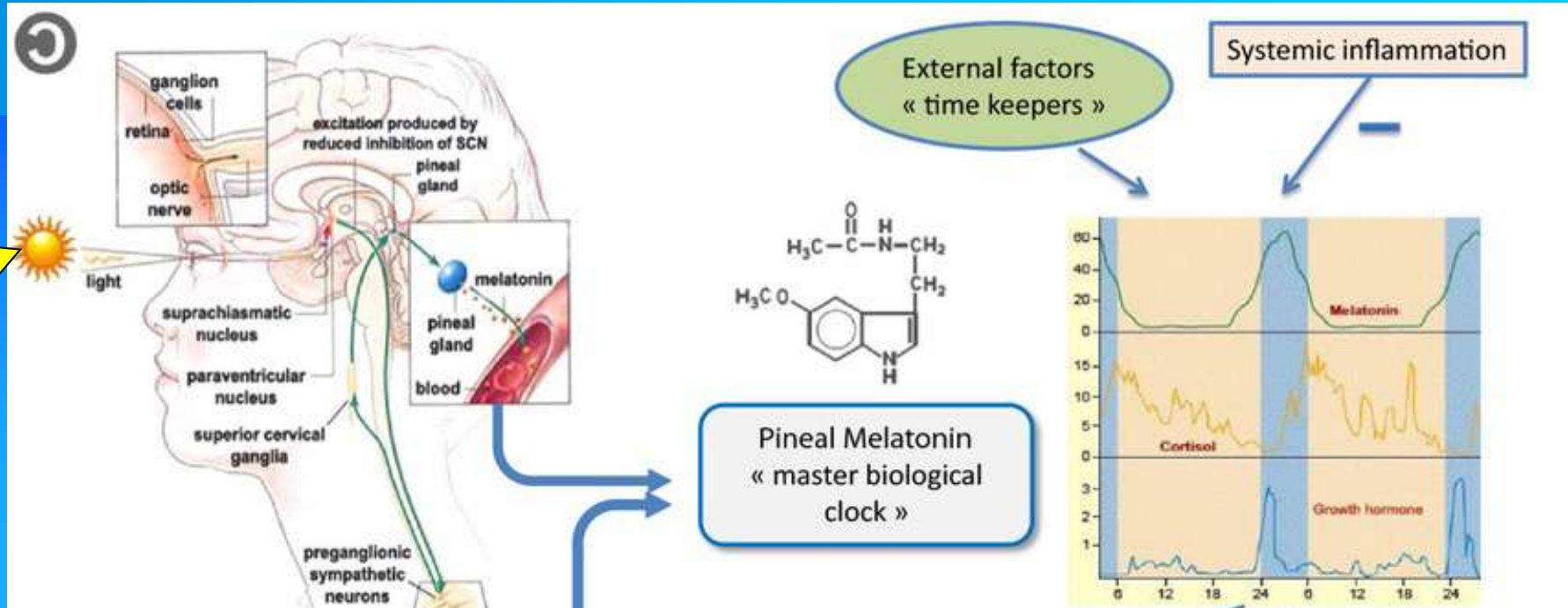
**Pancreas**

Insulin secretion  
Islet cell proliferation



**Adipose tissue**

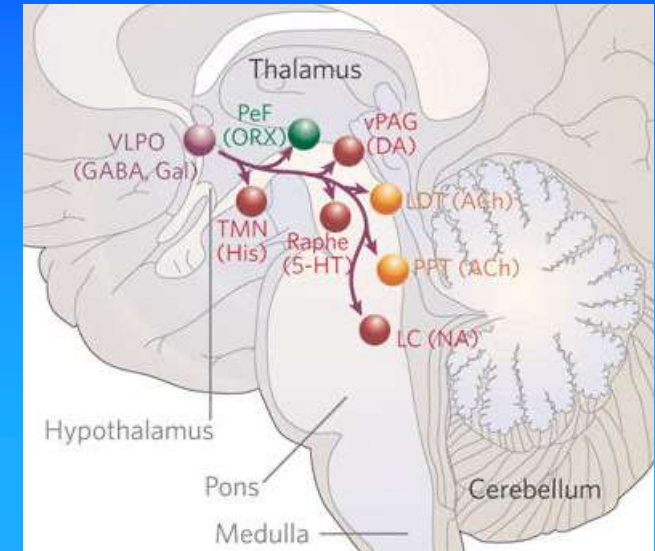
Adipogenesis  
Lipogenesis  
Fatty acid oxidation  
Lipolysis



**CIRCADIAN RHYTHM  
ABSENT IN  
NEONATES**

# Ultradian and circadian rhythms

*Ultradian:*  
Repeated during  
(single circadian) 24  
hour period



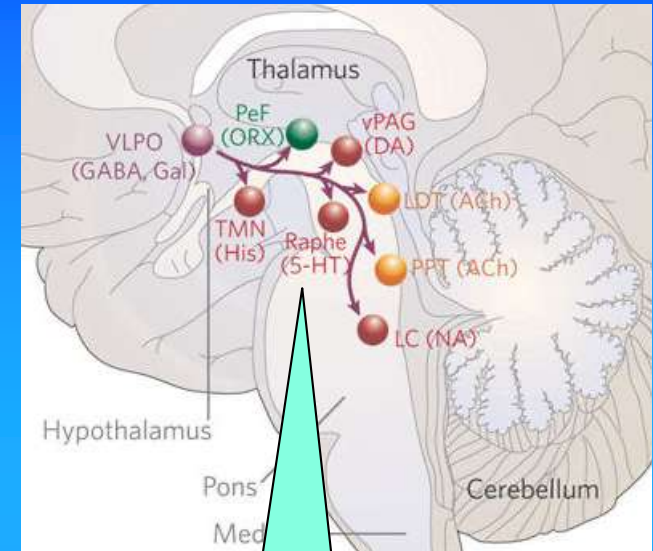
Lohr B, Siegmund R. 1999. *Chronobiol Int*  
16(2): 129-48.

# Ultradian and circadian rhythms of sleep-wake and food-intake behavior during early infancy.

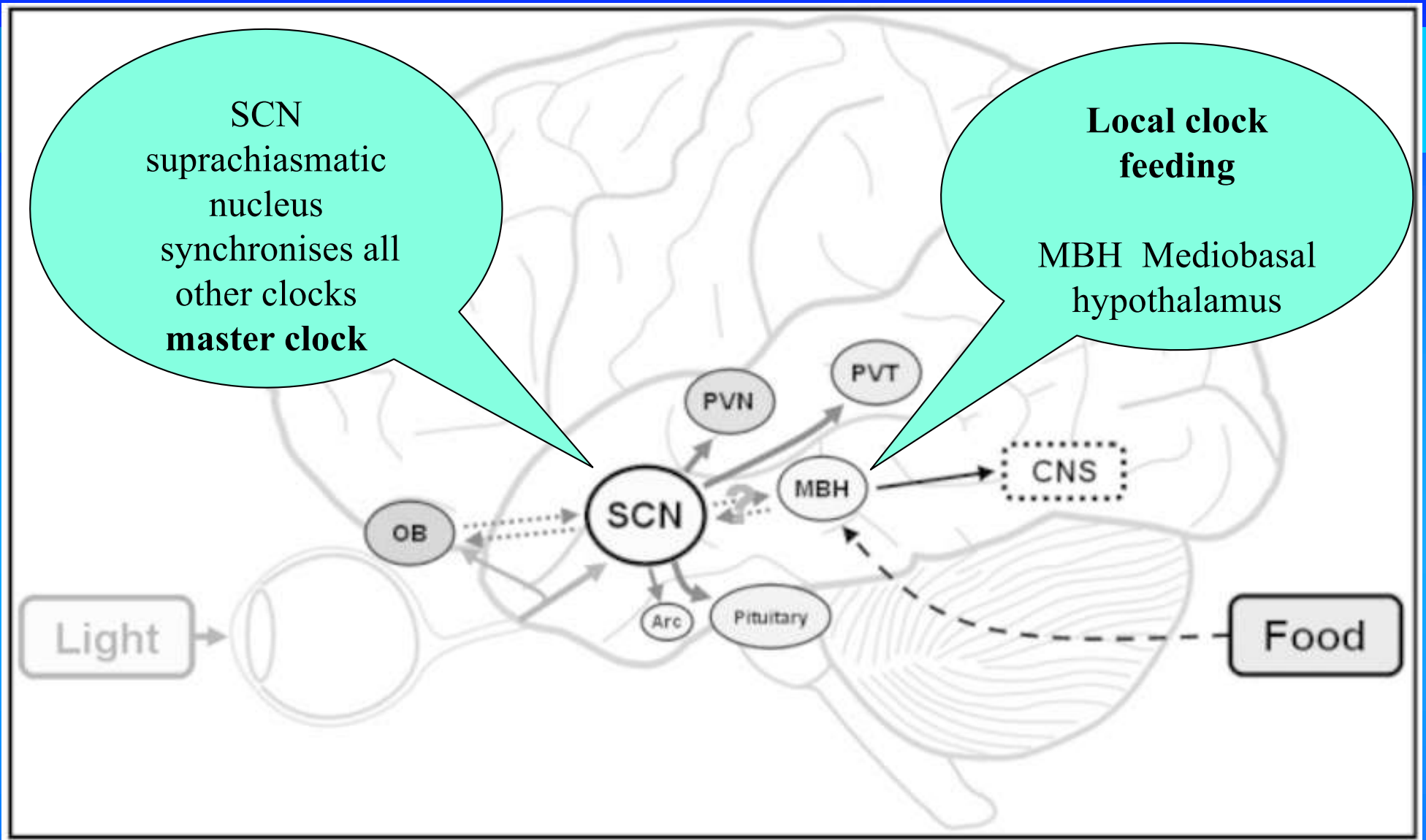
*Ultradian:*  
Repeated during  
(single circadian) 24  
hour period

## Pleasurable feeding - and sleeping -

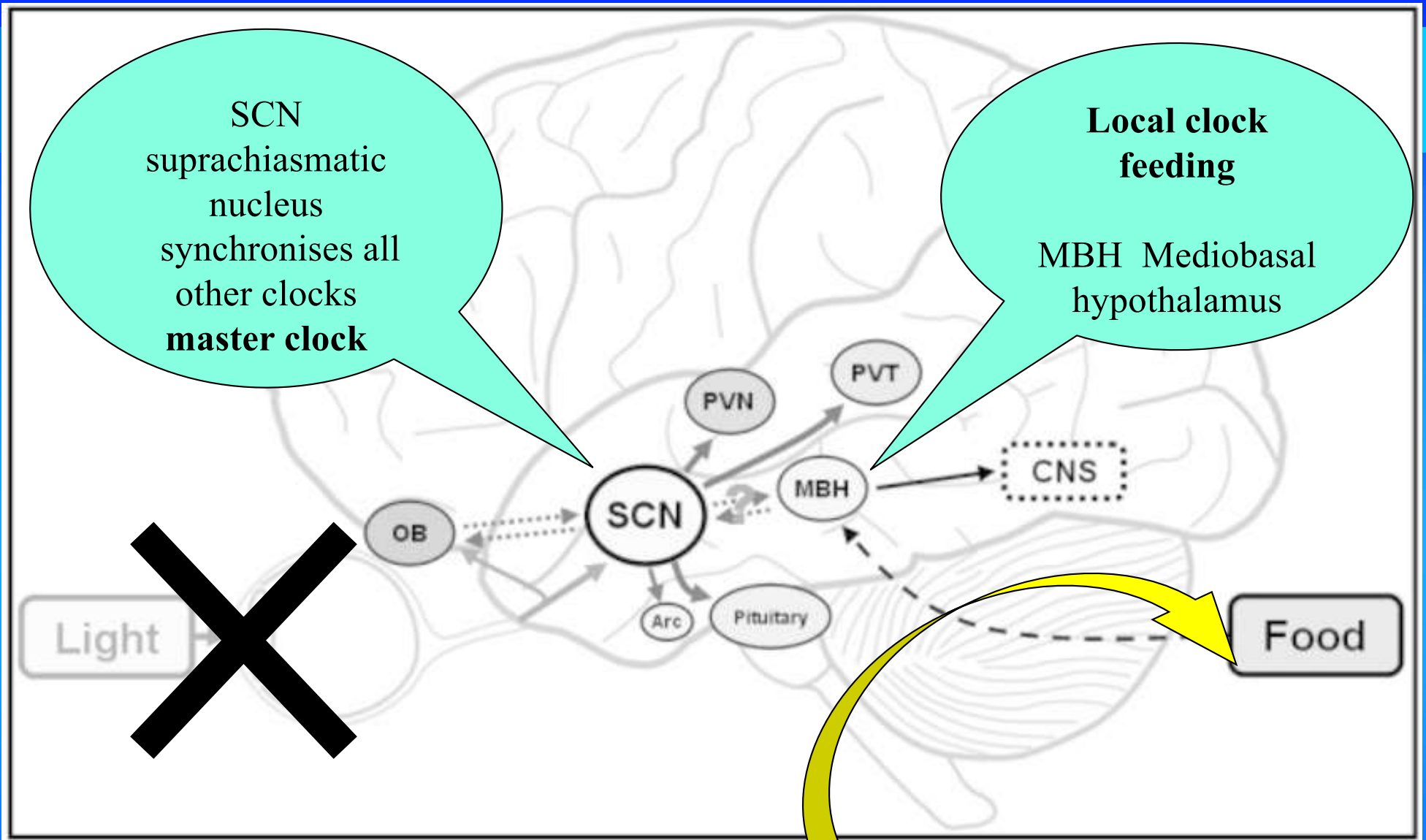
Lohr B, Siegmund R. 1999. *Chronobiol Int*  
16(2): 129-48.



**Hypothalamic  
local clocks  
communicate and  
coordinate**

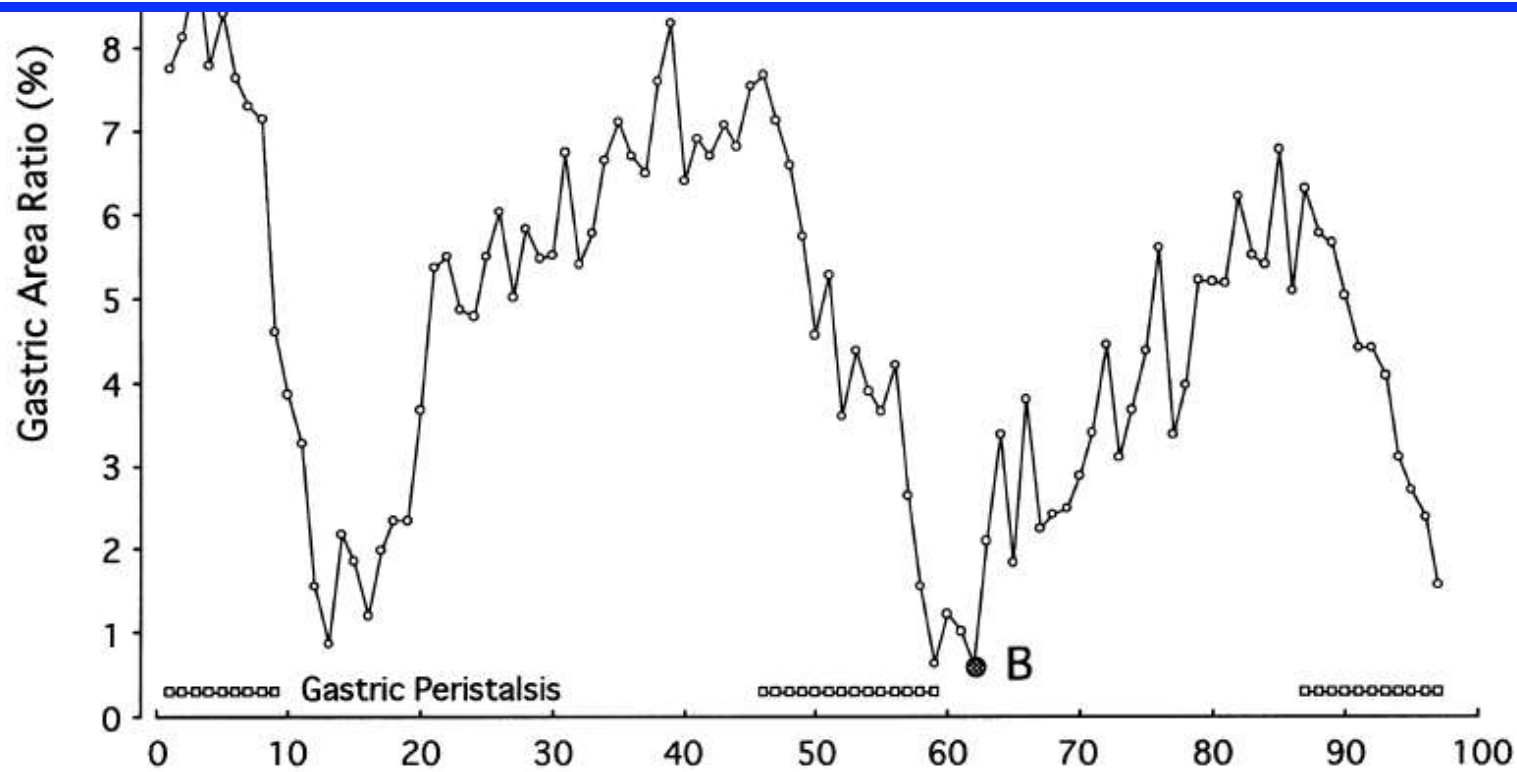


[https://www.researchgate.net/figure/Circadian-clocks-in-the-SCN-and-other-regions-of-the-brain-In-addition-to-the-central\\_fig3\\_51823898](https://www.researchgate.net/figure/Circadian-clocks-in-the-SCN-and-other-regions-of-the-brain-In-addition-to-the-central_fig3_51823898)



The 'zeitgeber' is  
not light, it is feeding.





note rhythmicity  
of fetal stomach → 40 - 50 minutes

The 'zeitgeber' is  
not light, it is feeding.

# Gastric clock: 40-50 minutes

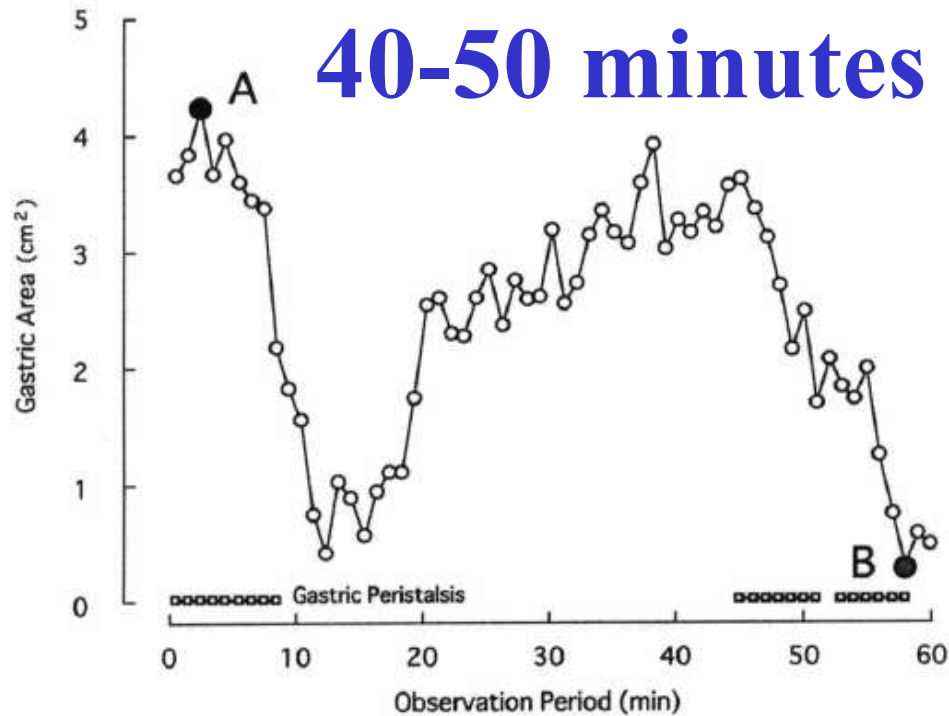
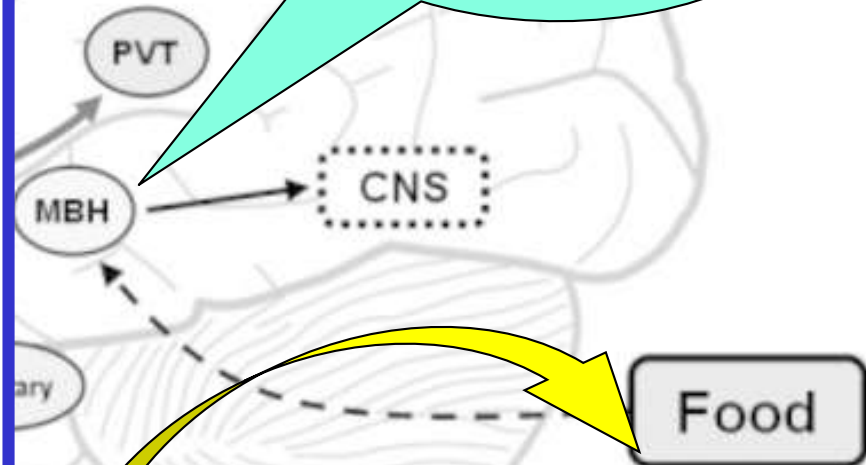


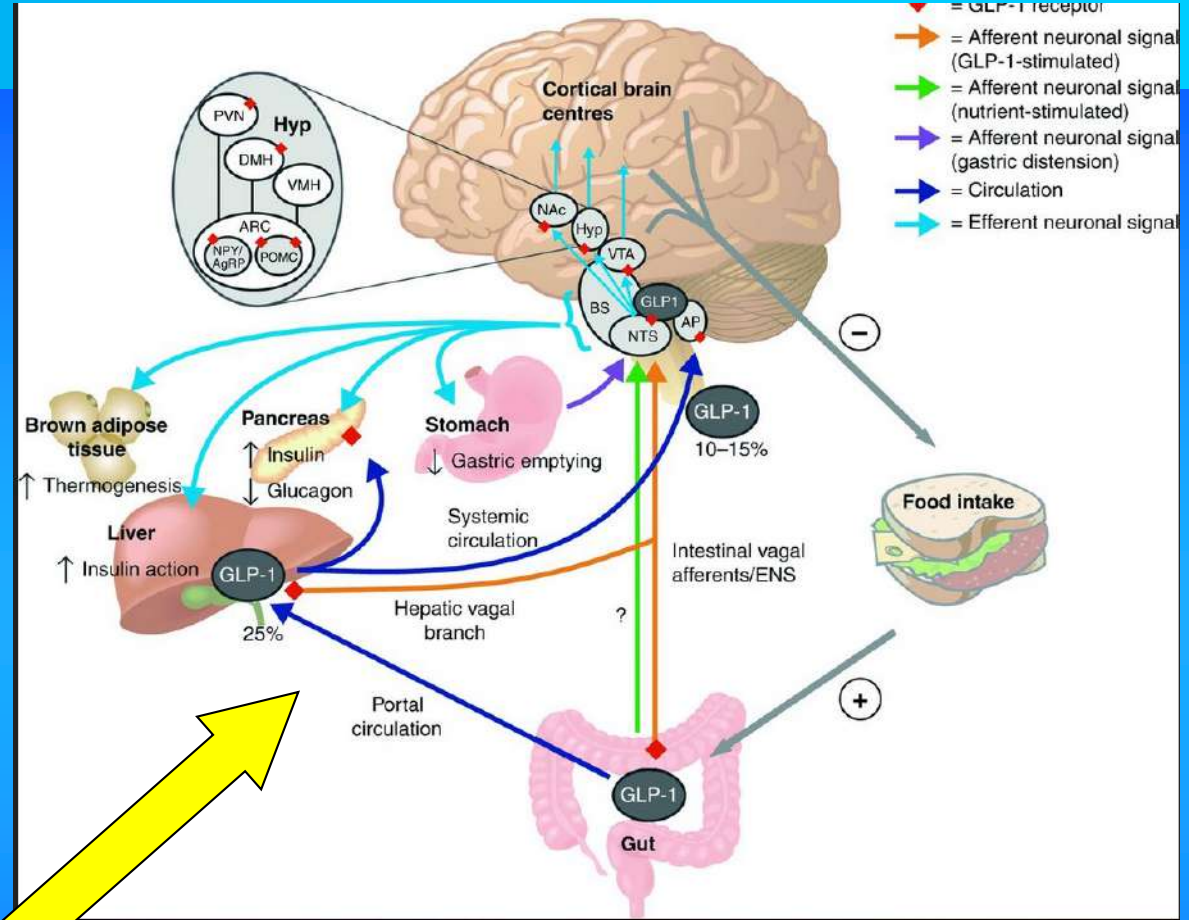
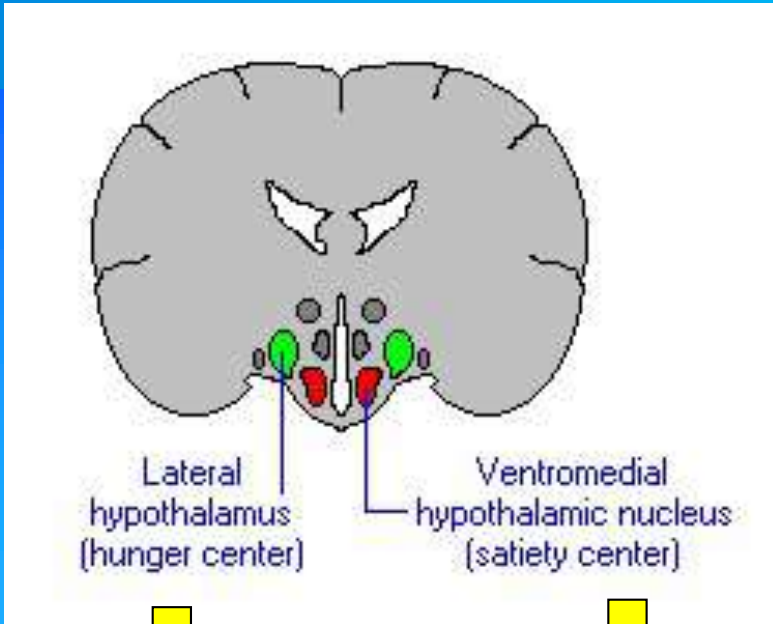
Figure 2. Changes of gastric area in a representative fetus at 33 weeks of gestation, in association with gastric peristalsis. The maximum gastric area (A) and the minimum gastric area (B) [27].

Local clock  
feeding

MBH Mediobasal  
hypothalamus



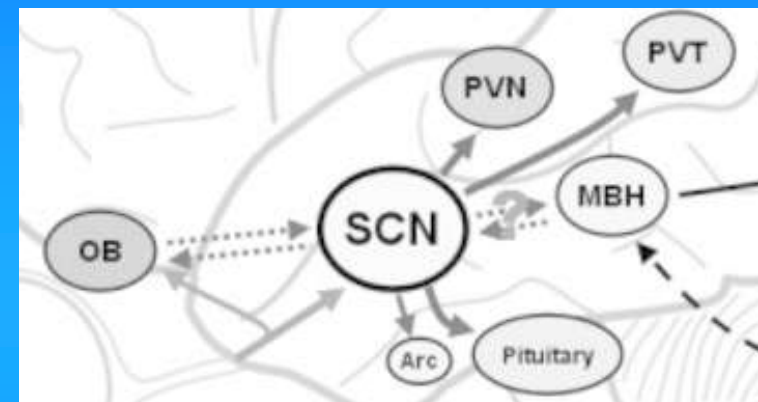
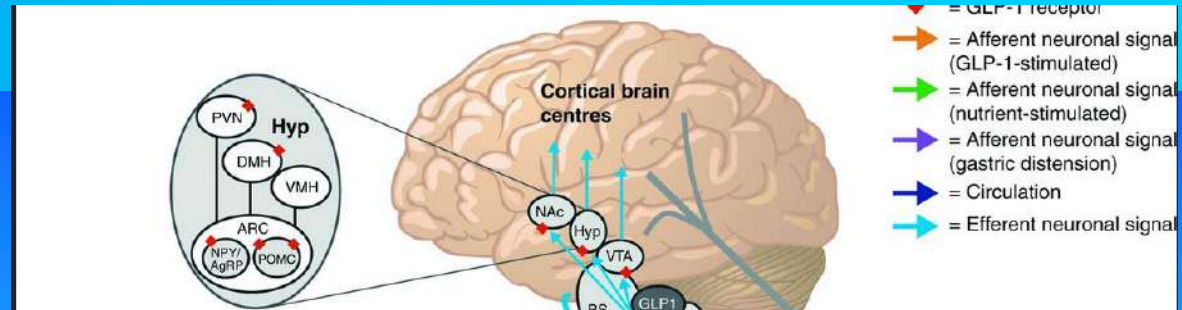
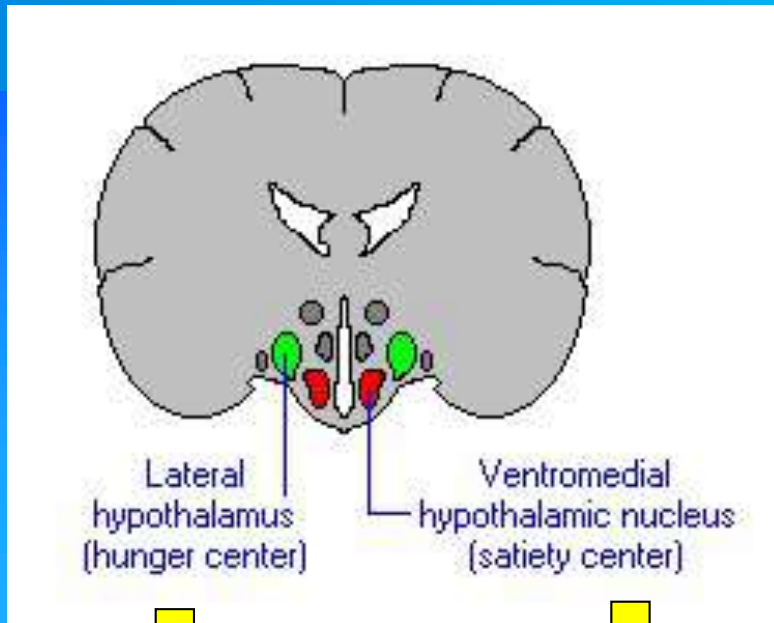
The 'zeitgeber' is  
not light, it is feeding.



Hunger & Satiety rhythms

regulate all metabolic processes

<http://joe.endocrinology-journals.org/content/221/1/T1/F1.expansion.html>



Hunger & Satiety rhythms

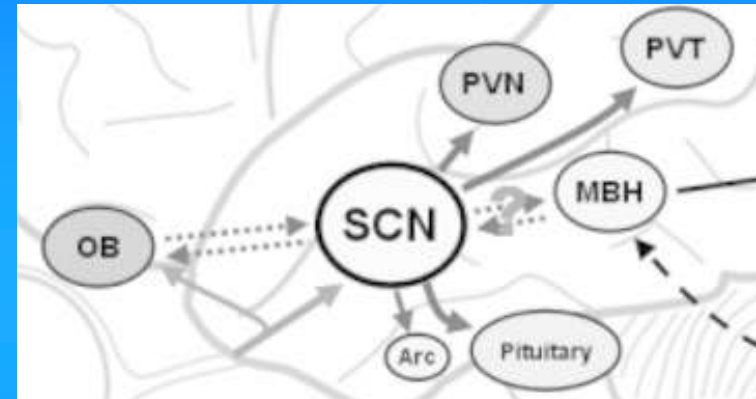
Sleep & Awake rhythms

regulate all metabolic processes

regulate all neurological processes

# SMELL

**OB – Olfactory Bulb  
drives the SCN  
(primary clock)**



Hunger & Satiety  
rhythms 

regulate all  
metabolic processes

Sleep & Awake  
rhythms

regulate all  
neurological processes

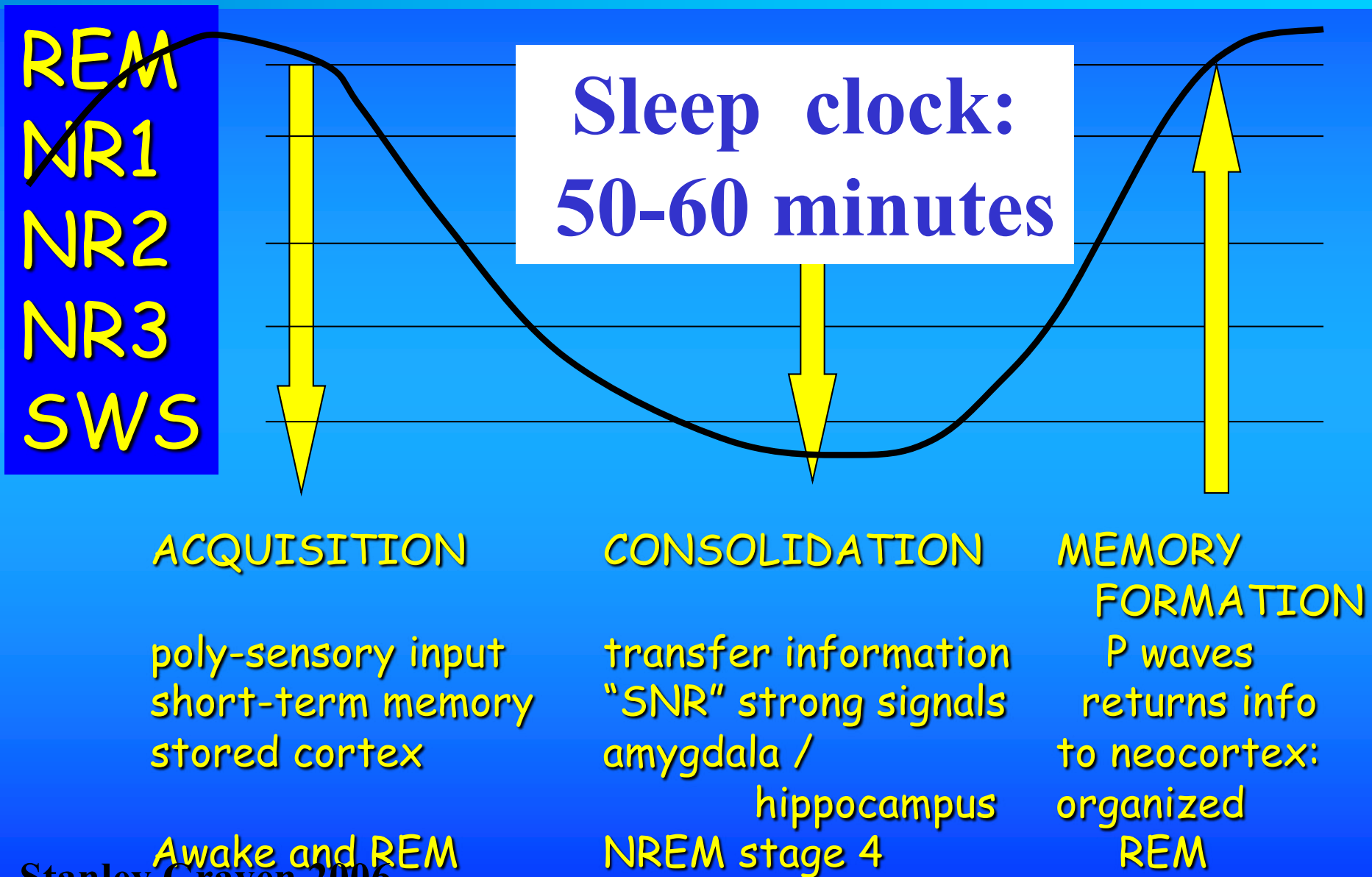
# SMELL



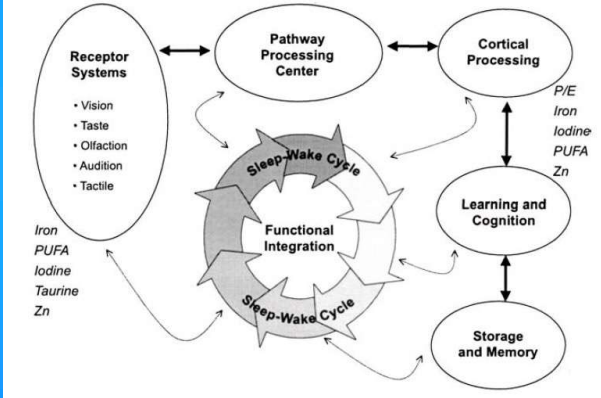
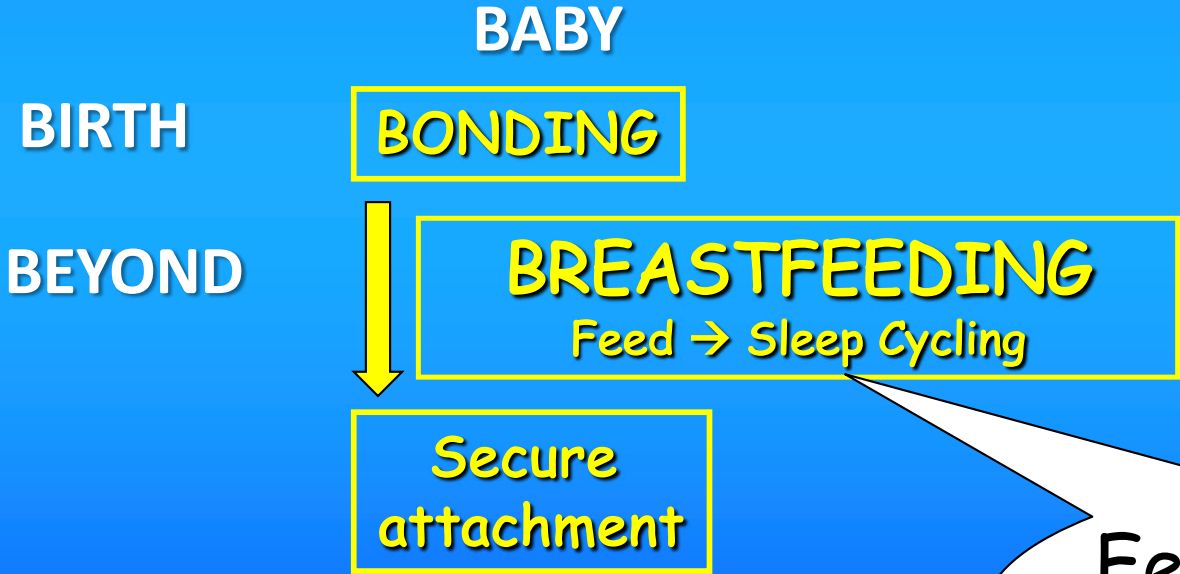
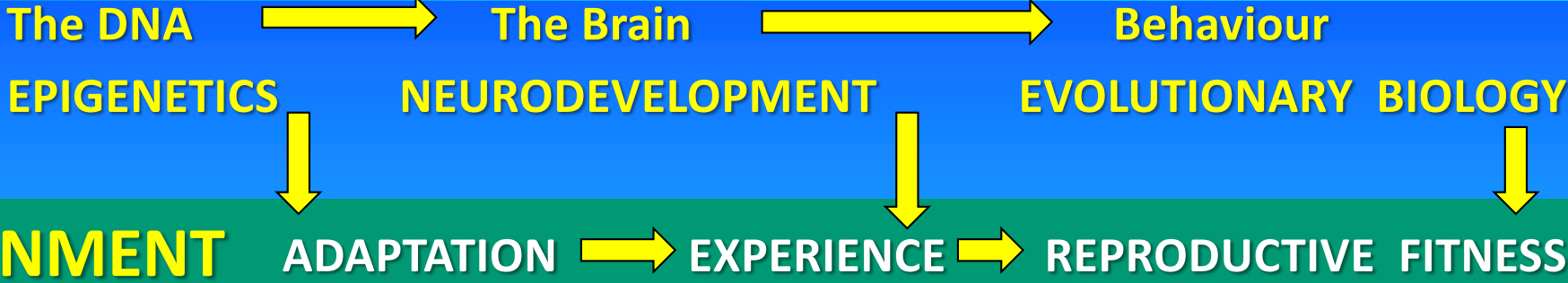
modulates state organisation  
elicits emotional behaviours

activates pre-feeding actions  
anticipatory digestive physiology  
regulates pace of ingestive behaviour

# BRAIN WIRING



# The Neuroscience of Birth & Breastfeeding



Feed interval is one sleep cycle



EHD 01145

The emergence of adrenocortical circadian function  
in newborns and infants and its relationship to sleep,  
feeding and maternal adrenocortical activity

Gottfried Spangler

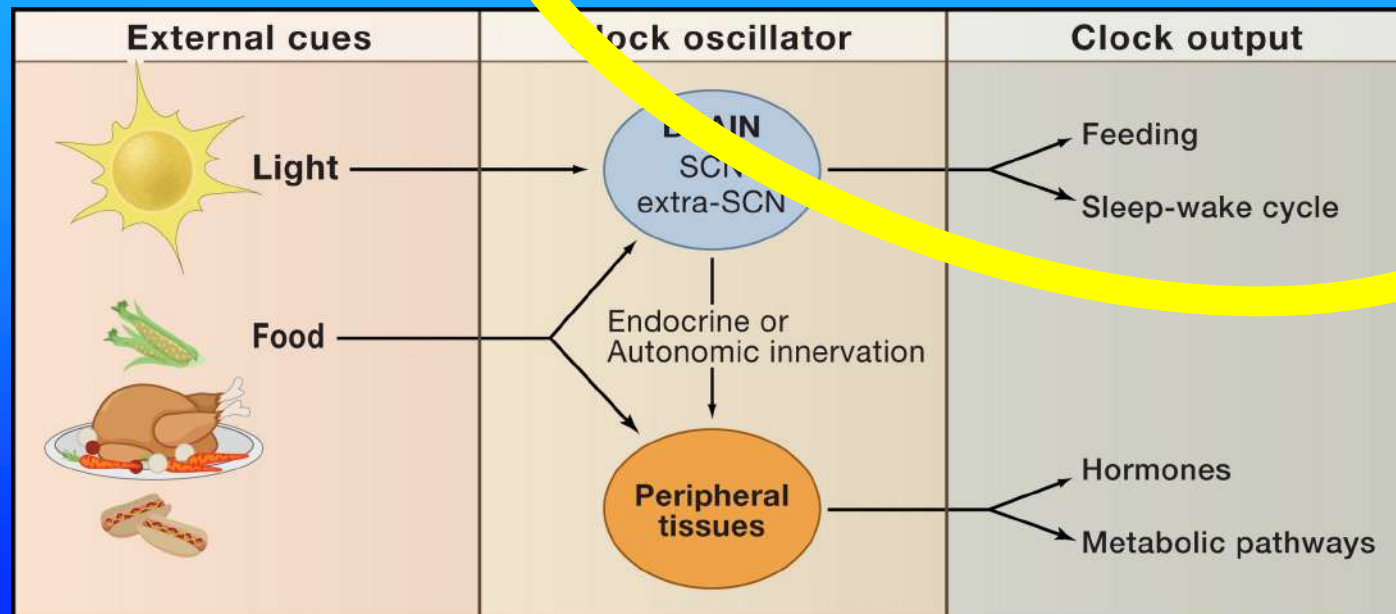
Sleeping, feeding and maternal-  
infant interaction rhythms are  
established much earlier.

# External Cues and Clock Outputs

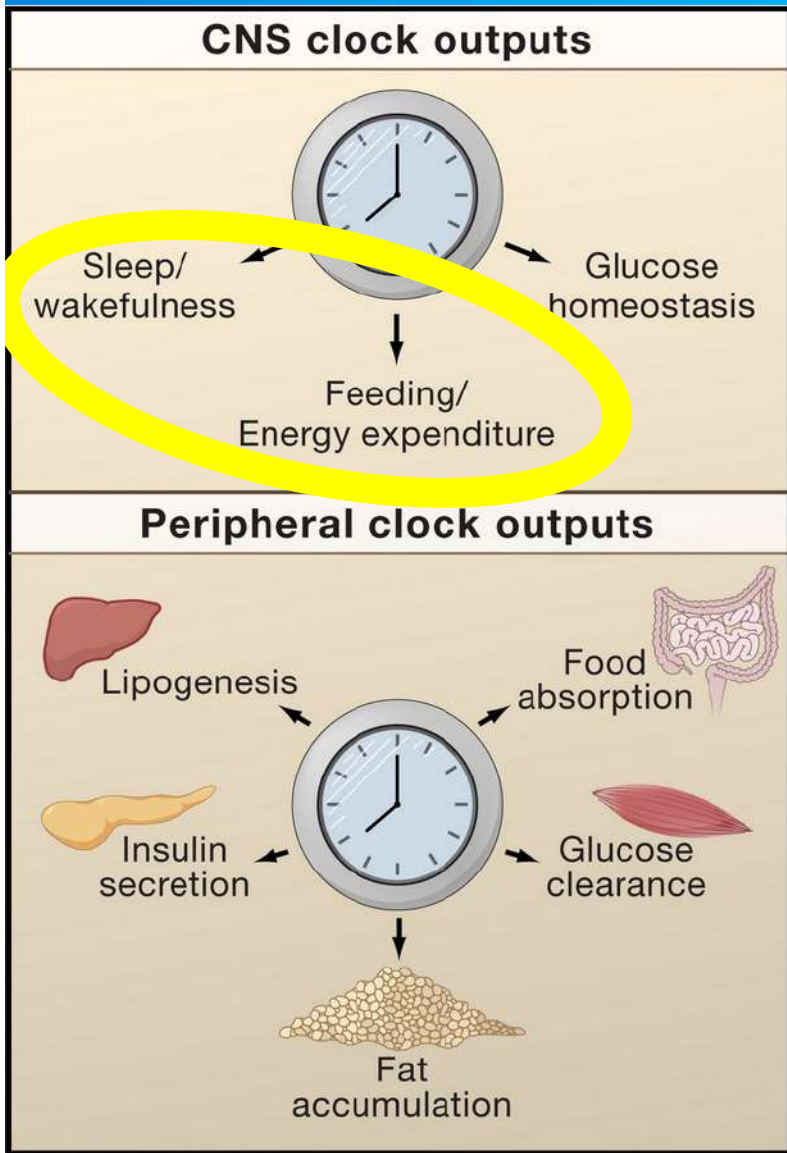
The predominant external cue (zeitgeber) of the SCN clock is light.

Clocks in peripheral tissues such as the liver also can be entrained by food.

Outputs of both the SCN and peripheral clocks impact behavioral and metabolic responses such as feeding, sleep-wakefulness ...



# Central Pacemaker and Peripheral Clocks



The master pacemaker encoding the mammalian clock resides within the SCN, although clock genes are also expressed in other regions of the brain and in most peripheral tissues. Emerging evidence suggests that peripheral tissue clocks are synchronized through humoral, nutrient, and autonomic wiring and that the cell-autonomous function of the clock is important in pathways involved in fuel storage and consumption.

clocks are synchronized

# Joseph 2014

Arch Dis Child Fetal Neonatal Ed. 2014 Sep 22. pii: fetalneonatal-2014-306104.  
doi: 10.1136/archdischild-2014-306104. [Epub ahead of print]

## Getting rhythm: how do babies do it?

**MELATONIN**  
day-night rhythm

**H3f3b gene**  
detected

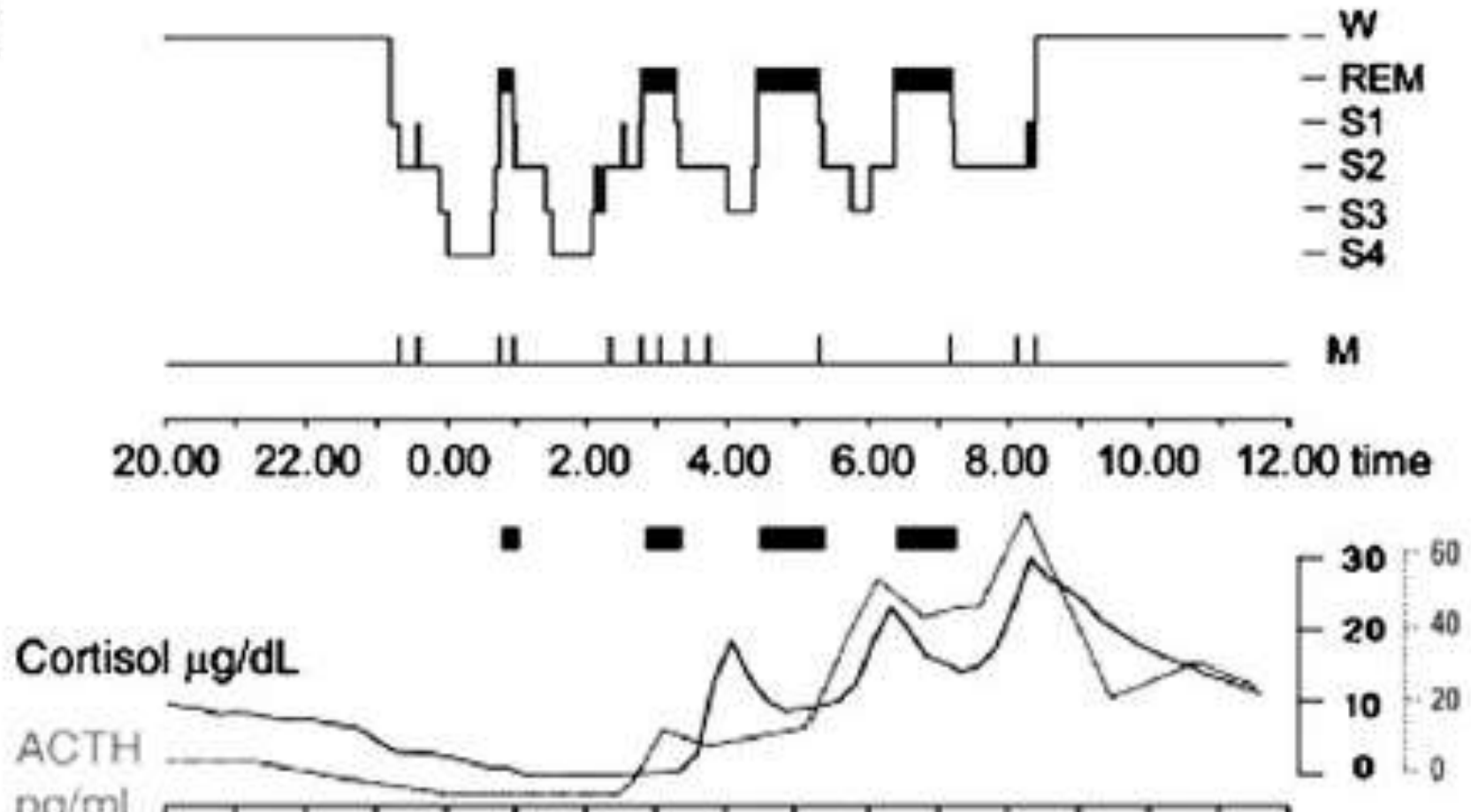
**CORTISOL**  
day-night  
rhythm

**TEMPERATURE**  
day-night  
rhythm

Birth ~ / ~ 8w 9w 10w 11w

dates averaged → “between 6 and 18 weeks”

B



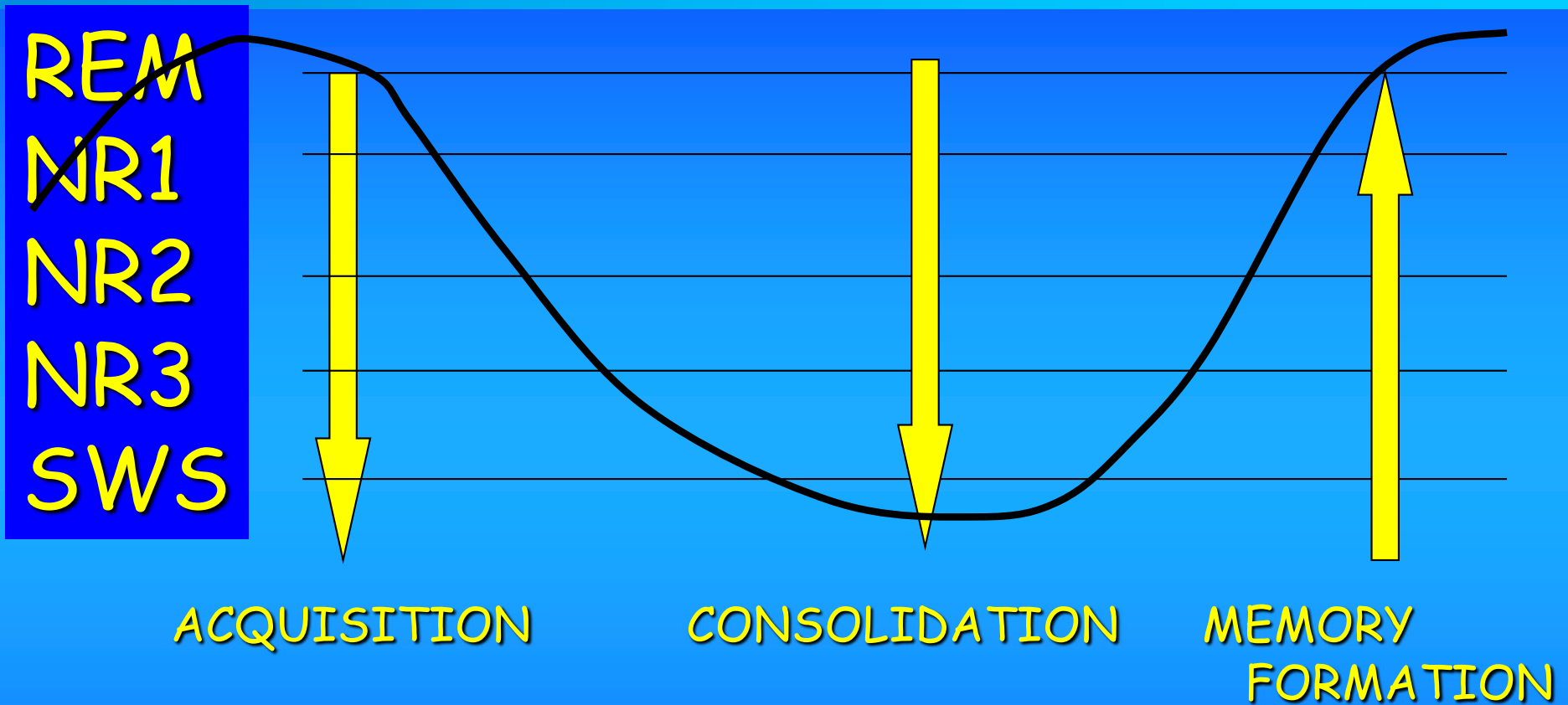
**CORTISOL**  
day-night  
rhythm

**TEMPERATURE**  
day-night  
rhythm

Birth ~ / ~ 8w 9w 10w 11w

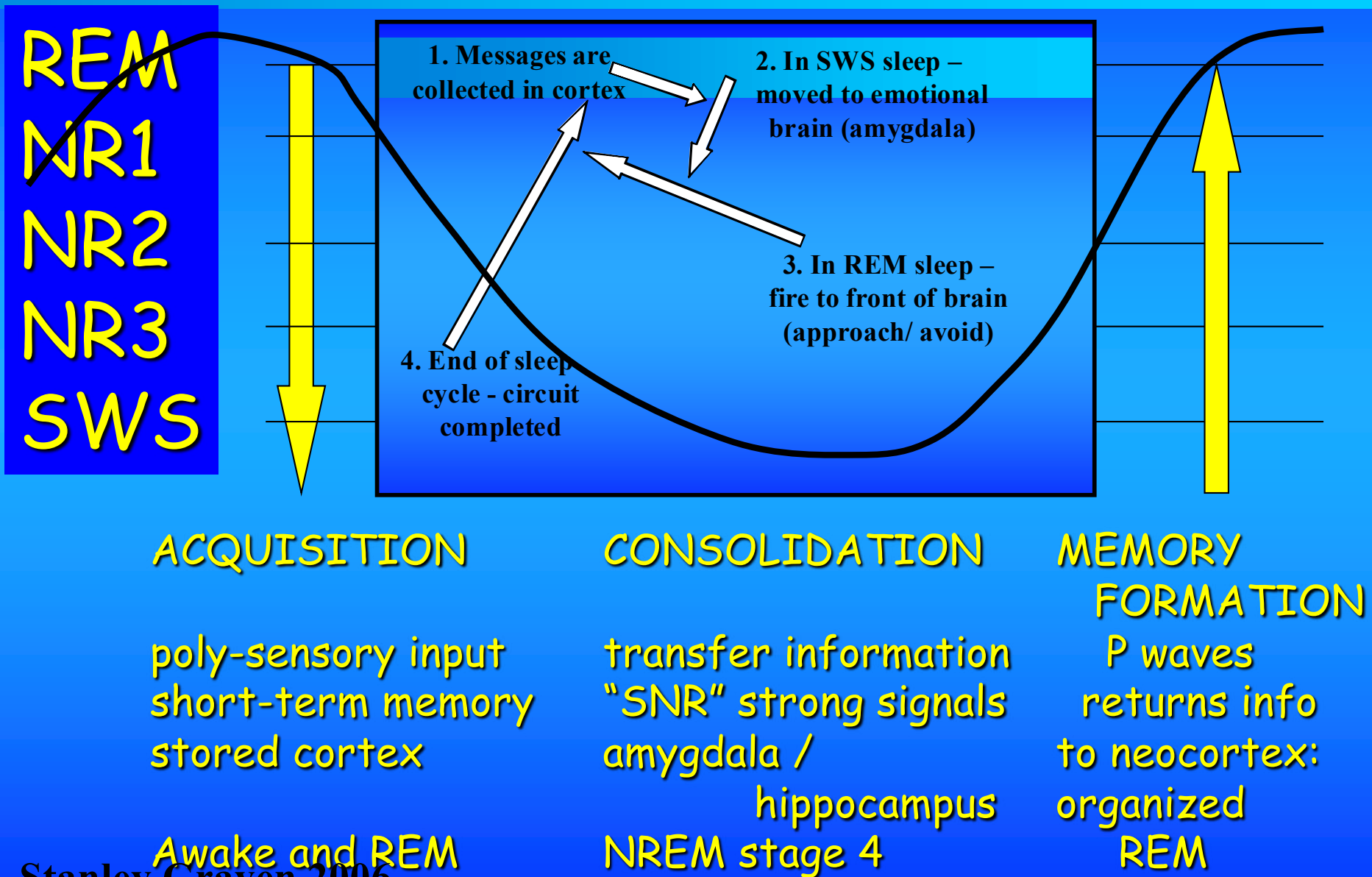
dates averaged → “between 6 and 18 weeks”

# BRAIN WIRING



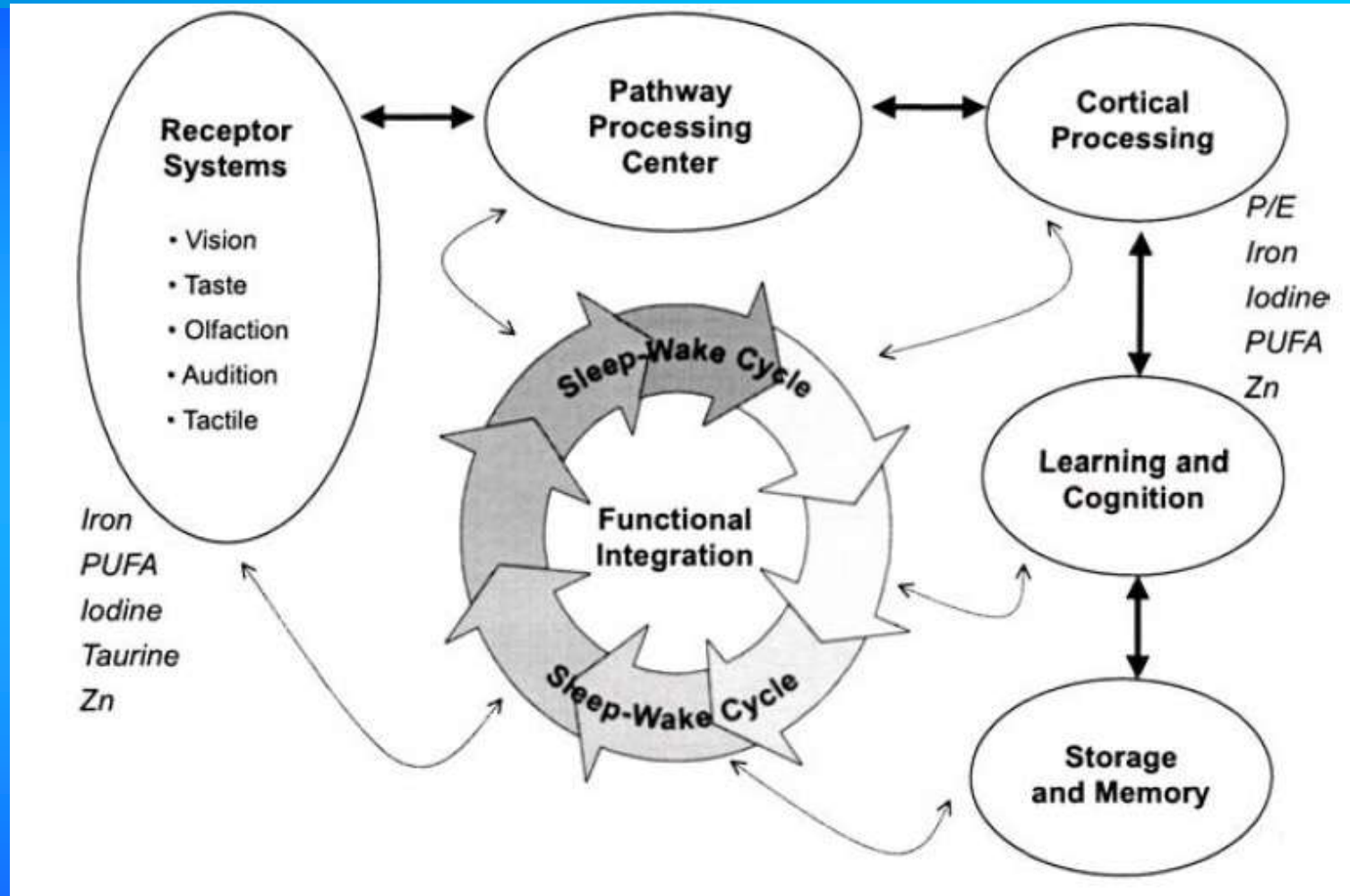
SLEEP CYCLE IS ONE HOUR

# BRAIN WIRING



Stanley Graven 2006

# BRAIN WIRING



**Fig 4.** Schematic representation of the interaction between sensory receptors and CNS functions within the framework of the sleep-wake cycle. Nutrients with proven effects on sensory receptors and/or cortical processing are included (*PUFA*, polyunsaturated fatty acids; *Zn*, zinc; *P/E*, protein/energy).



EHD 01145

The emergence of adrenocortical circadian function  
in newborns and infants and its relationship to sleep,  
feeding and maternal adrenocortical activity

Gottfried Spangler

Sleeping, feeding and maternal-  
infant interaction rhythms are  
established much earlier.

# CIRCADIAN CORTISOL

Newborn

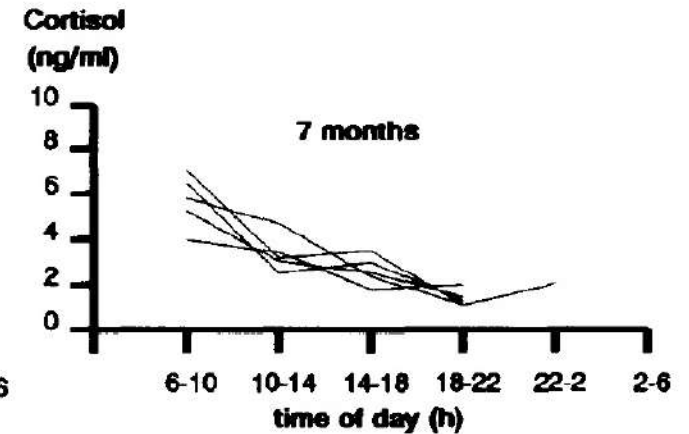
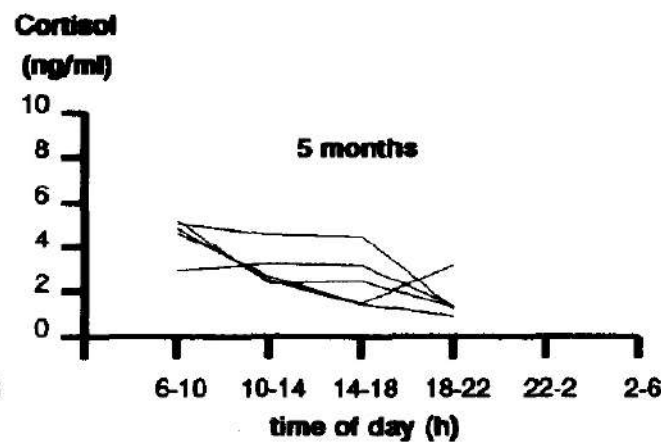
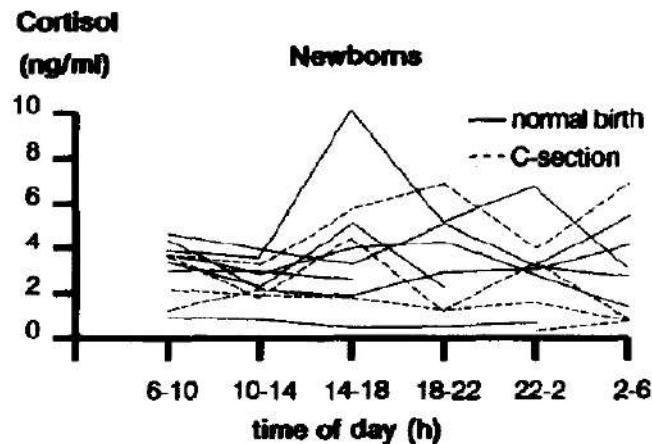
none

5 months

some

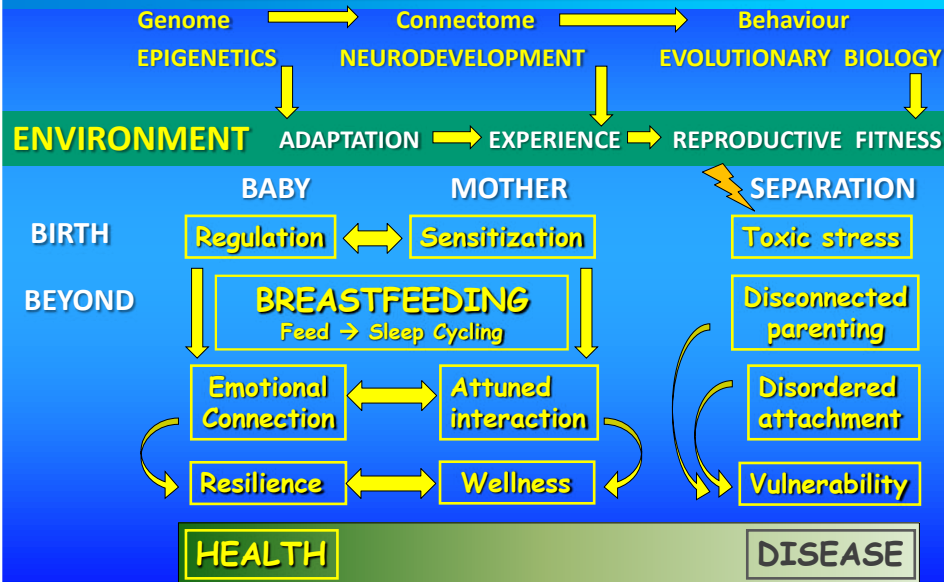
7 months

most



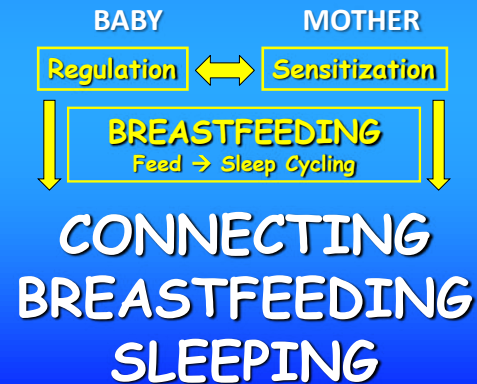
Sleeping, feeding and maternal-infant interaction rhythms are established much earlier.

# NURTURESCIENCE



# NURTURESCIENCE

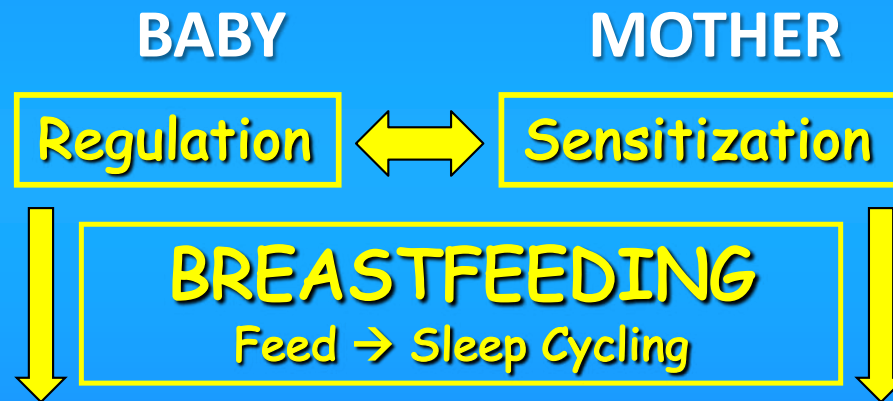
3 primary occupations:



Sleeping, feeding and maternal-infant interaction rhythms are established much earlier.

# NURTURESCIENCE

3 primary occupations:



CONNECTING  
BREASTFEEDING  
SLEEPING

Pleasurable feeding  
- and sleeping -  
a physiological rhythm for  
premature infants.



one hour sleep-wake cycles  
feed cycles

*What evidence ?*

**Karen Edmond, MBBS, MSc (Epidemiology), PhD**  
*London School of Hygiene and Tropical Medicine,  
London, U.K.*

**Rajiv Bahl, MD, PhD**  
*Department of Child and Adolescent  
and Development, WHO, Geneva*

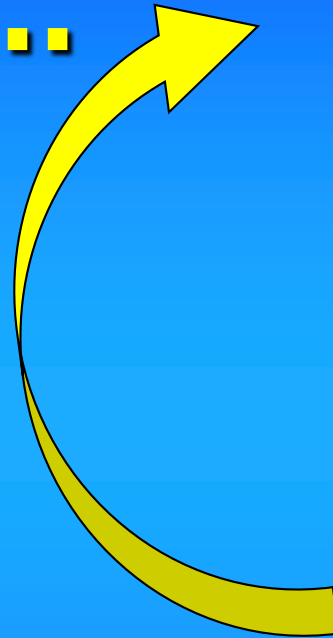
# **EVIDENCE FOR FEEDING FREQUENCY ?????**

**Edmond 2006**



**No RCT's ...**

**Because  
no one did  
the study.**



Conclusions and implications

Only case series and descriptive studies were located in this section. These describe the

about the safest or most effective regimens. No implications can be drawn for infants of particular gestational ages or birth weights.

**No RCT's ...**

**Insufficient  
evidence**

# NEVERTHELESS:

**No RCT's ...**

**Because  
no one did  
the study.**

**SOME  
FACTS →**

Conclusions and implications

Only case series and descriptive studies were located in this section. These describe the

about the safest or most effective regimens. No implications can be drawn for infants of particular gestational ages or birth weights.

**No RCT's ...**

**Insufficient  
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**FEEDING  
FREQUENCY**

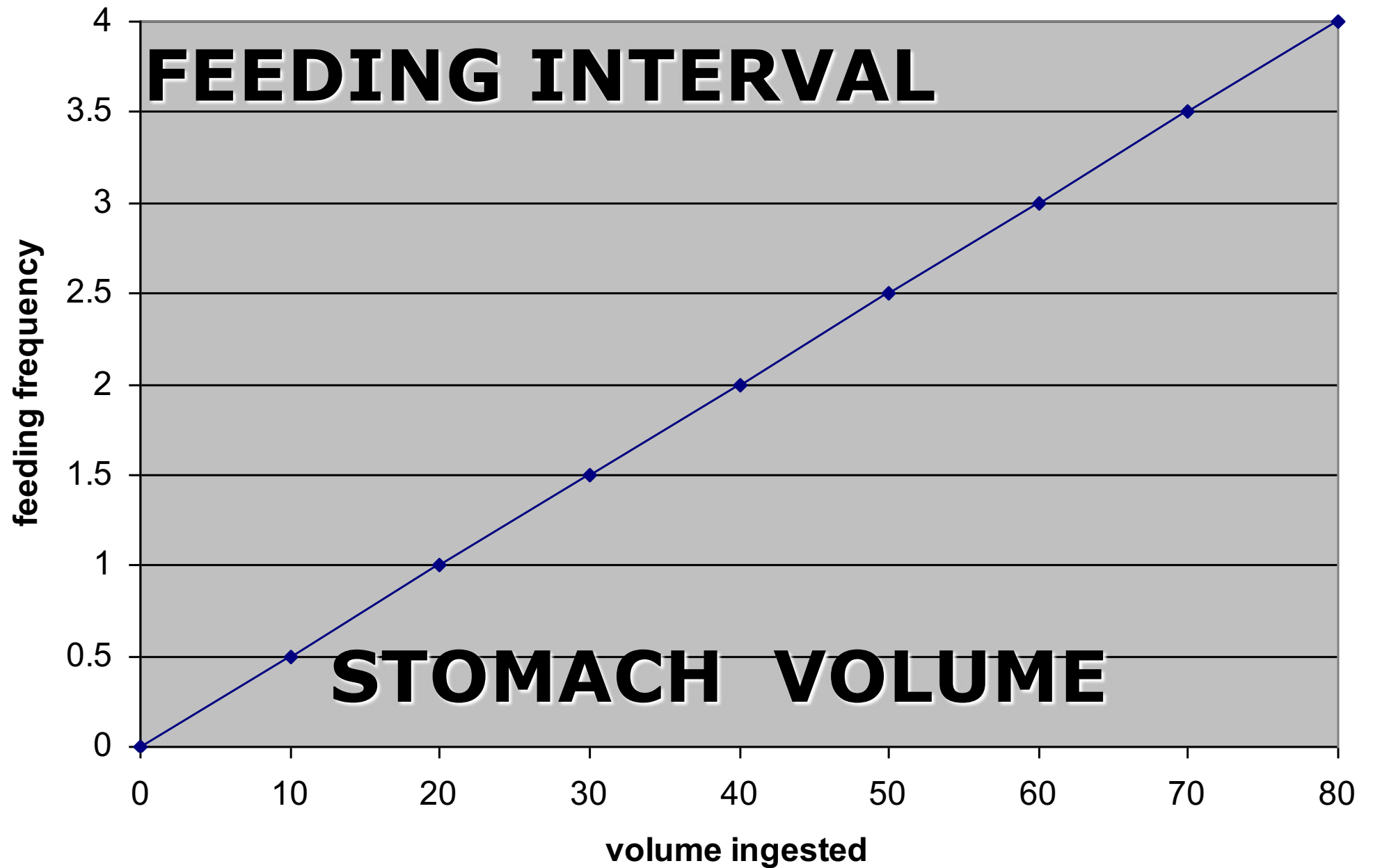
**NEVERTHELESS:**

**SOME  
FACTS →**

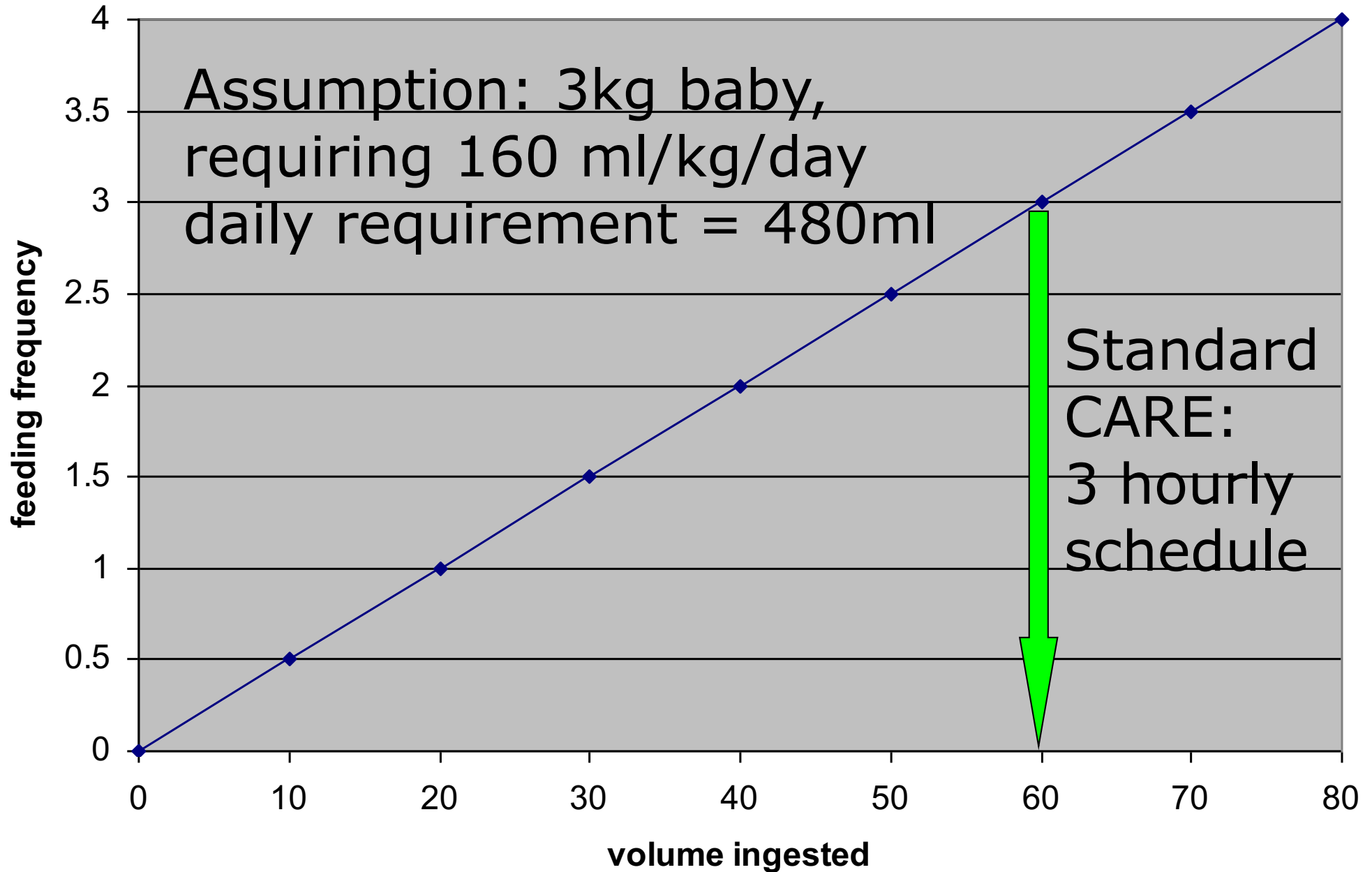
**$\frac{1}{\text{FEEDING  
INTERVAL}}$**

**STOMACH VOLUME**

# FEEDING INTERVAL



# STOMACH VOLUME



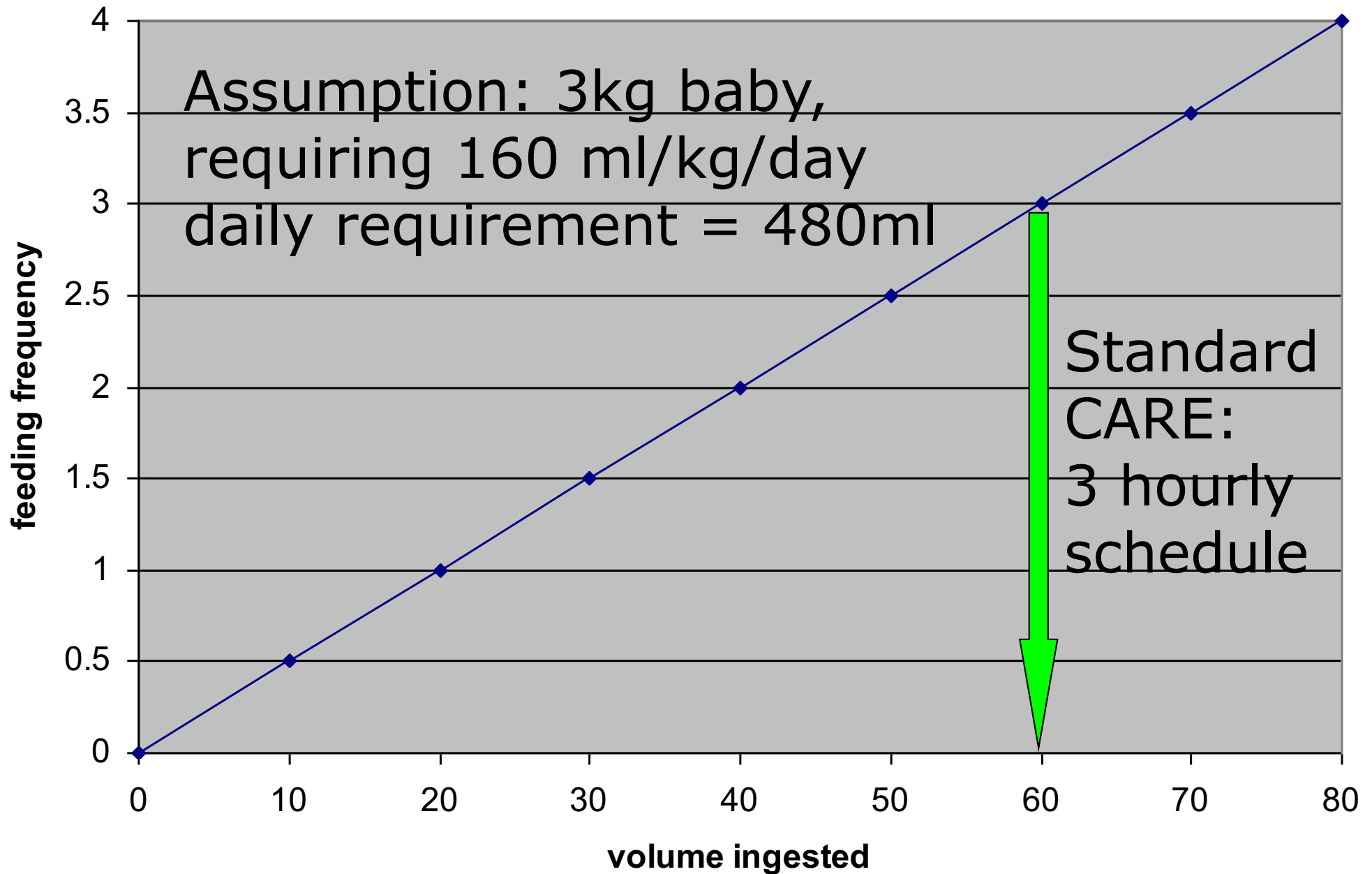
**KEY QUESTION:**  
**WHAT IS THE**  
**STOMACH**  
**VOLUME**  
**OF THE**  
**NEONATE ???**

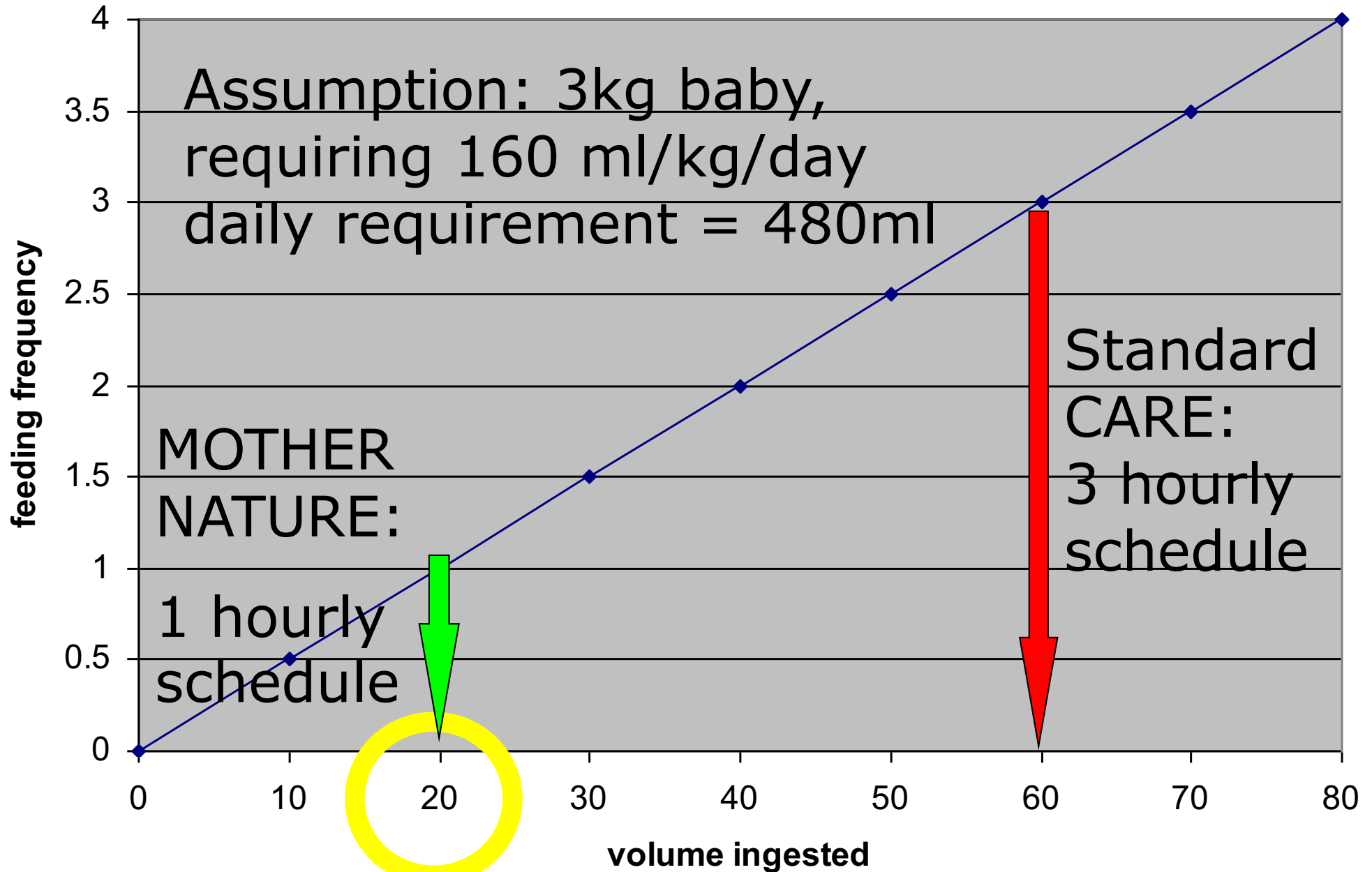
# EVIDENCE: (NBn 111009)

<u>Author</u>	<u>Capacity</u>	<u>Note:</u>
Sase	10-15 ml	Live, term fetus
Goldstein	10-15 ml	Live, term fetus
Widstrom	10 mls	Live, newborn
Zangen	20 mls	Live, (pressure)
Naveed	20 mls	Autopsy (SB)
	20 mls	Autopsy (ENND)
Kernessuk	15 mls	Autopsy (in situ)
Scammon (Alliot)	30-35 ml	Autopsy (water pressure)

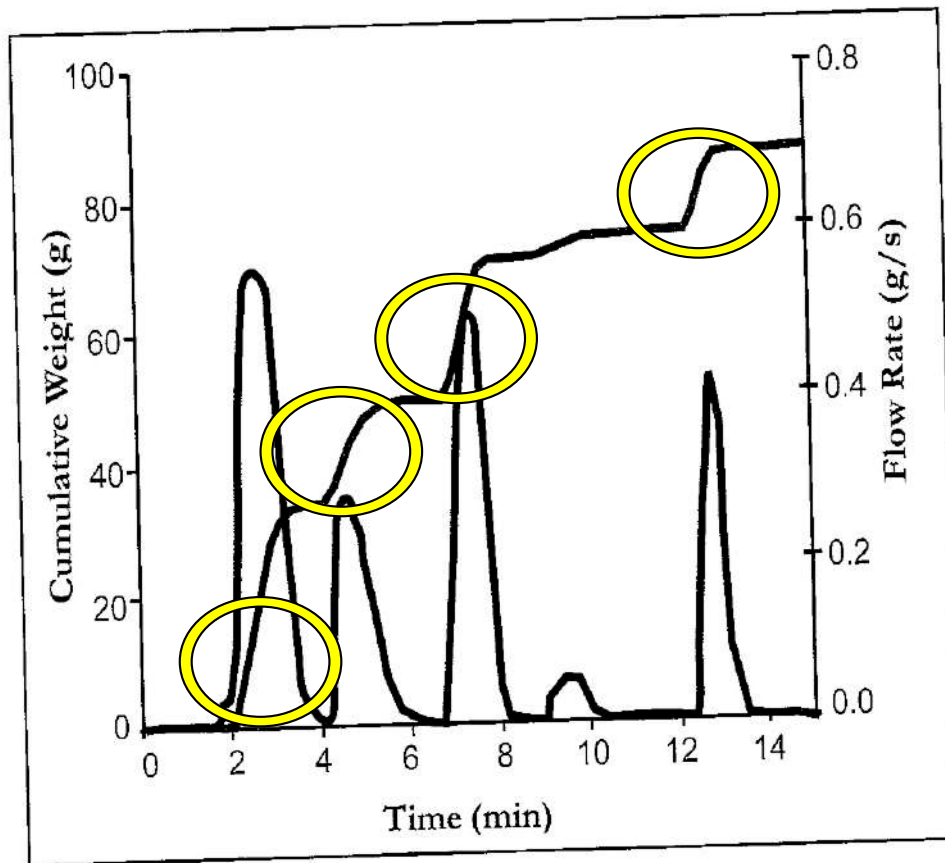
# PROPOSAL:

The CAPACITY of a neonate's stomach is **approx 20 ml.**  
**(7ml / kg)**









A single MER  
(milk ejection  
reflex)  
is 20 ml

Regardless of  
breast size,  
mammary gland  
tissue fairly  
constant

# AMYLIN peptide

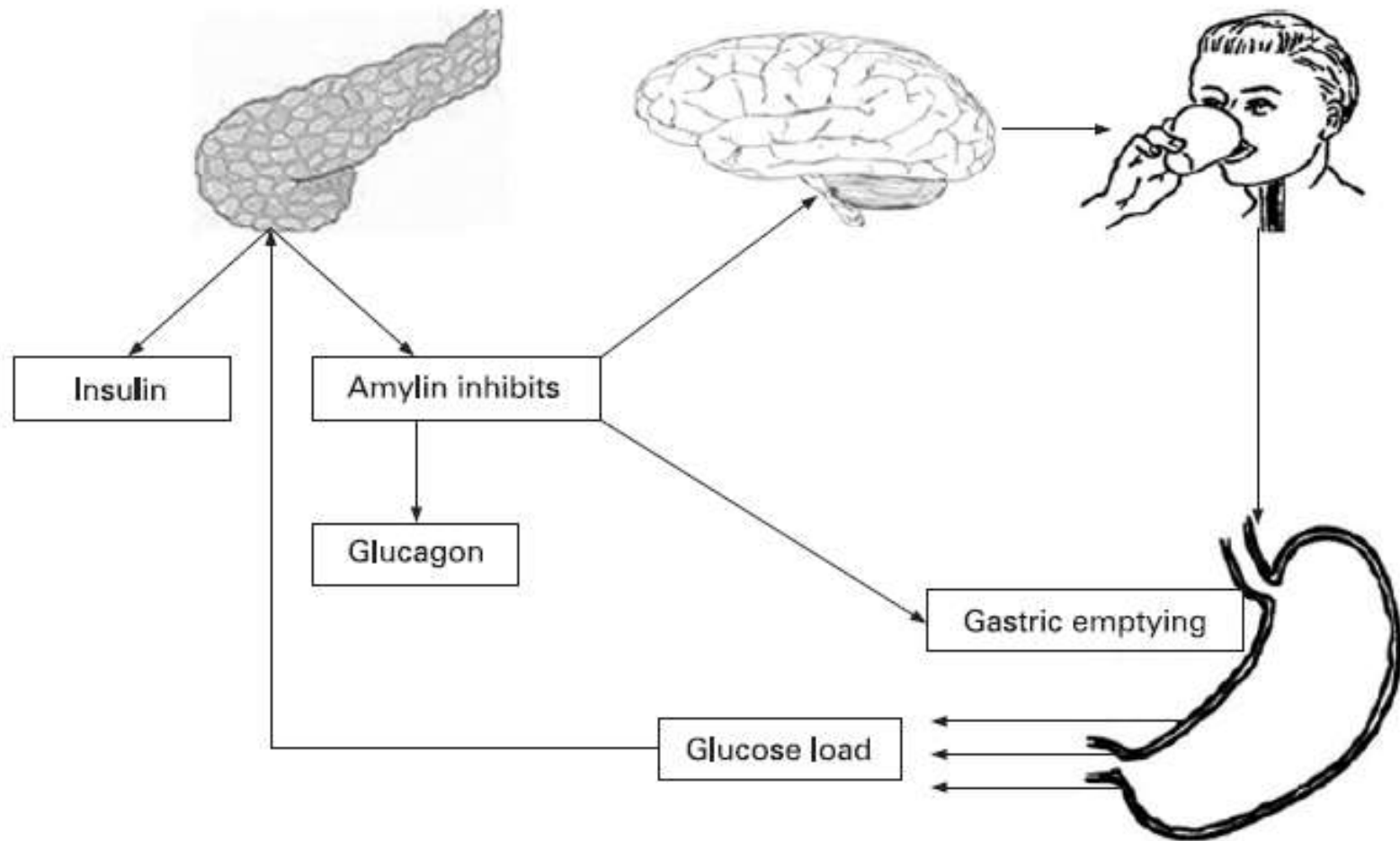
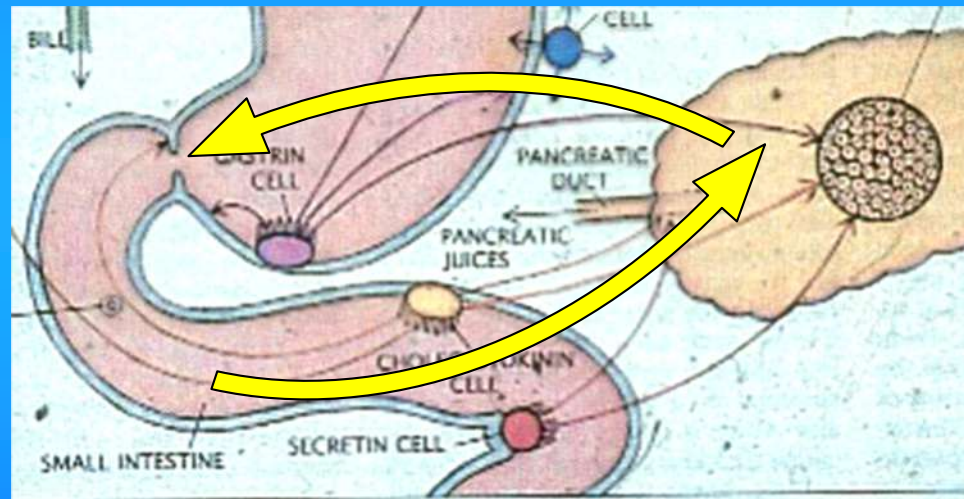


Figure 4 Proposed mechanism of action of amylin.

Kairamkonda 2008

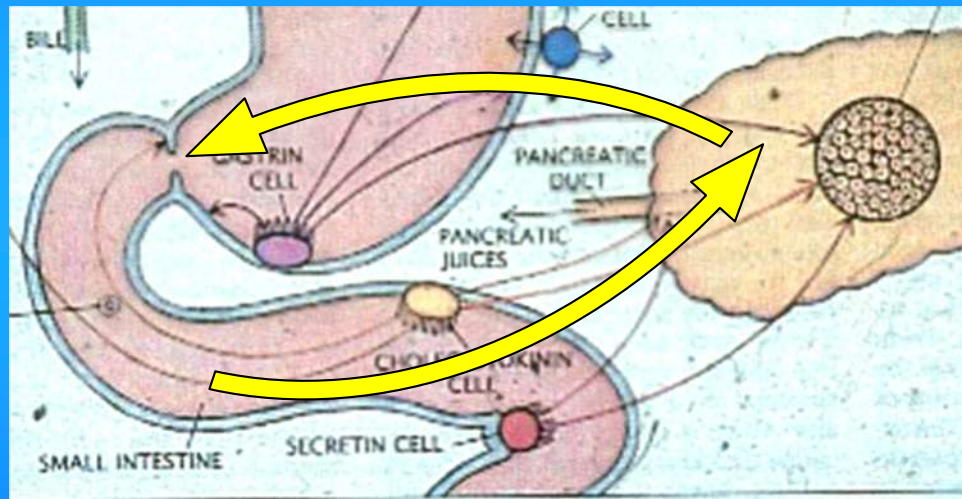
**AMYLIN  
released**



**Food in  
duodenum**

**Closes  
pylorus**

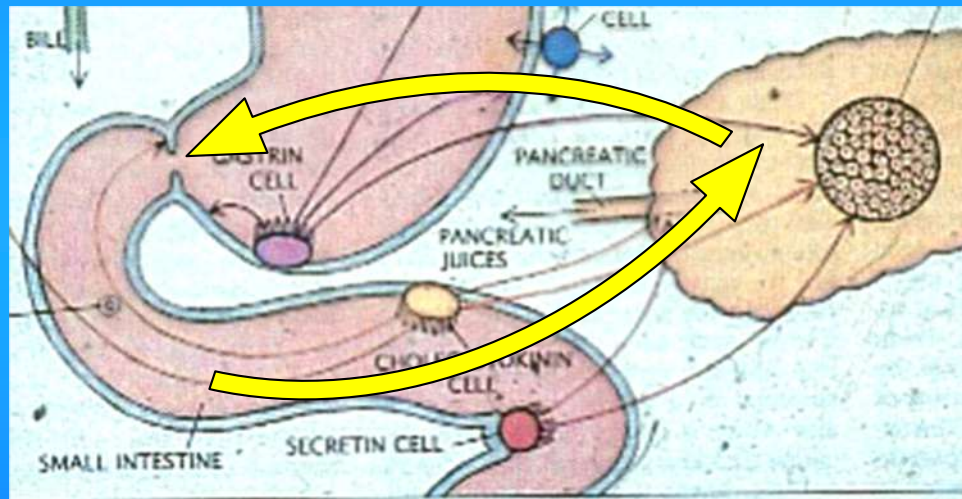
**AMYLIN  
released**



**Food in  
duodenum**

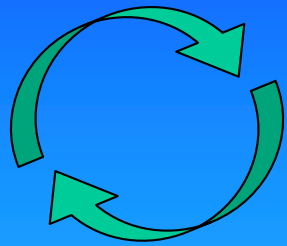
**Closes  
pylorus**

**AMYLIN  
released**



**Duodenum  
empty**

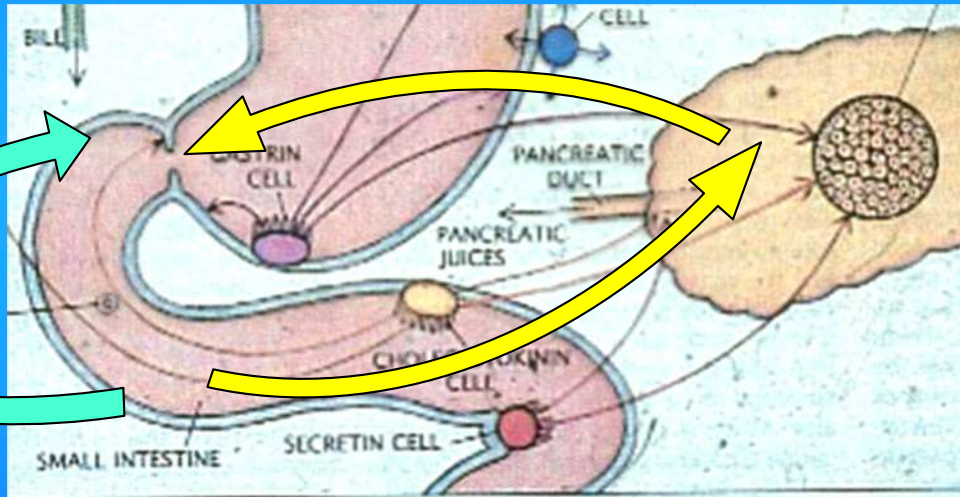
**Food in  
duodenum**



**Closes pylorus**

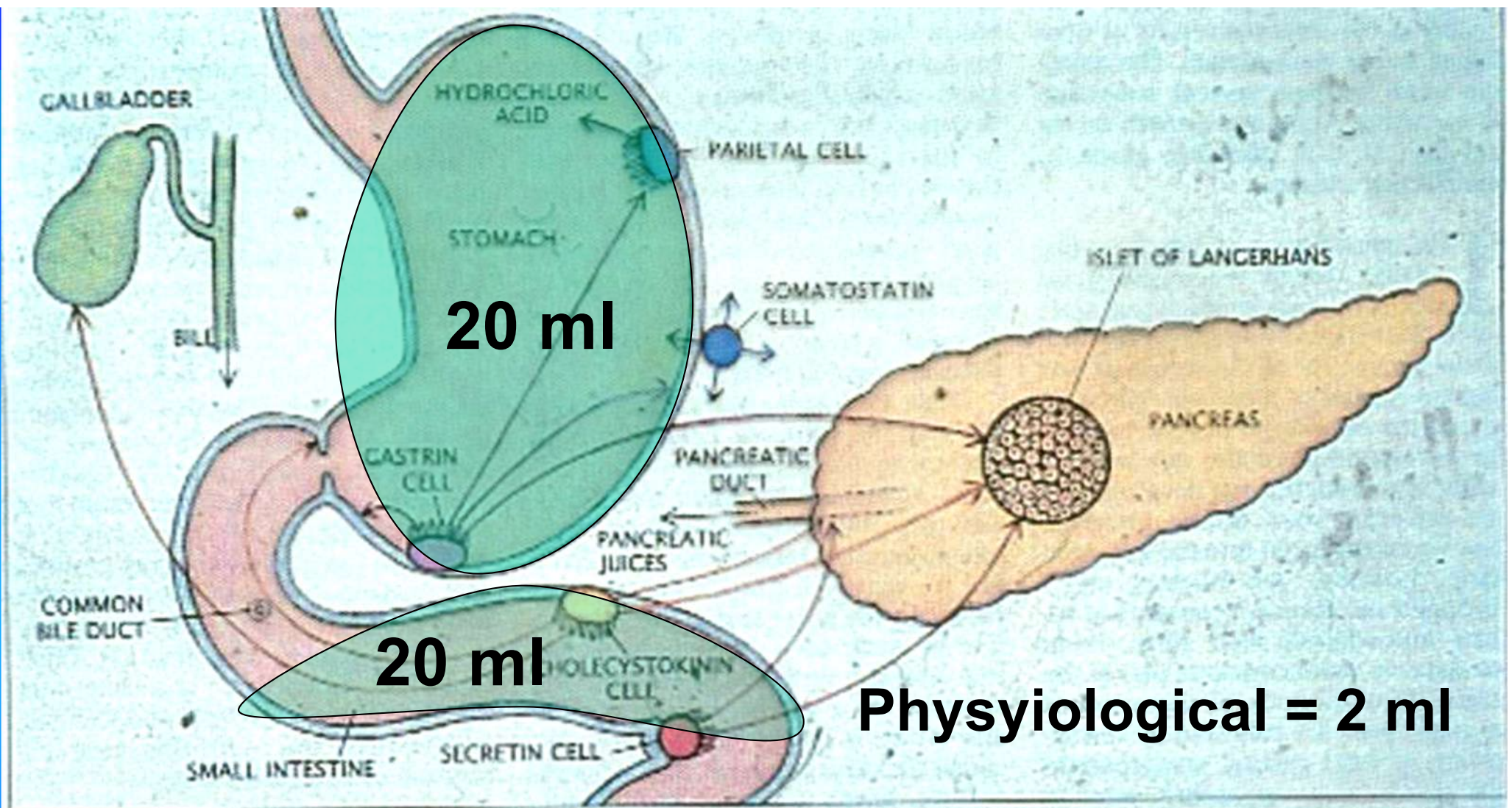
**AMYLIN released**

**Pylorus opens**



**Duodenum empty**

**Food in duodenum**

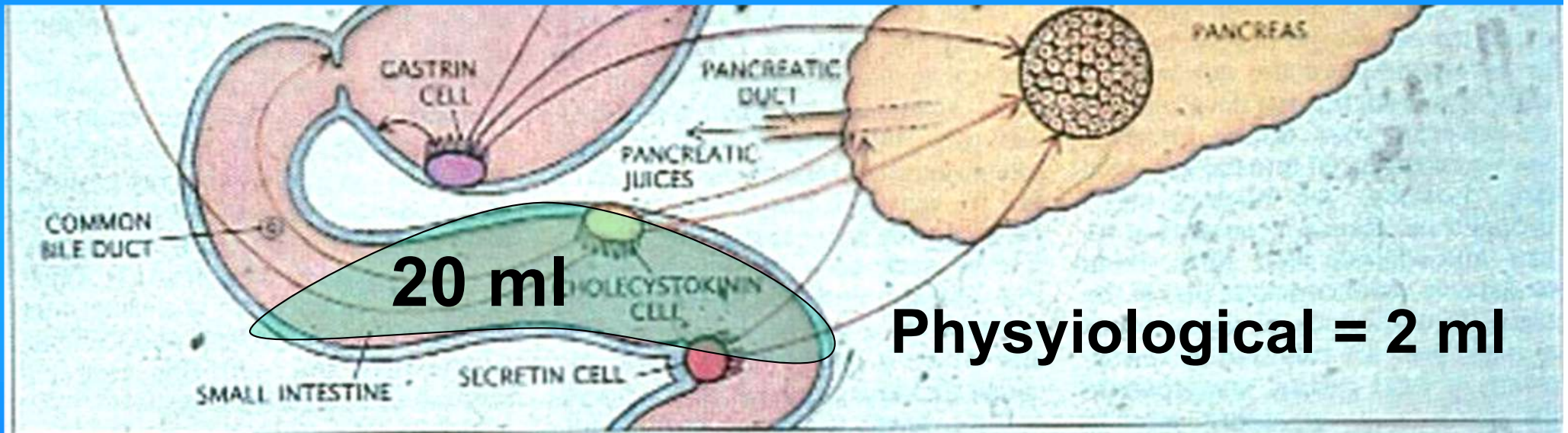


GASTROINTESTINAL HORMONES are secreted into the gut and the circulation by endocrine cells in the wall of the stomach and small intestine. Gastrin, cholecystikinin and secretin enhance pancreatic insulin secretion. Gastrin also stimulates release of hydrochloric acid, growth of mucosal cells and gas-

tric motility. Cholecystikinin slows emptying of the stomach and stimulates discharge of bile from the gallbladder and secretion of digestive enzymes by the pancreas; secretin stimulates pancreatic bicarbonate secretion. Somatostatin inhibits secretion of gut hormones and counteracts their effects.

# Amylin peptide is increased in preterm neonates with feed intolerance

V R Kairamkonda,<sup>1</sup> A Deorukhkar,<sup>2</sup> C Bruce,<sup>3</sup> R Coombs,<sup>2</sup> R Fraser,<sup>3</sup> A-P T Mayer<sup>4</sup>



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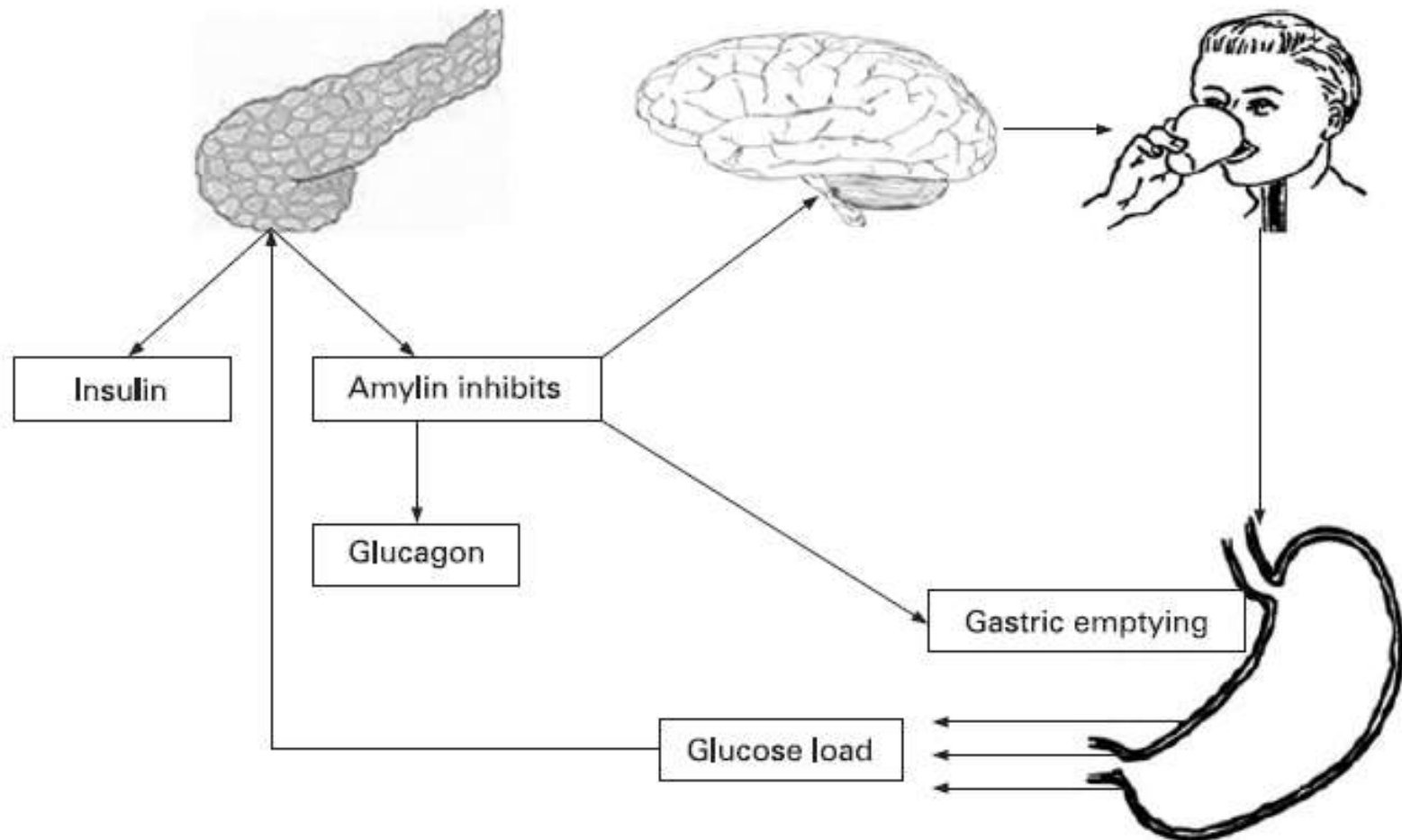


Figure 4 Proposed mechanism of action of amylin.

Kairamkonda 2008

Amylin peptide is increased in preterm neonates with feed intolerance

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**“Feed intolerance” ...  
... or VOLUME intolerance?**

**2 - 3 hourly feeds are  
not physiological ...  
... not pleasurable**

# CONTINUOUS FEEDING PROMOTES GASTROINTESTINAL TOLERANCE AND GROWTH IN VERY LOW BIRTH WEIGHT INFANTS

ANN DSILNA, RN, BASc, KYLLIKE CHRISTENSSON, RNM, PhD, LARS ALFREDSSON, PhD, HUGO LAGERCRANTZ, MD, PhD,  
AND MATS BLENNOW, MD, PhD

In VLBW infants, continuous feeding seems to be better than intermittent feeding with regard to gastrointestinal tolerance and growth.

(J Pediatr 2005;147:43-9)

# CONTINUOUS FEEDING PROMOTES GASTROINTESTINAL TOLERANCE AND GROWTH IN VERY LOW BIRTH WEIGHT INFANTS

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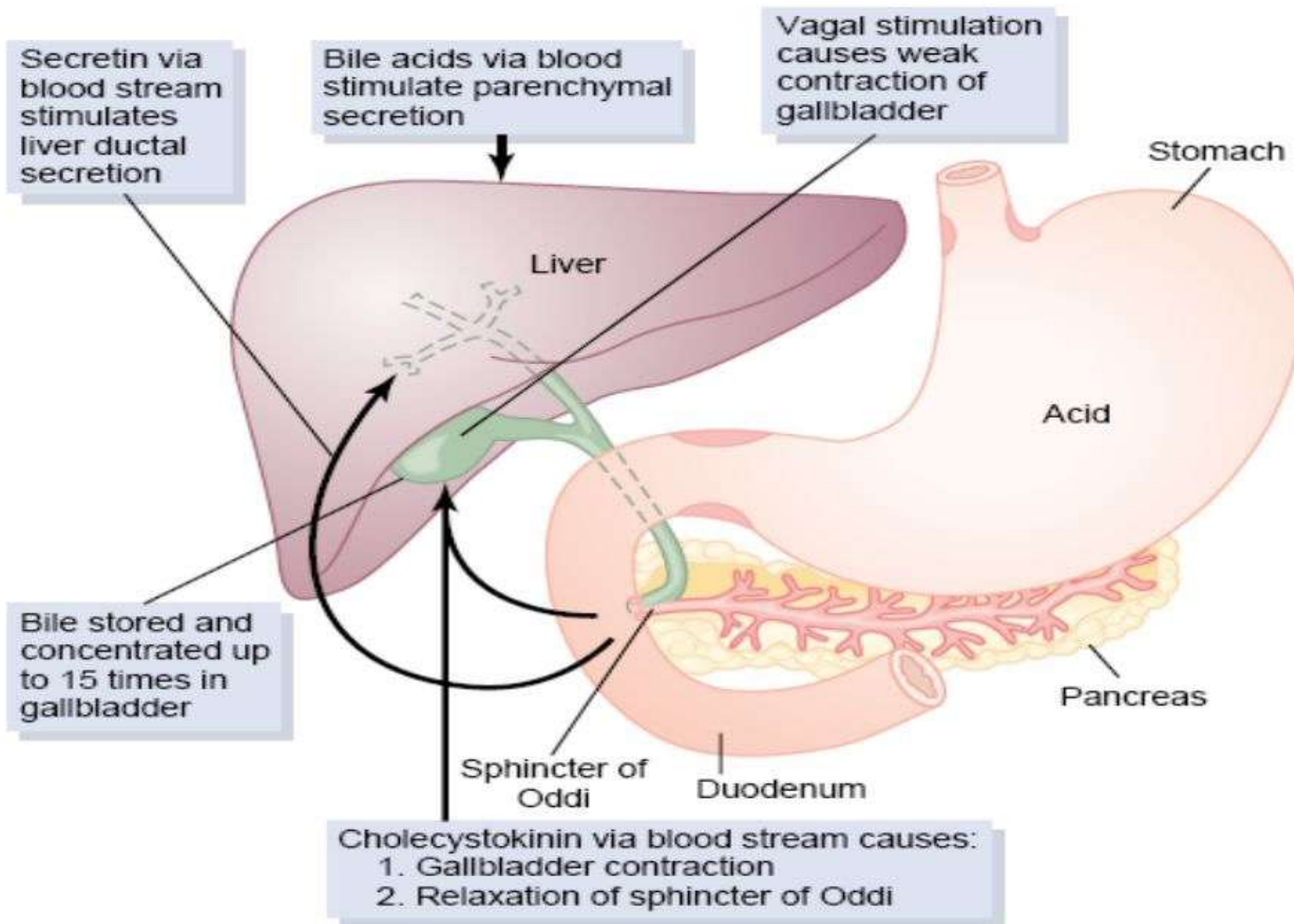
In VLBW infants, continuous feeding seems to be better than intermittent feeding with regard to gastrointestinal tolerance and growth.

(J Pediatr 2005;147:43-9)

**no rhythmicity ...**

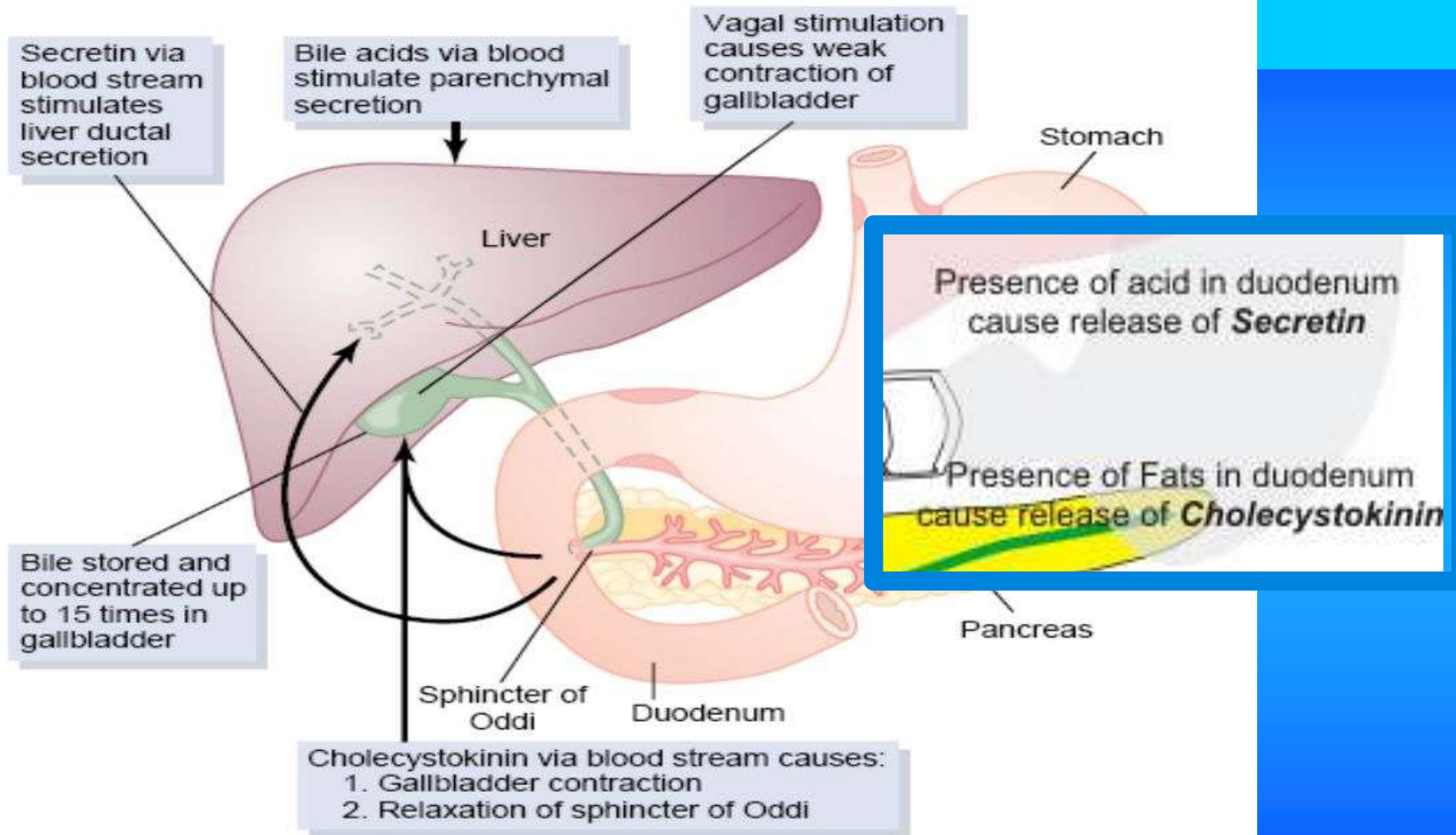
**how physiological is this ???**

# Liver secretion and gallbladder emptying.



**how physiological is this ???**

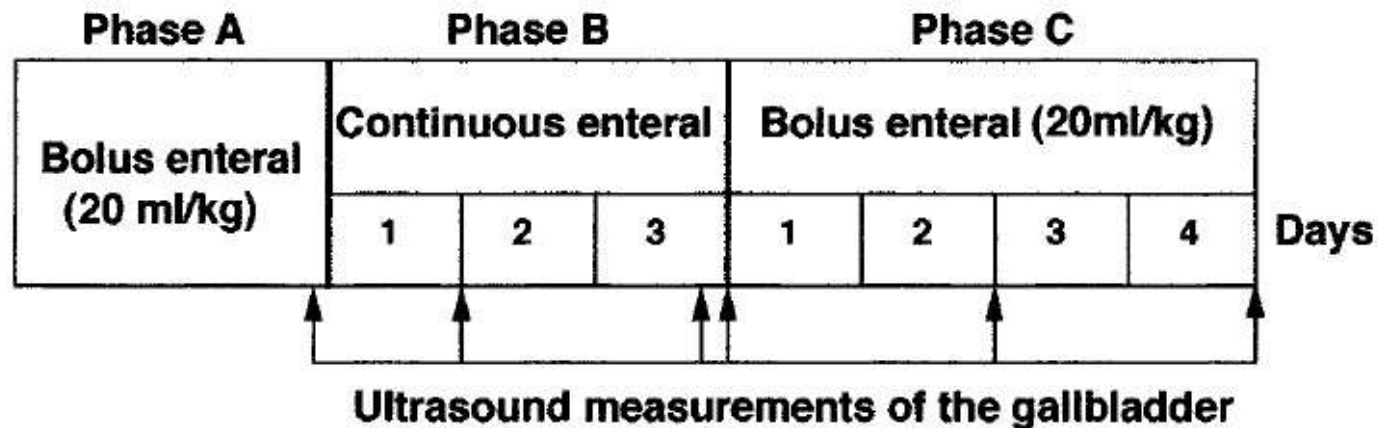
# Liver secretion and gallbladder emptying.



**how physiological is this ???**

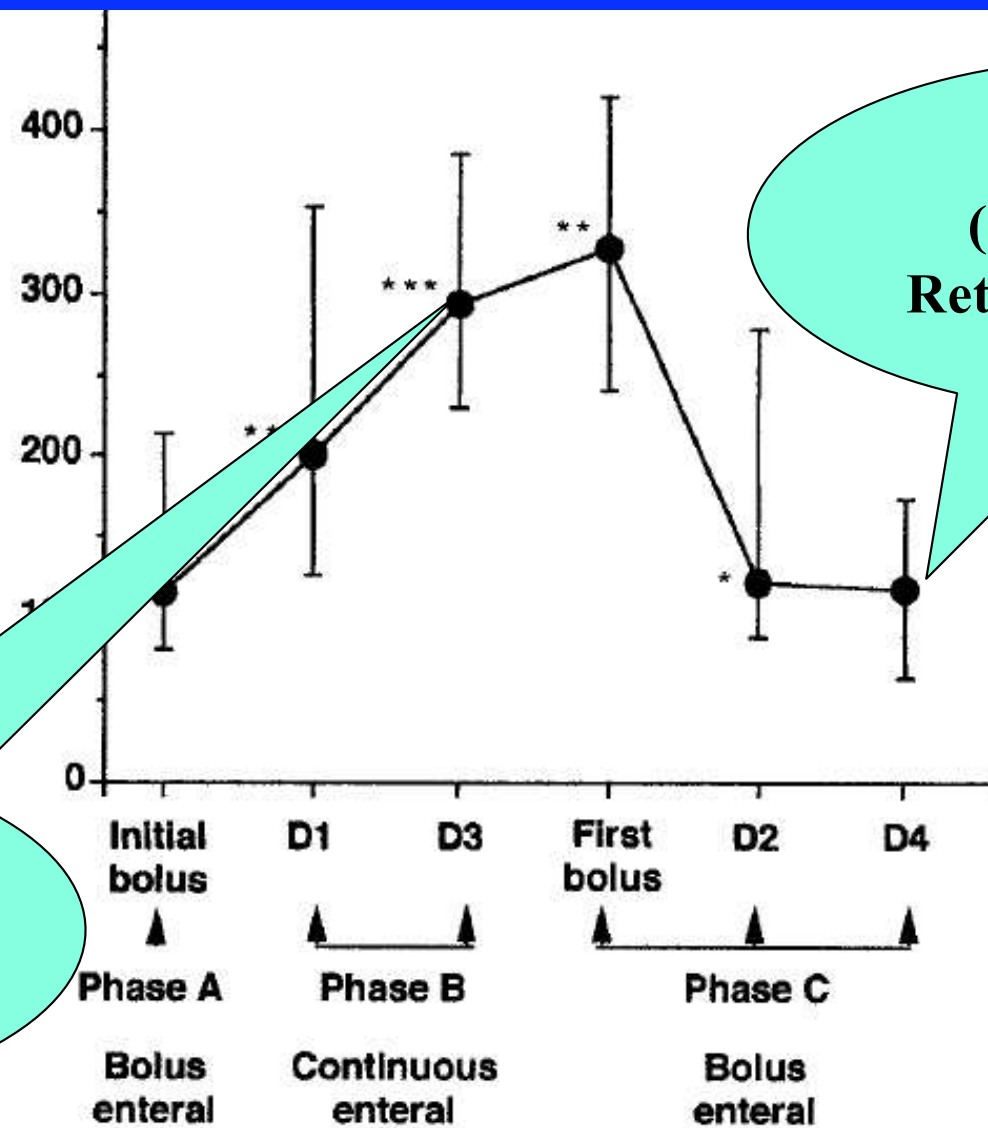
# Continuous enteral feeding impairs gallbladder emptying in infants

*Girish Jawaheer, FRCS, Nigel J. Shaw, MD, MRCP, and Agostino Pierro, MD, FRCS*



*Fig 1.* Study design. In phase A, infants received bolus enteral feeds. In phase B, bolus feeds were stopped and replaced with continuous enteral feeds for 3 days. In phase C, bolus enteral feeds were resumed. Ultrasound measurements of gallbladder were made at time of last bolus feed in phase A, after 1 and 3 days of phase B, after first resumed bolus feed, and after 2 and 4 days of phase C.

Gallbladder volume (mm<sup>3</sup>)

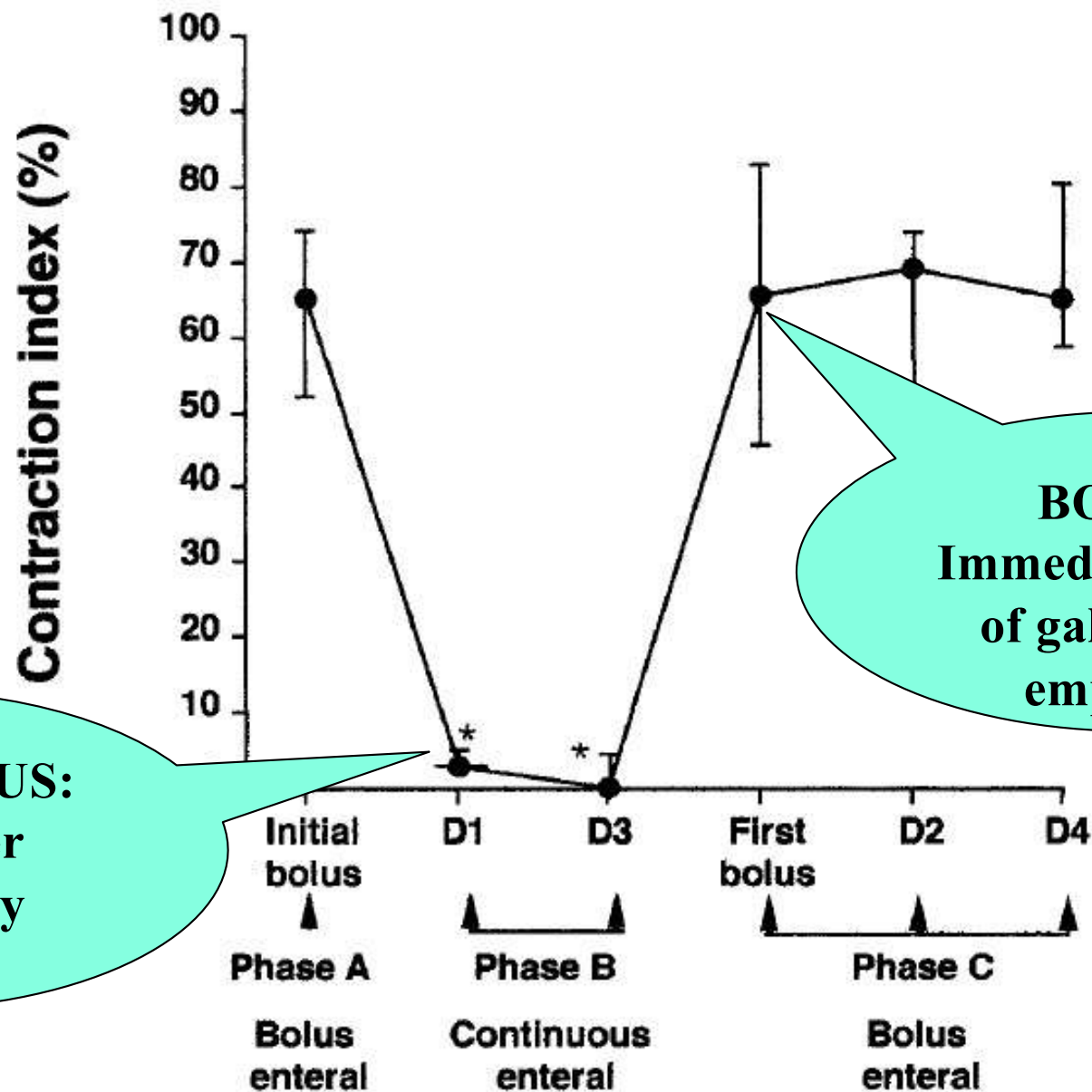


**BOLUS:**  
( 2-4 hourly)  
Return to normal  
in 4 days.

**CONTINUOUS:**  
2.6-fold increase  
gallbladder volume

*Fig 2.* Effect of continuous enteral feeding on gallbladder volume. Continuous enteral feeding in phase B causes 2.6-fold increase in gallbladder volume, compared with phase A. Resumption of bolus feeds in phase C causes gallbladder volume to return to normal within 4 days. Results are expressed as median. Error bars indicate interquartile range. Prefix D indicates experimental day. (\*\*\* $P < .001$ ; \* $P < .01$ ; \* $P < .05$  compared with phase A).





**CONTINUOUS:**  
Gallbladder  
contractility  
impaired

**BOLUS:**  
Immediate return  
of gallbladder  
emptying.

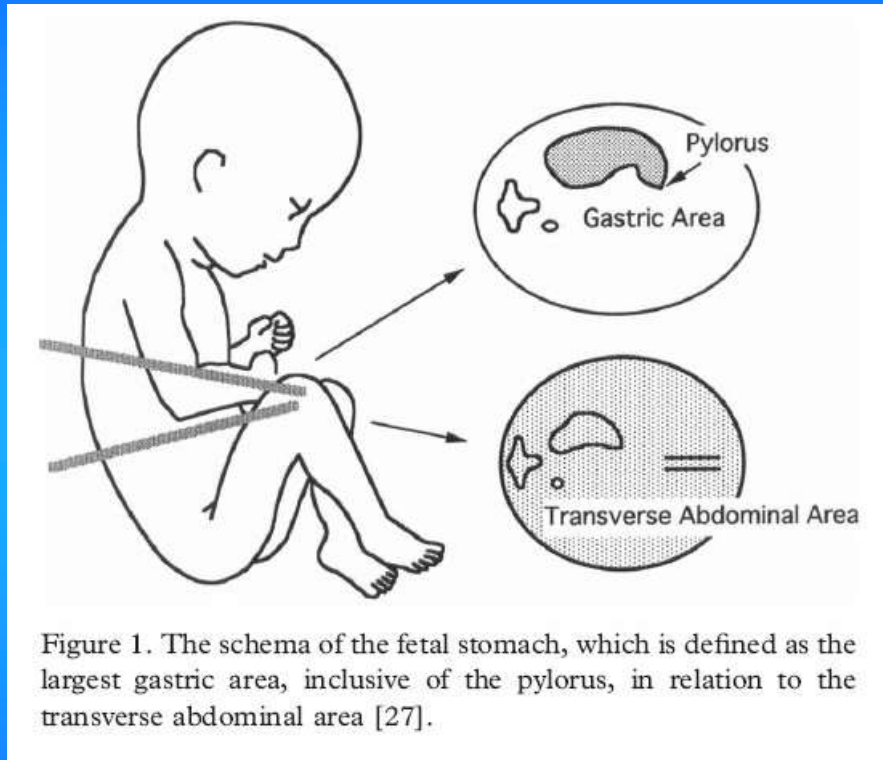
*Fig 3.* Effect of continuous enteral feeding on contraction index. Gallbladder contractility is impaired during continuous enteral feeding in phase B. Resumption of bolus feeds in phase C causes immediate return of normal gallbladder emptying. Results are expressed as median. Prefix D indicates experimental day. (\* $P < .001$  compared with phase A).

# Continuous enteral feeding impairs gallbladder emptying in infants

*Girish Jawaheer, FRCS, Nigel J. Shaw, MD, MRCP, and Agostino Pierro, MD, FRCS*

... it can be inferred that the continuous feeding modality, enteral or parenteral, may play a role in inducing stasis in the extrahepatic biliary tree.

# “Ontogeny of gastric emptying patterns in the human fetus”



**note rhythmicity  
of fetal stomach**

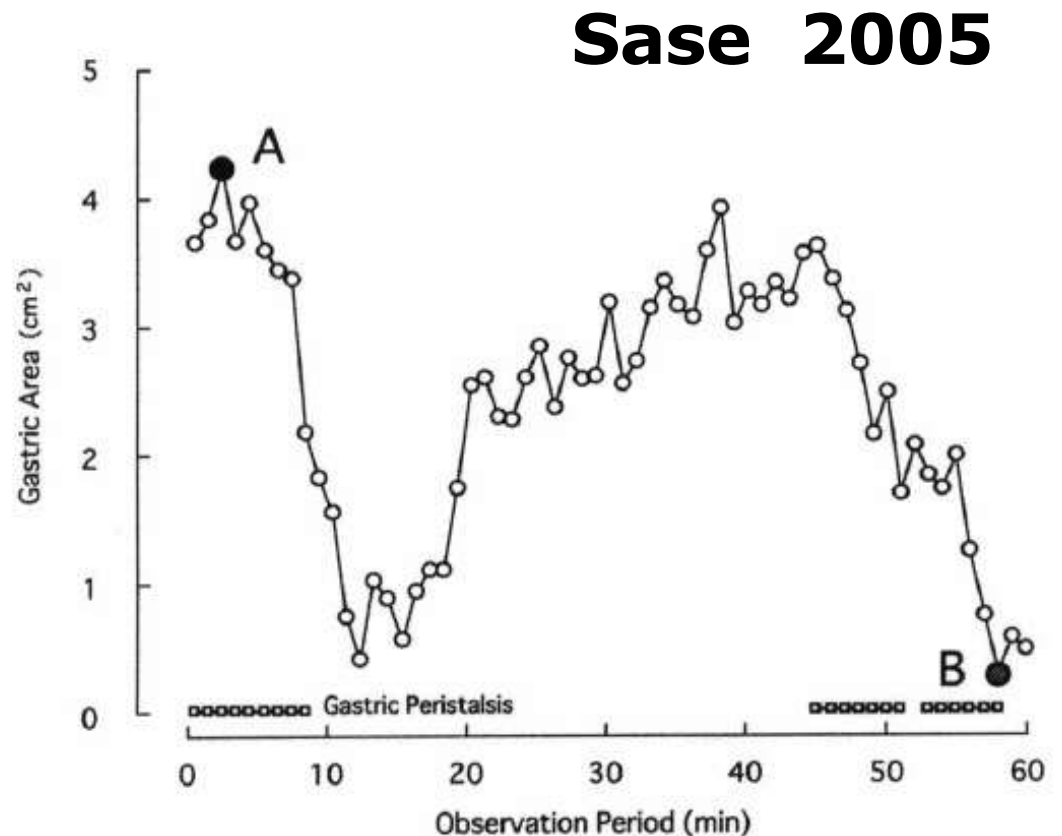
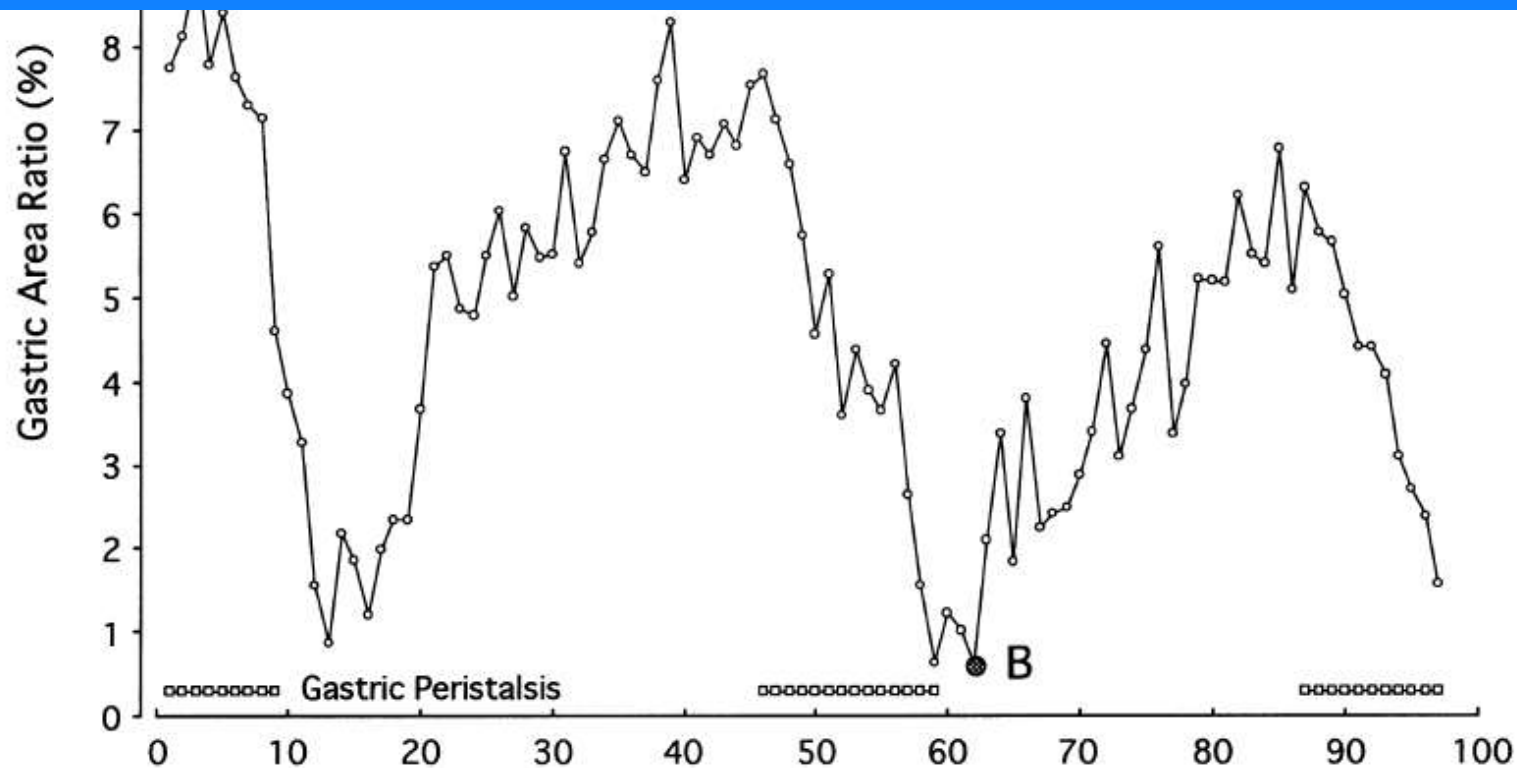


Figure 2. Changes of gastric area in a representative fetus at 33 weeks of gestation, in association with gastric peristalsis. The maximum gastric area (A) and the minimum gastric area (B) [27].

12 - 15 ml volumes at term.



note rhythmicity  
of fetal stomach → 40 - 50 minutes

Pleasurable feeding  
- and sleeping -  
a physiological rhythm for  
premature infants.



note rhythmicity  
of fetal stomach → 40 - 50 minutes

Pleasurable feeding  
- and sleeping -  
a physiological rhythm for  
premature infants.



Sleep cycling → 50 - 70 minutes

note rhythmicity  
of fetal stomach → 40 - 50 minutes

# Gastric overfilling syndrome?

## Excessive volumes

reflux, aspiration, colic

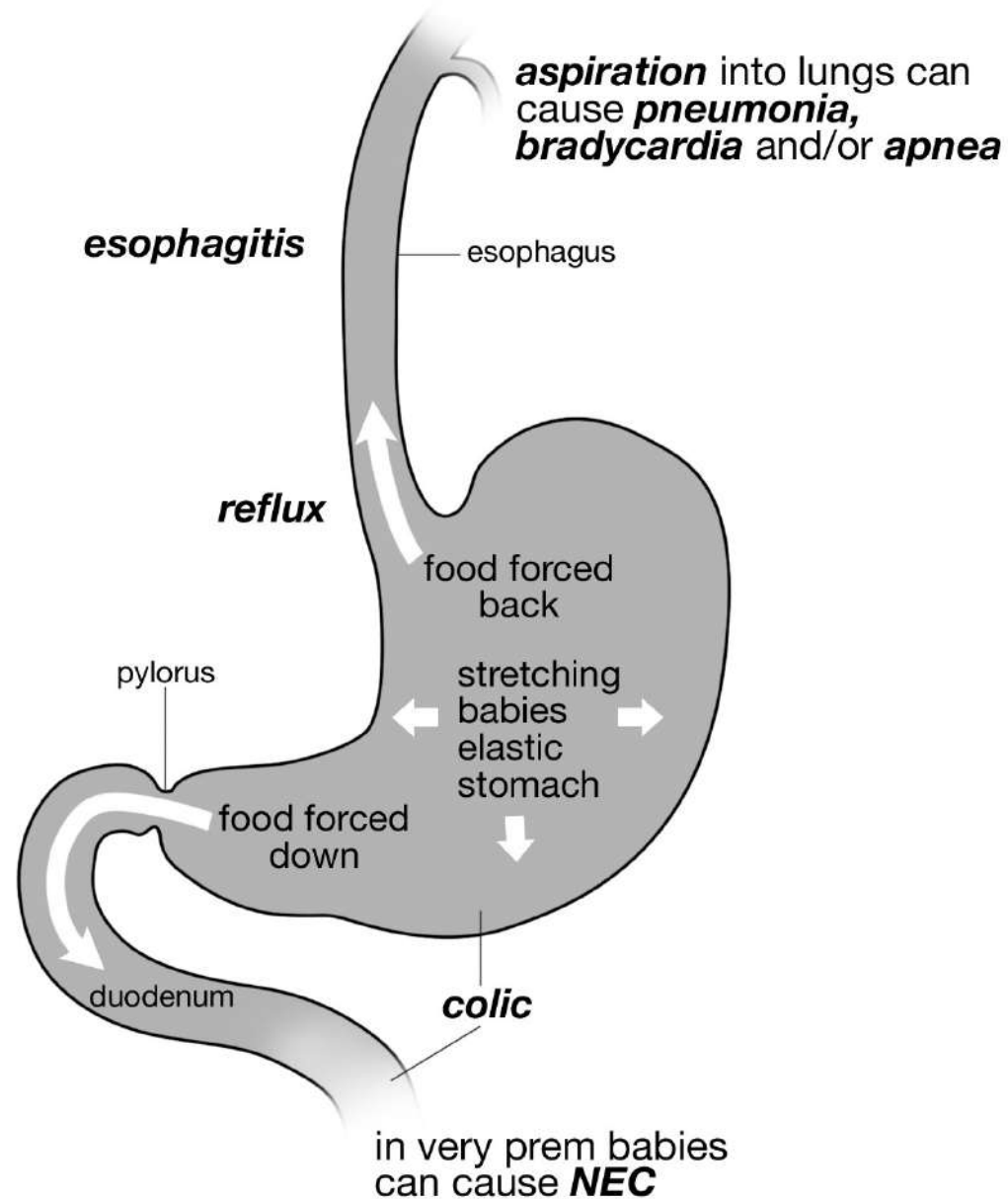
## Excessive time interval

hypoglycaemia

## Adaptations

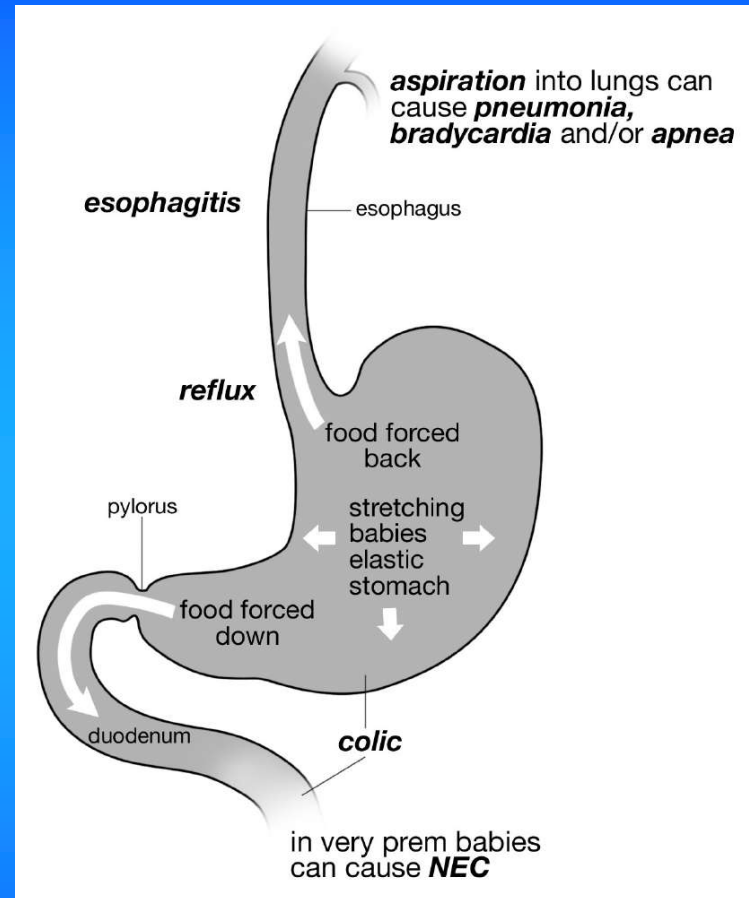
diabetic diathesis, obesity

# Gastric overfilling syndrome?





# Gastric overfilling syndrome?

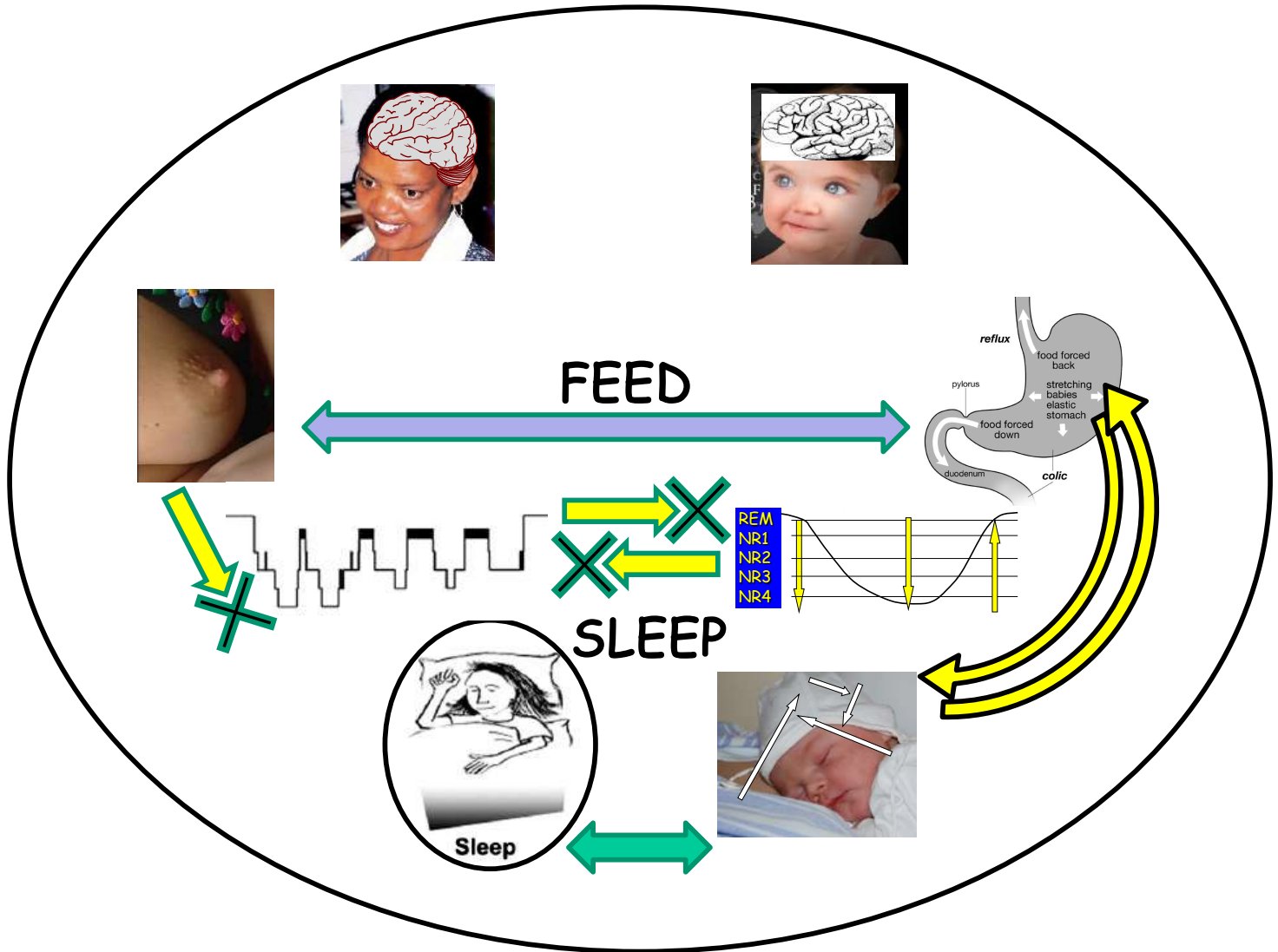


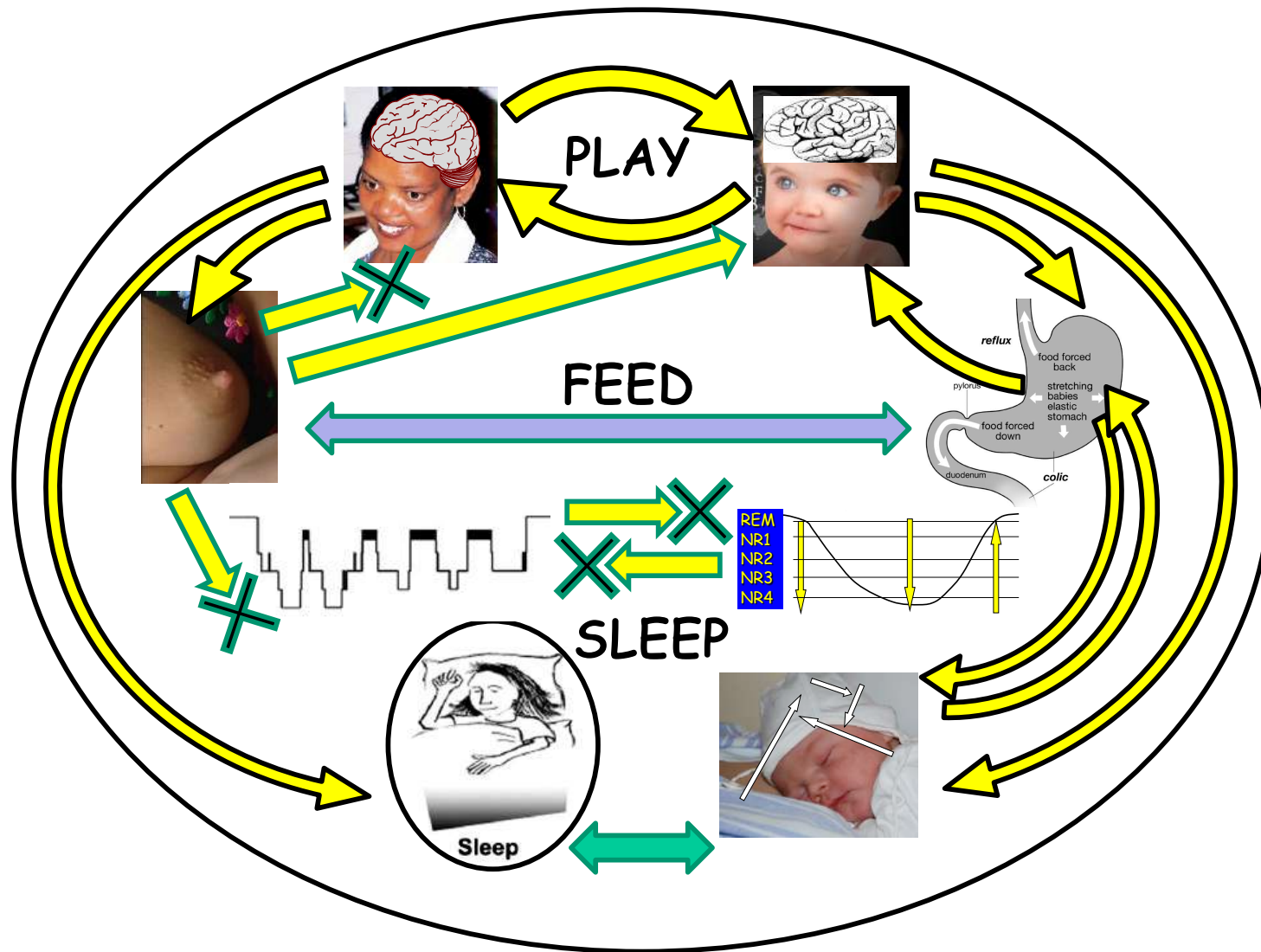
**Proposed Management →**

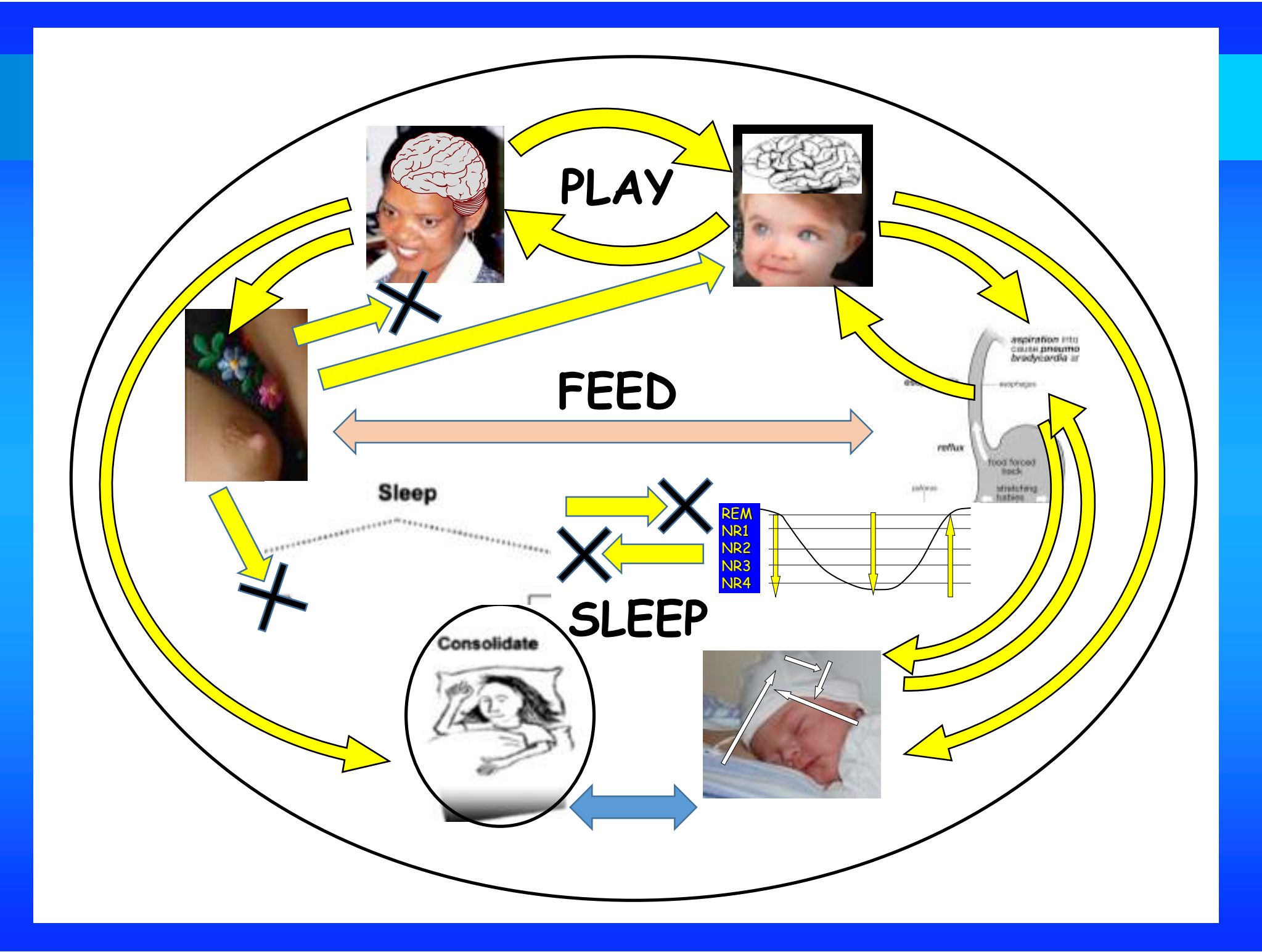


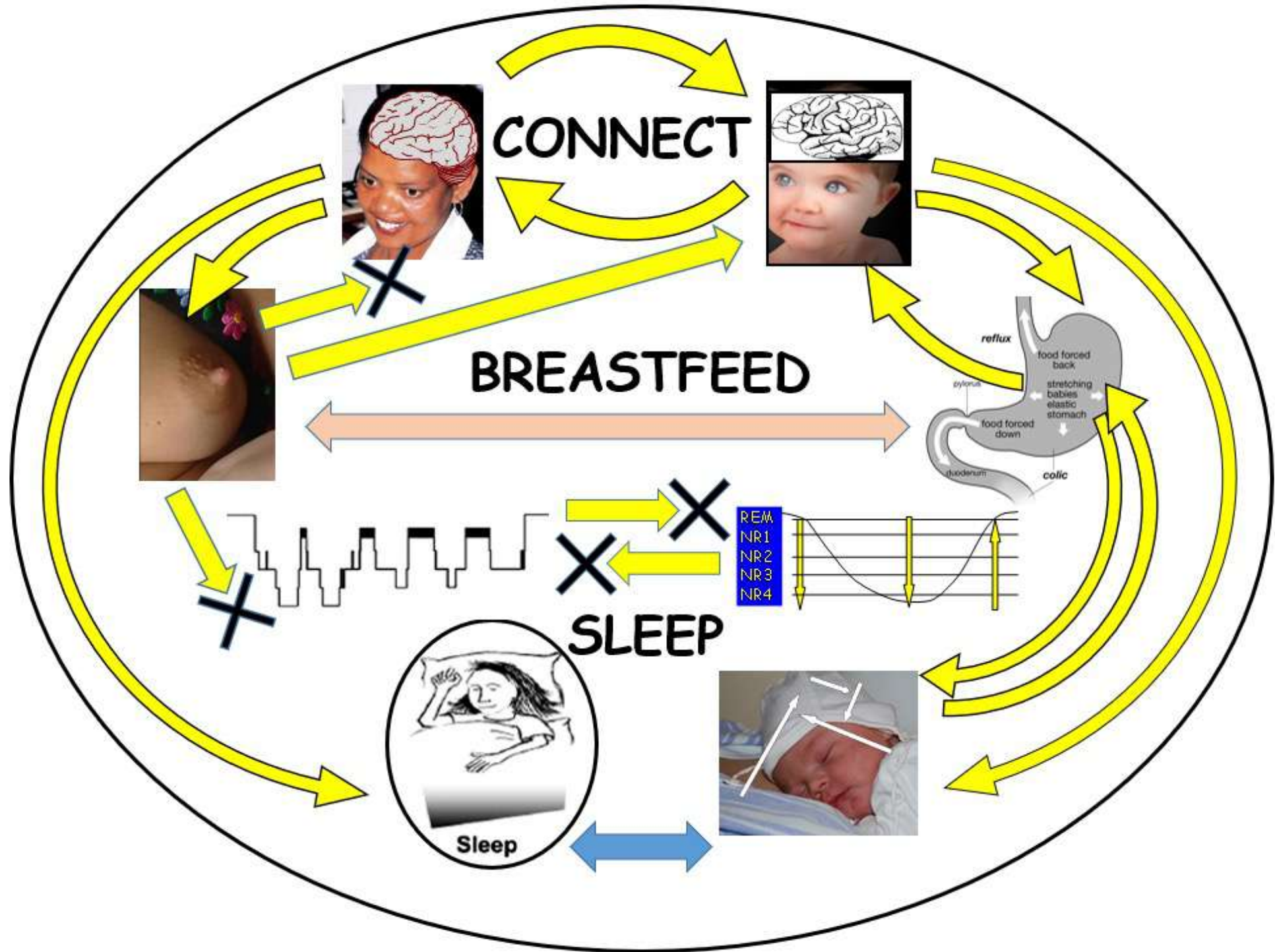
SLEEP







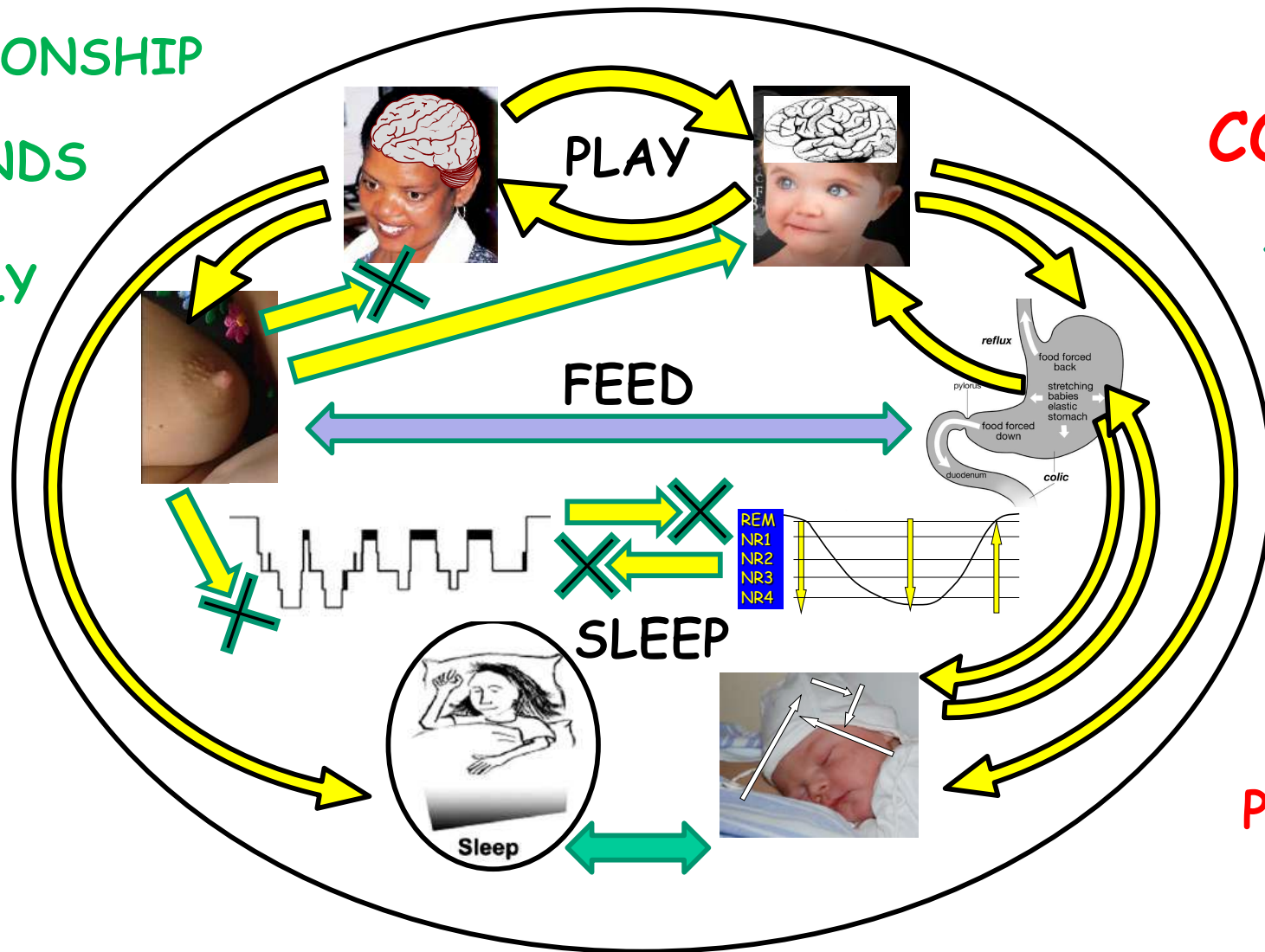




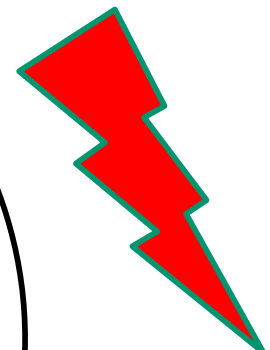
RELATIONSHIP

FRIENDS

FAMILY



CONTROL

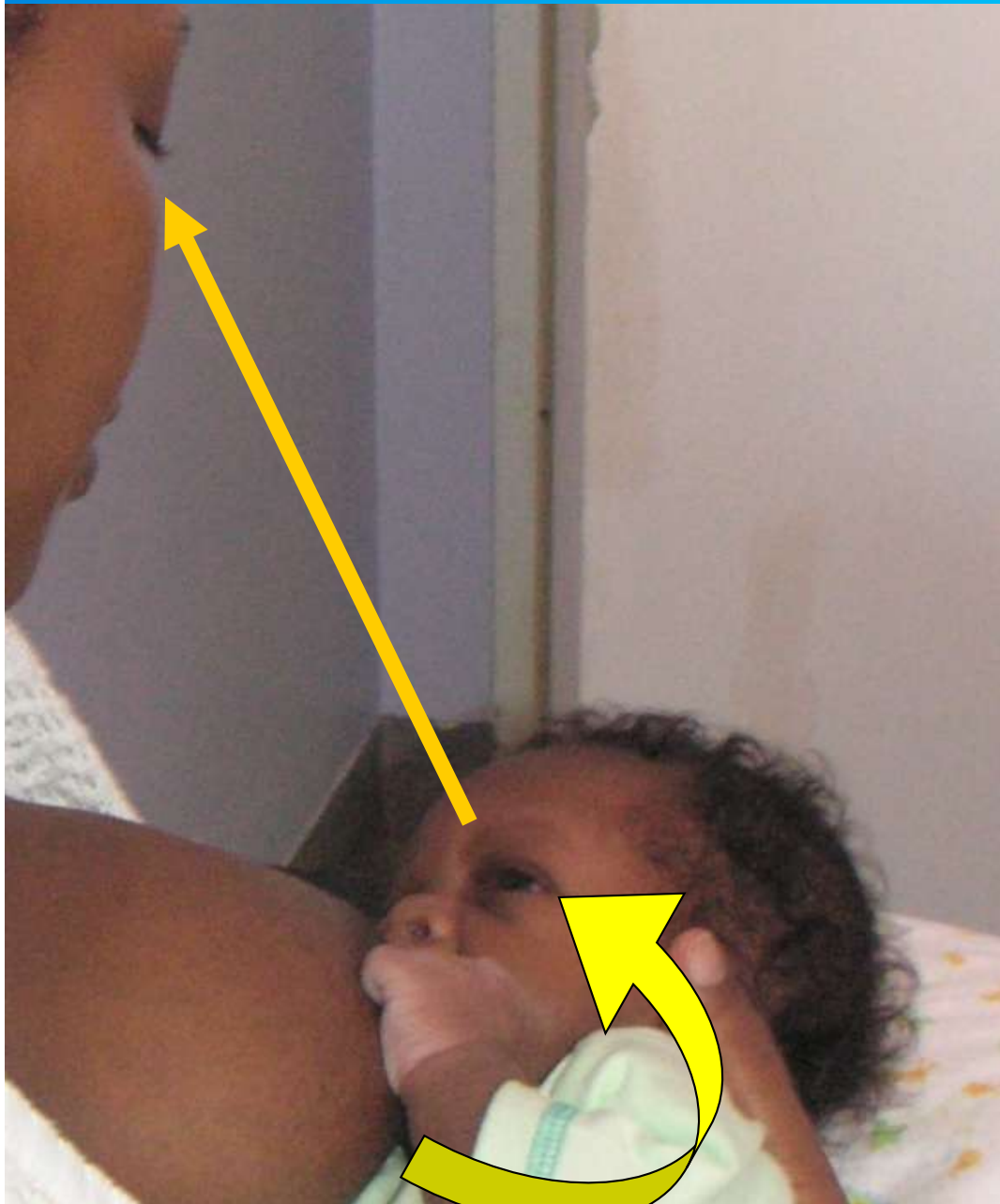


TOYS

WORK

PACIFIER

Consolidation of dyadic lifestyle leads to emotional and social competence



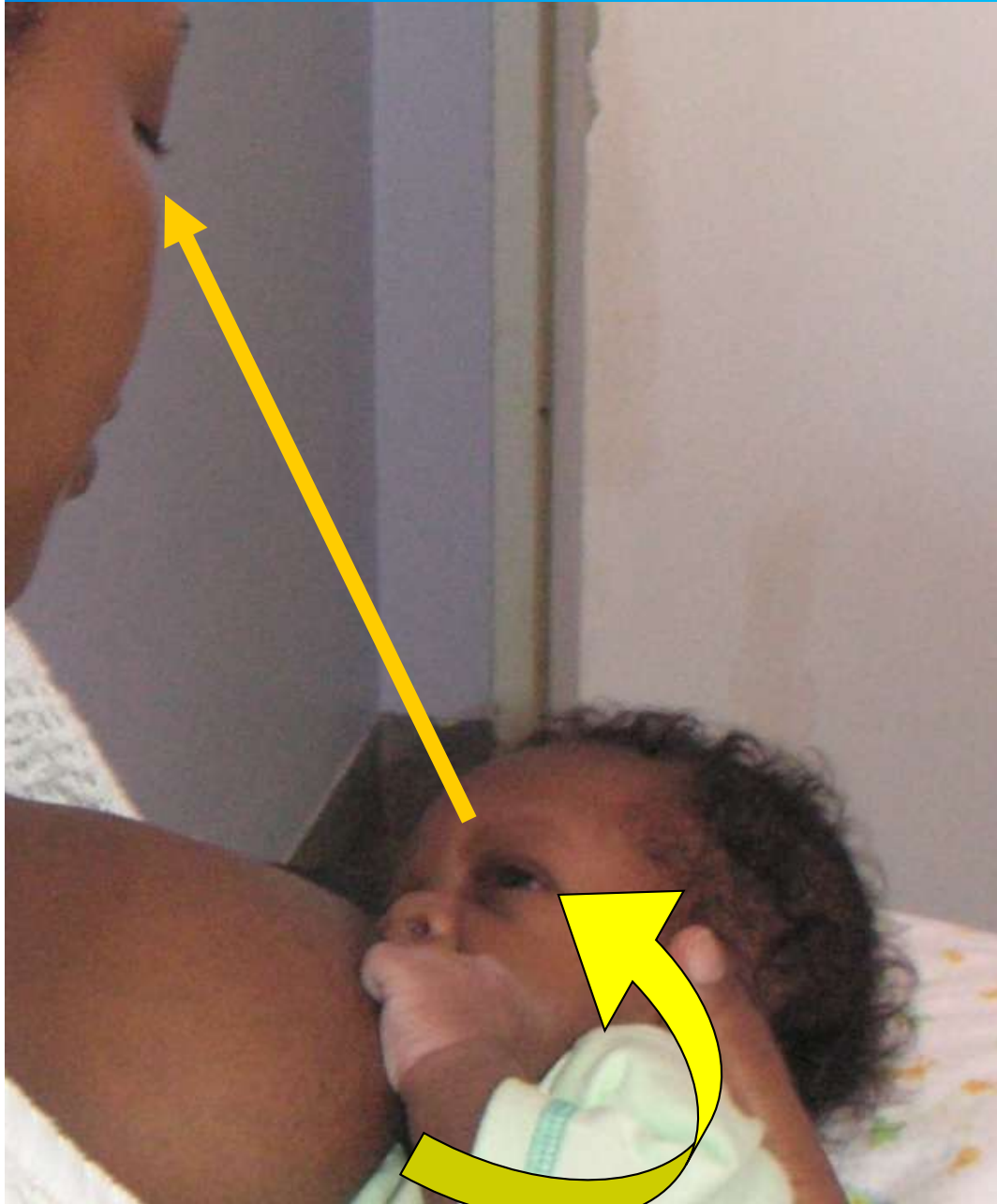
Amygdala



SSC

*says "mother"*





PFOC



Amygdala *says "safe"*



SSC *says "mother"*



Visual  
cortex



PFOC

*says "approach"*



Amygdala

*says "safe"*



SSC

*says "mother"*



Eyes

Visual  
cortex

PFOC

Amygdala

SSC

*says "open eyes"*

*says "approach"*

*says "safe"*

*says "mother"*



Eyes *says "contact"*

Visual cortex *says "open eyes"*

PFOC *says "approach"*

Amygdala *says "safe"*

SSC *says "mother"*

# Neural circuitry of bonding

Eyes

*says "contact"*

Visual  
cortex

*says "open eyes"*

PFOC

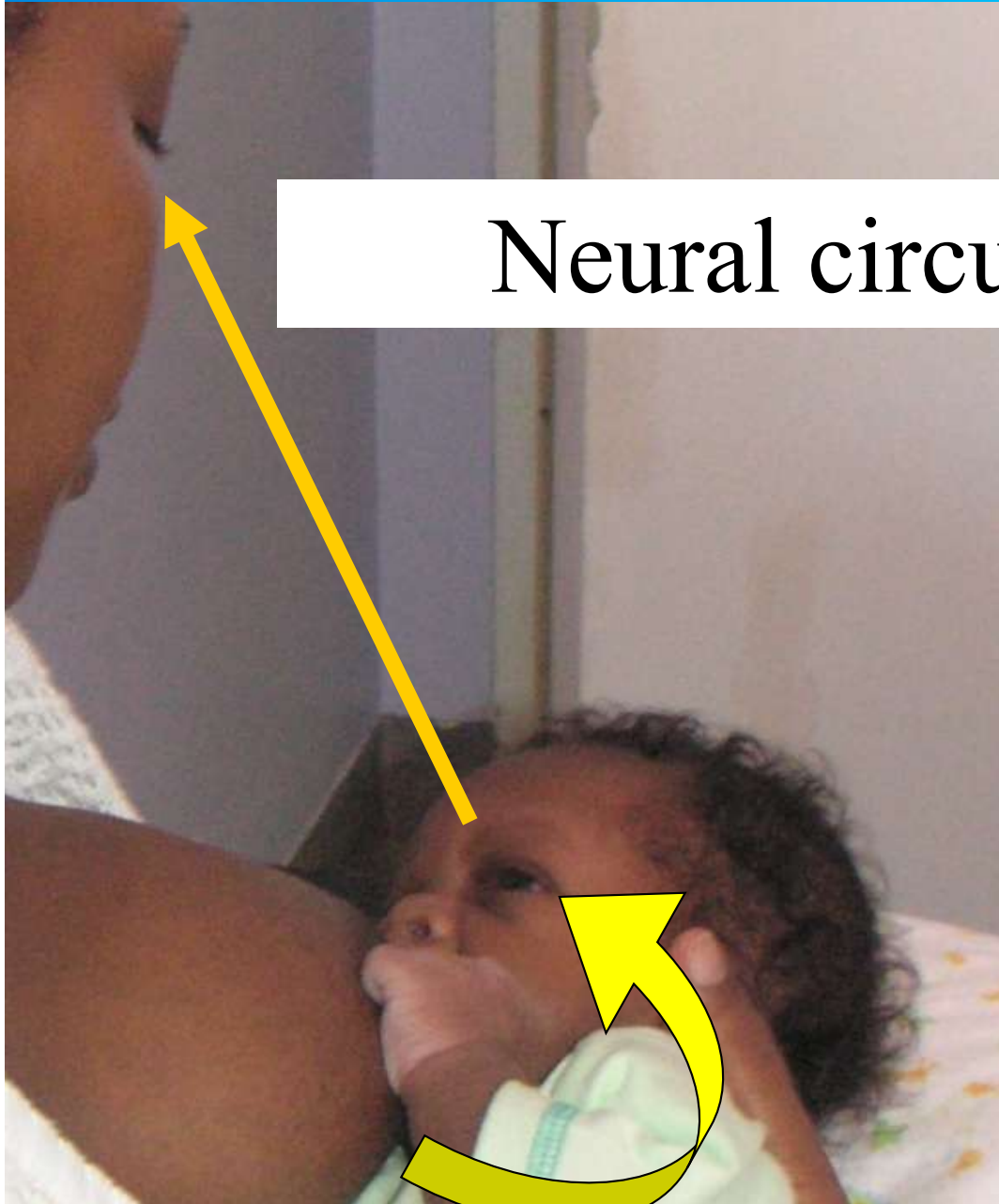
*says "approach"*

Amygdala

*says "safe"*

SSC

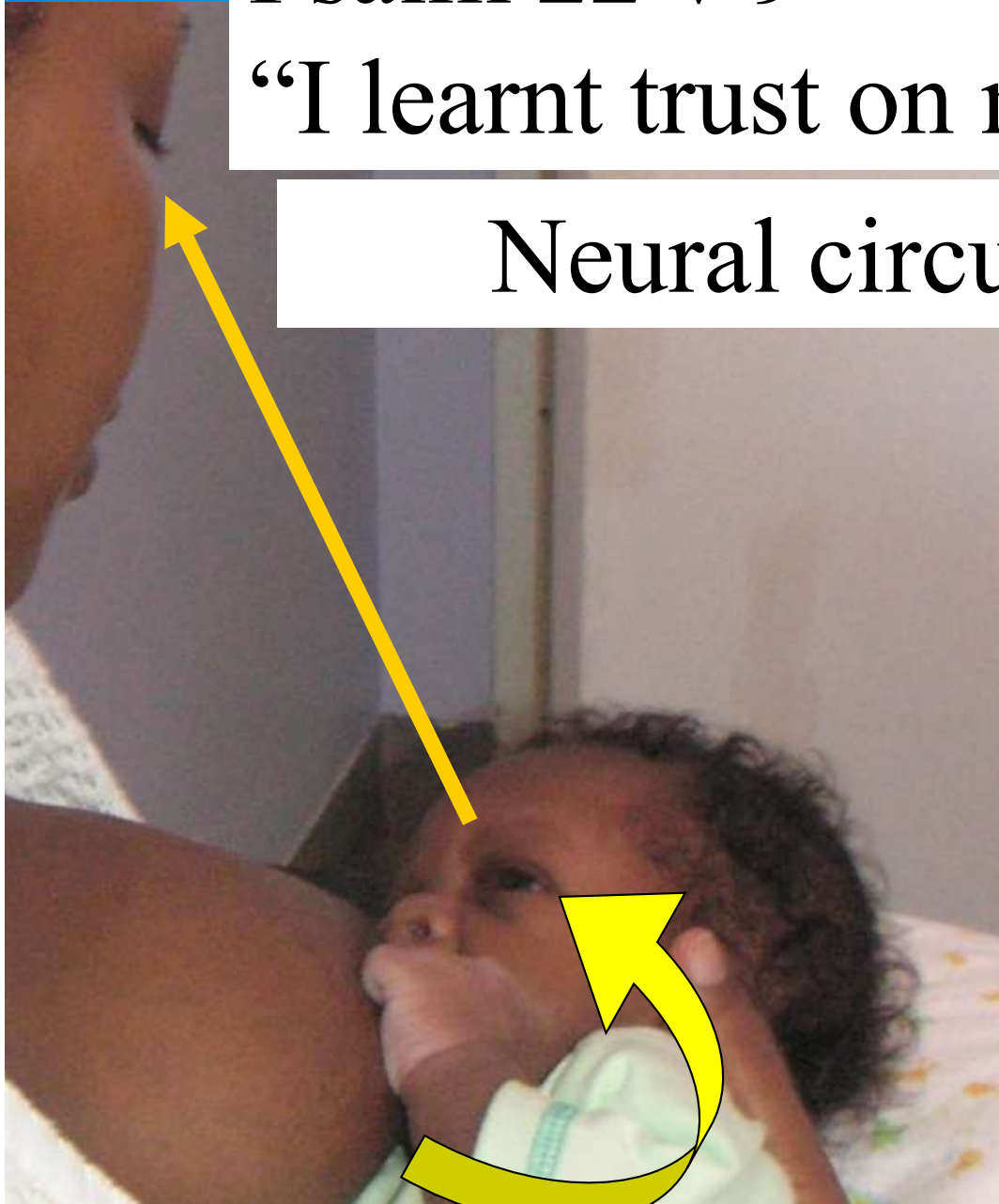
*says "mother"*



Psalm 22 v 9

“I learnt trust on my mother’s breasts”

## Neural circuitry of bonding



Eyes

*says "contact"*

Visual  
cortex

*says "open eyes"*

PFOC

*says "approach"*

Amygdala

*says "safe"*

SSC

*says "mother"*

# Psalm 22 v 9

“I learnt trust on my mother’s breasts”

“trust” (bāṭach)

to *hie* for refuge; figuratively to *trust*,  
be bold (confident, secure, sure),  
(make to hope, make to trust.)



“breast” (shôd)  
the *breast* of a woman  
or animal (as *bulging*):  
- breast, pap, teat.

# Psalm 22 v 9

“I learnt trust on my mother’s breasts”



Instituto Europeo de  
Salud Mental Perinatal

... with focus on long  
term mental health  
benefits.