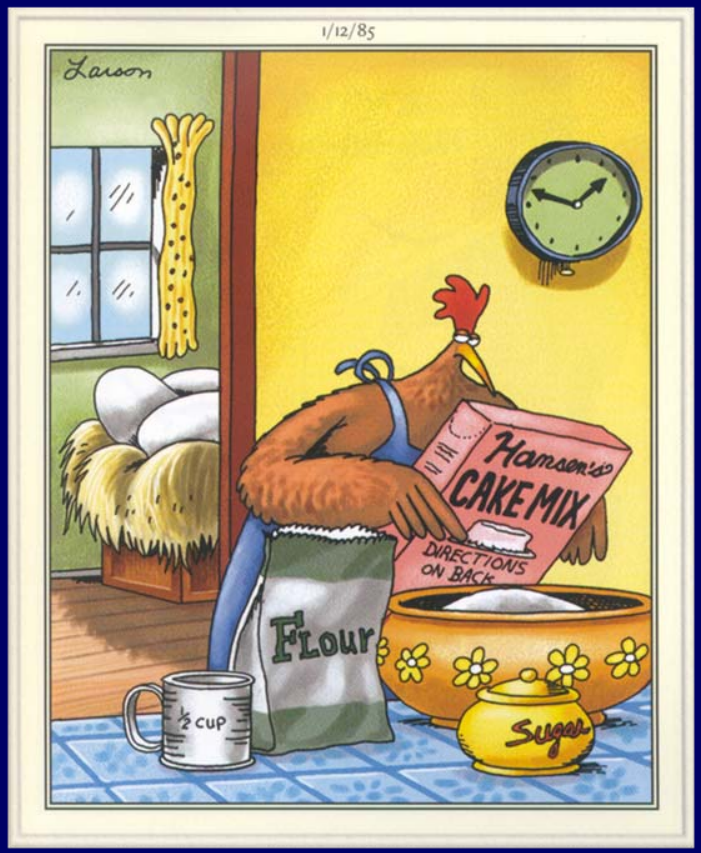
Conflict of Interest Disclosure: nothing to disclose ☺☺



Origins of mothering: role of affect, executive function, and the brain in its regulation

***Alison S. Fleming,* students and colleagues**

Psychology , UTM &
Institute for Human Development
University of Toronto

Maternal Behaviour: Human and Animal Models

South bldg, 1966

St Joseph's, Hosp1907

Hedonics
Affect
Attention
Memory

mediated by

Hormones
Brain
NTs

affected by

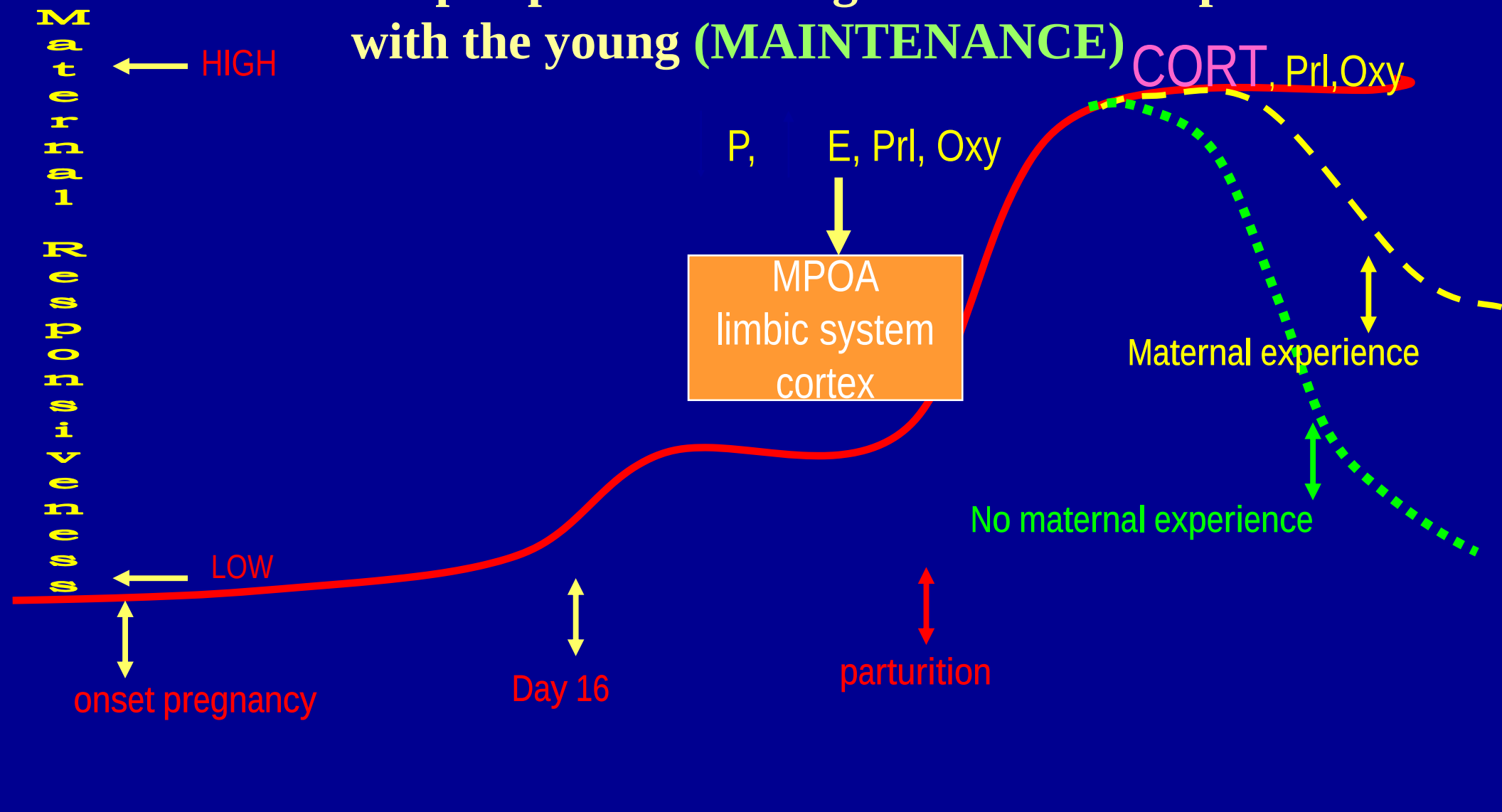
early experience
genetics

Today's task is to describe maternal behavior in terms of psychological components and-if time permits- their underlying neural mechanisms

- ONSET OF MB
  - –stimulus salience, 'reward'
  - –Affect
    - *Nucleus accumbens (NAcc)*
    - *Amygdala*

- ONGOING QUALITY OF MB
  - –attention, response inhibition, memory
    - *Medial prefrontal cortex (mPFC)*

Maternal responsiveness peaks at parturition under influence of hormones (ONSET) and is sustained postpartum through interactive experiences with the young (MAINTENANCE)



HORMONES: Changes in the estrogen /progesterone ratio during pregnancy associated with onset of PP maternal behavior (rats) and early attachment attitudes (human)

In rats and humans

Prolactin,

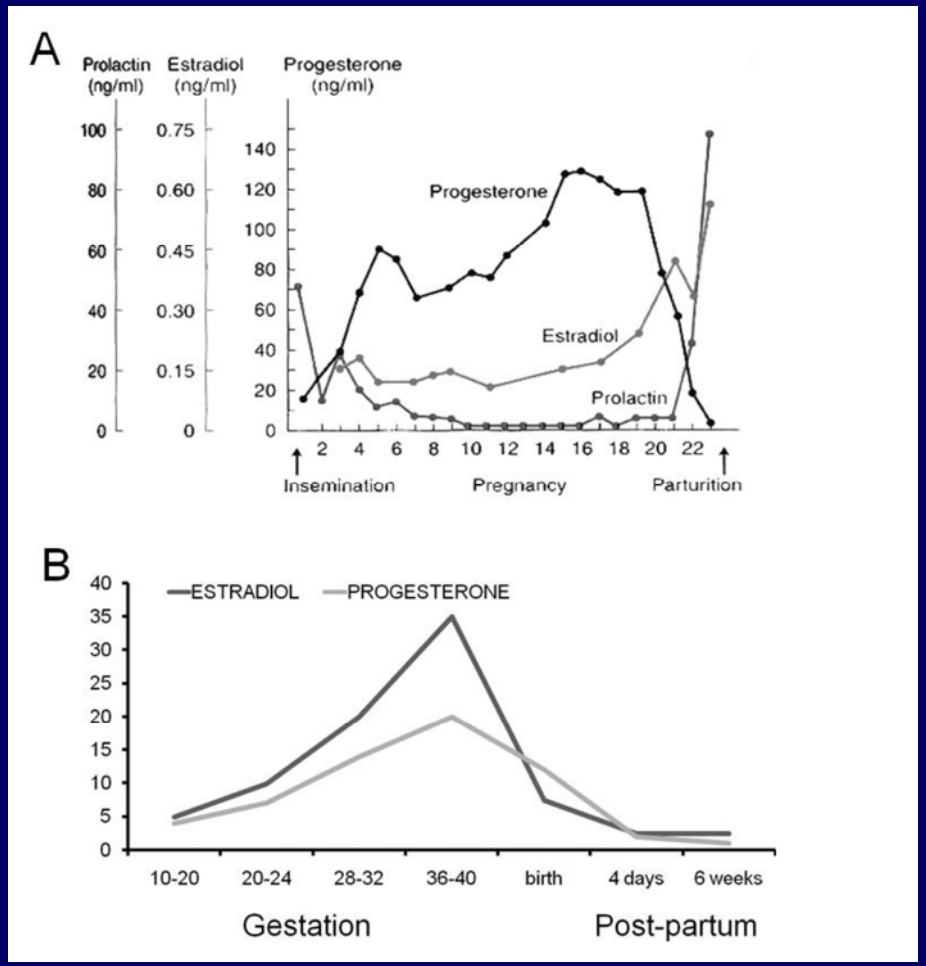
Oxytocin, and

Glucocorticoids also

Associated with an

Enhancement of

mothering



Reviewed in Numan, Fleming, & Levy, 2006

- We believe that these hormonal changes affect mothers' maternal behavior by affecting brain systems and neurotransmitters related to
  - Affect
  - Stimulus salience
  - Reward
  - Attention/executive function
  - Memory



Background for todays talk derives from 40+ years of work on the psychobiology of maternal behavior in rat (YIKES!!)

Let me now describe some of the relevant work to lay the groundwork for the human studies that constitute the focus of the rest of the talk

Reviewed in Fleming & Li, 2002;Numan, Fleming, & levy, 2006; Barrett & Fleming, 2011

Virgin females are ‘timid’ (neophobic) in general and normally avoid pups

Hormones and pup exposure shift mothers’ affect and mothers do not avoid young

Reviewed in Numan, Fleming, & Levy, 2006; Barrett & Fleming, 2011

Pups have salience for the new mother

- Among rats and other mammalian mothers, new mother rats are attracted to the odours and ultrasonic vocalizations of newborn rat pups, whereas virgin non-mothers are not.

- Salience enhanced by
  - Hormones
  - Prior maternal experience
  - Early rearing experience

Pups are rewarding stimuli to the new mother and motivate her approach

- With interactive experience early PP with young mothers learn about the young and this maintains their maternal behavior after hormones have subsided

- Through experience pups come to take on rewarding properties for the mother and can sustain an instrumental response (mothers will bar press for pups) Virgin rats will not bar press for pups (Lee et al., 2000)

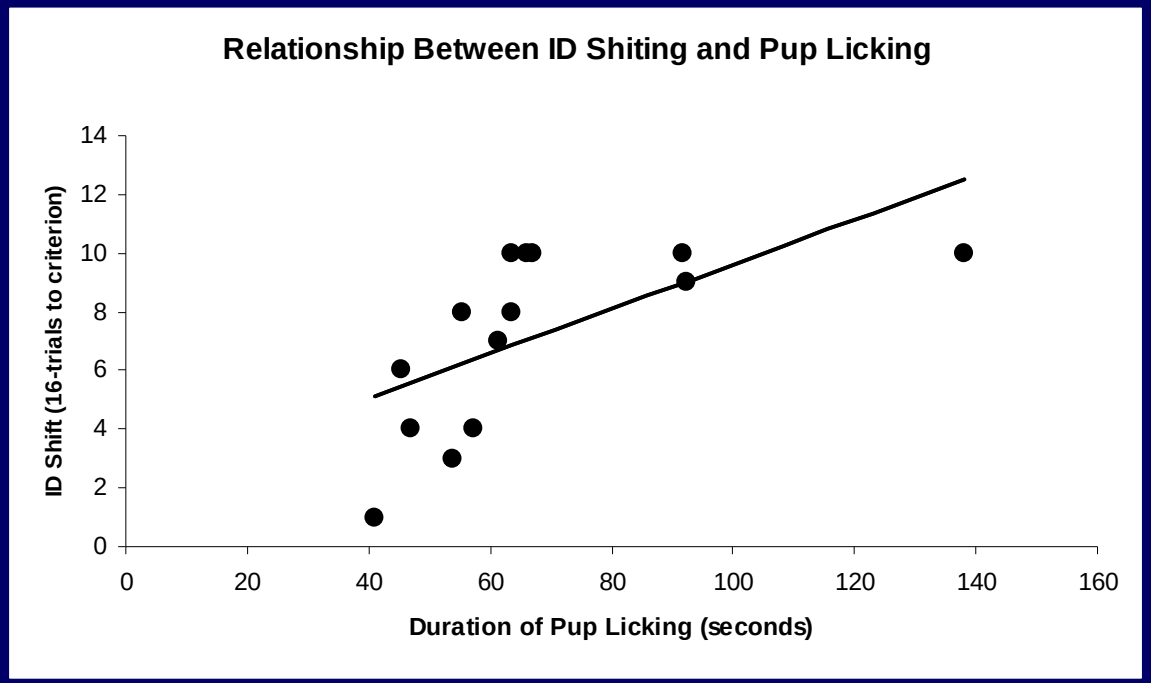
Once maternal, appropriate behavioral Interactions depend on good attention and executive function

Mothers lick, retrieve, build nests and and forage for food . Normal execution of these behaviors and their sequential nature requires that mothers have good executive functions: that they can pay attention, easily shift attention, show good working memory, are not impulsive, and so on.

(Lovic et al., 2004, 2010,2011; Kinsely al. , 2008).

but one example,

- In new mother rats there is a strong positive correlation between attentional performance on a set shifting task and licking behavior..(Lovic & Fleming, 2004)



Early adversity (in rat, early social isolation rearing) disrupts later maternal behavior, affect, and executive function: replacement lick-like stroking reverses these effects

- mothers who are reared apart from their own mothers and siblings grow up to show
  - reduced licking and crouching (motivation is present, intensity is reduced)
  - Greater 'anxiety', reduced attraction to infant cues, reduced attention, increased impulsivity, and reduced social learning

Gonzalez et al., 2001; Lovic et al., 2004, 2010, 2011; Burton et al., 2006,2007,2011

SUMMMARY OF THE RAT WORK

- to understand behavioral processes that underlie mothering, the female undergoes a change that involves
  - Reducing natural withdrawal tendencies
  - Becoming attracted to young that act as ‘rewards’
  - Becoming more attentive, less impulsive, with good working memory
- AND, as we will see later, specific brain systems are involved in regulating these processes and are affected by early experiences

So these rats have taught us quite a bit

Numan , Fleming, & Levy, 2006; Barrett & Fleming, 2011

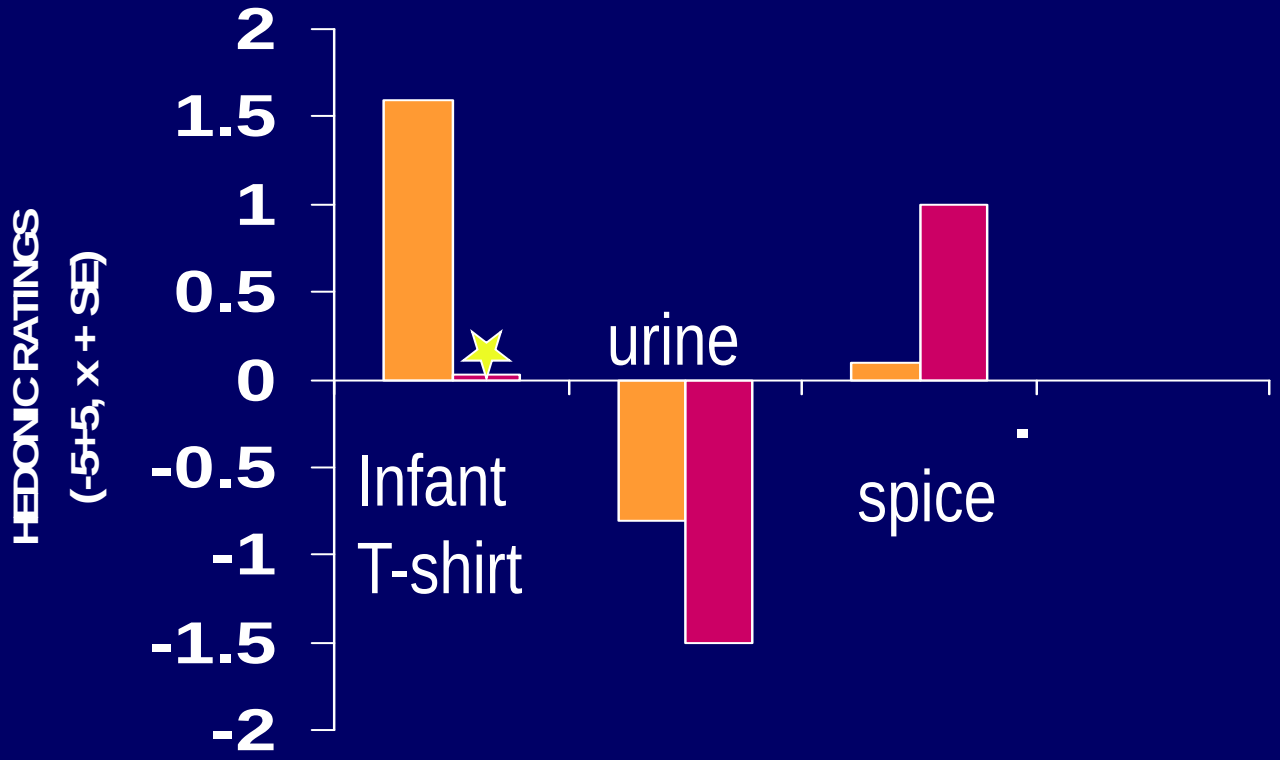
To what extent do similar processes apply to human mothers?

Human Studies




Among Humans as well, New Mothers are Often Very Responsive to Their Infants soon after birth and are Attracted to Infants and their Cues

New Mothers (day 2pp) are More Attracted to Infant Body Odors, But Not to Control Odors, Than are Non-mothers (VAS, pleasantness)

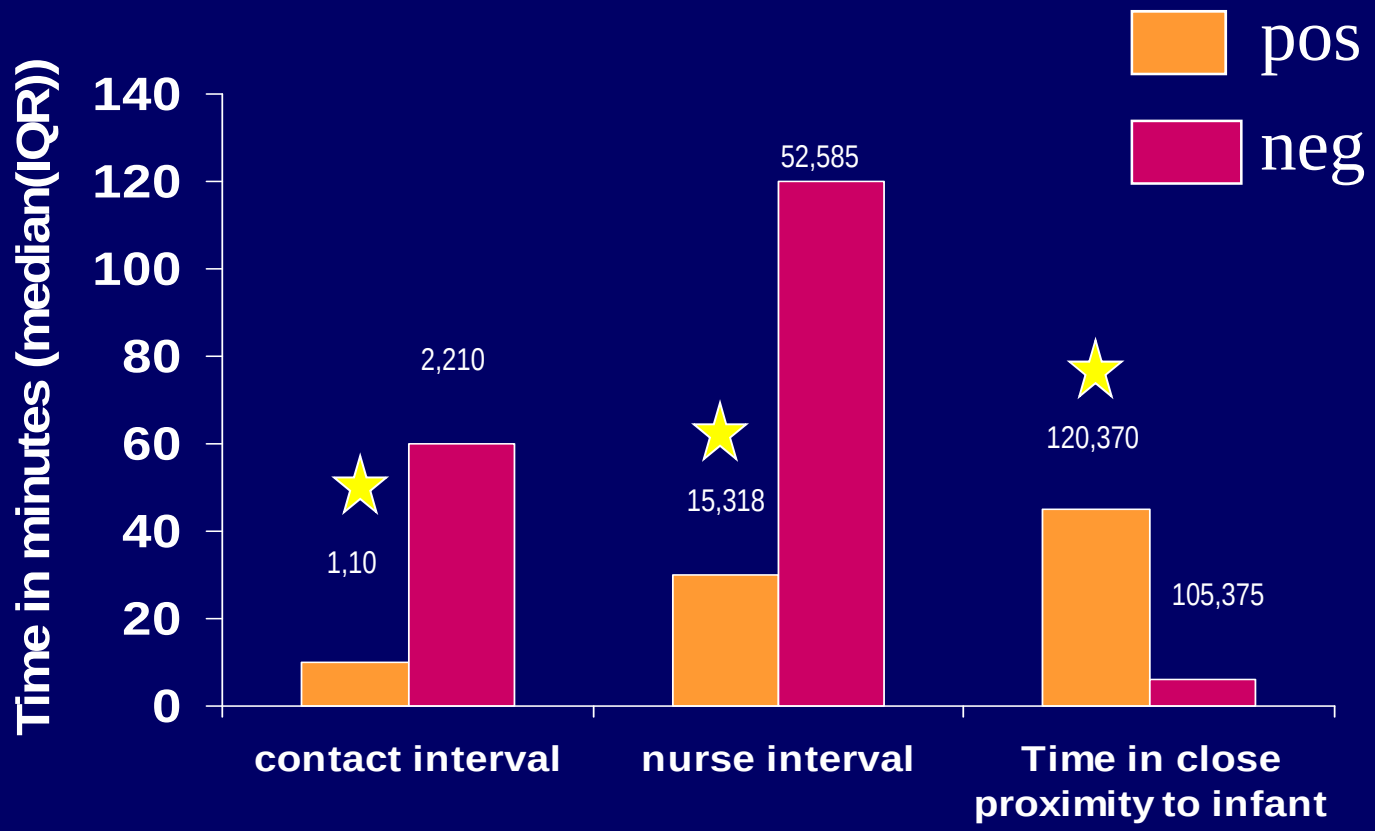


stimulus odor prsented in Baskin Robbins containers

Variances homogenous

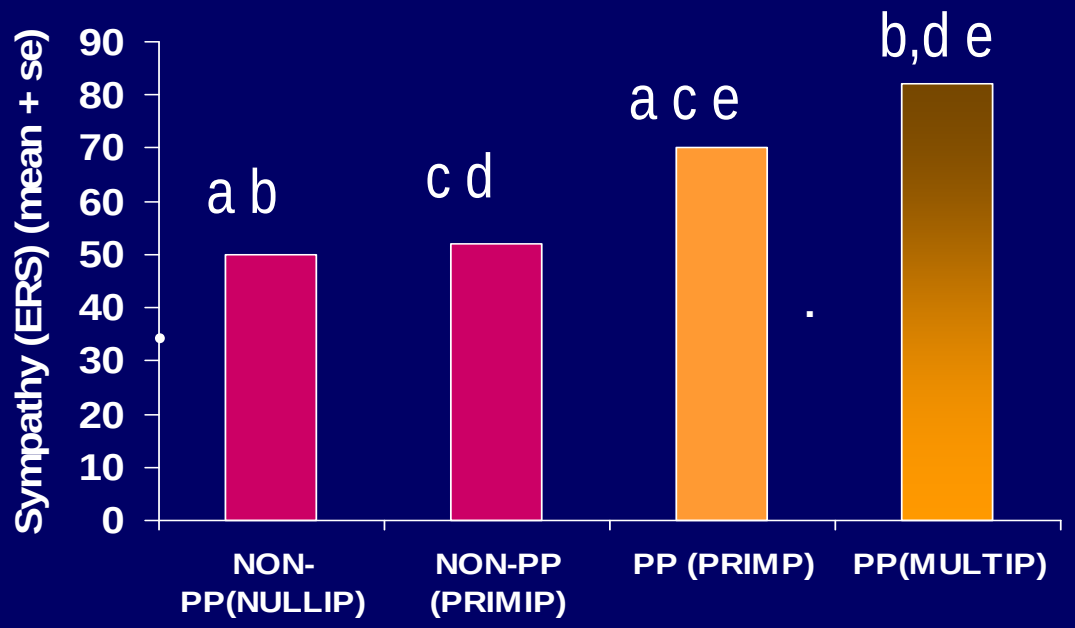
Fleming, Corter, Franks, Surbey, Schneider., & Steiner, 1993

Mothers with More Postpartum Experience tend to also Find Infant Odors to be More Attractive



Fleming, Corter et al., 1993

In terms of normal range of affect, new mothers are more sympathetic to infant pain cries than are non-mothers; experience (multiparity) increases feelings of sympathy



shared letter, p<.05

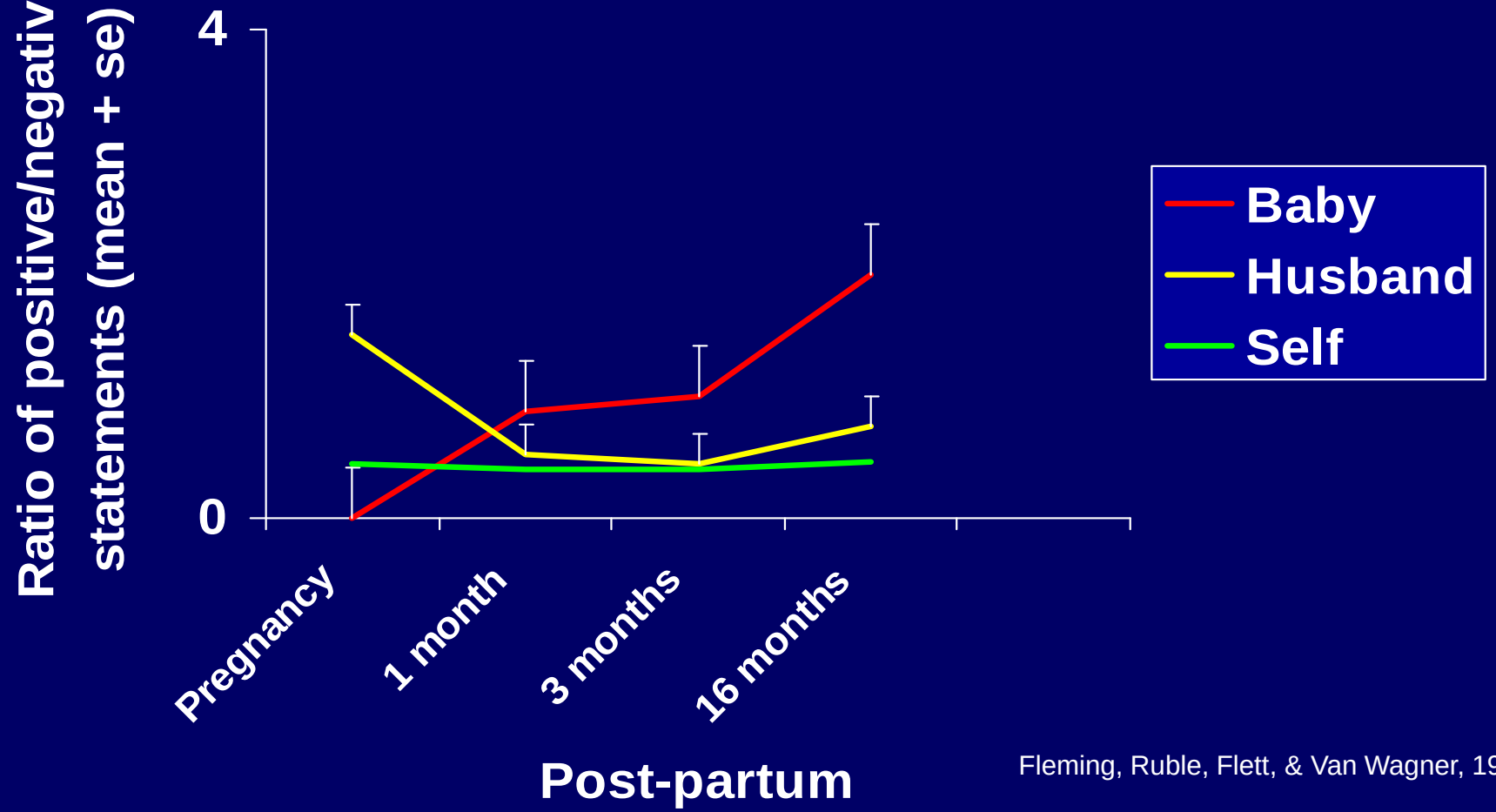
Stallings, Fleming, Corter, Worthman, & Steiner, 2001

- MORE ‘SYMPATHETIC’ MOTHERS
  - Have higher cortisol levels
  - Have higher heart rates
  - Don’t know which is primary, the affect or the physiology-need to consider prior ‘personality’ characteristics

Stallings, Fleming, Corter, Worthman, & Steiner, 2001

With Postpartum Experience New Mothers Become Increasingly More Positive About the Baby- and less positive about their partners

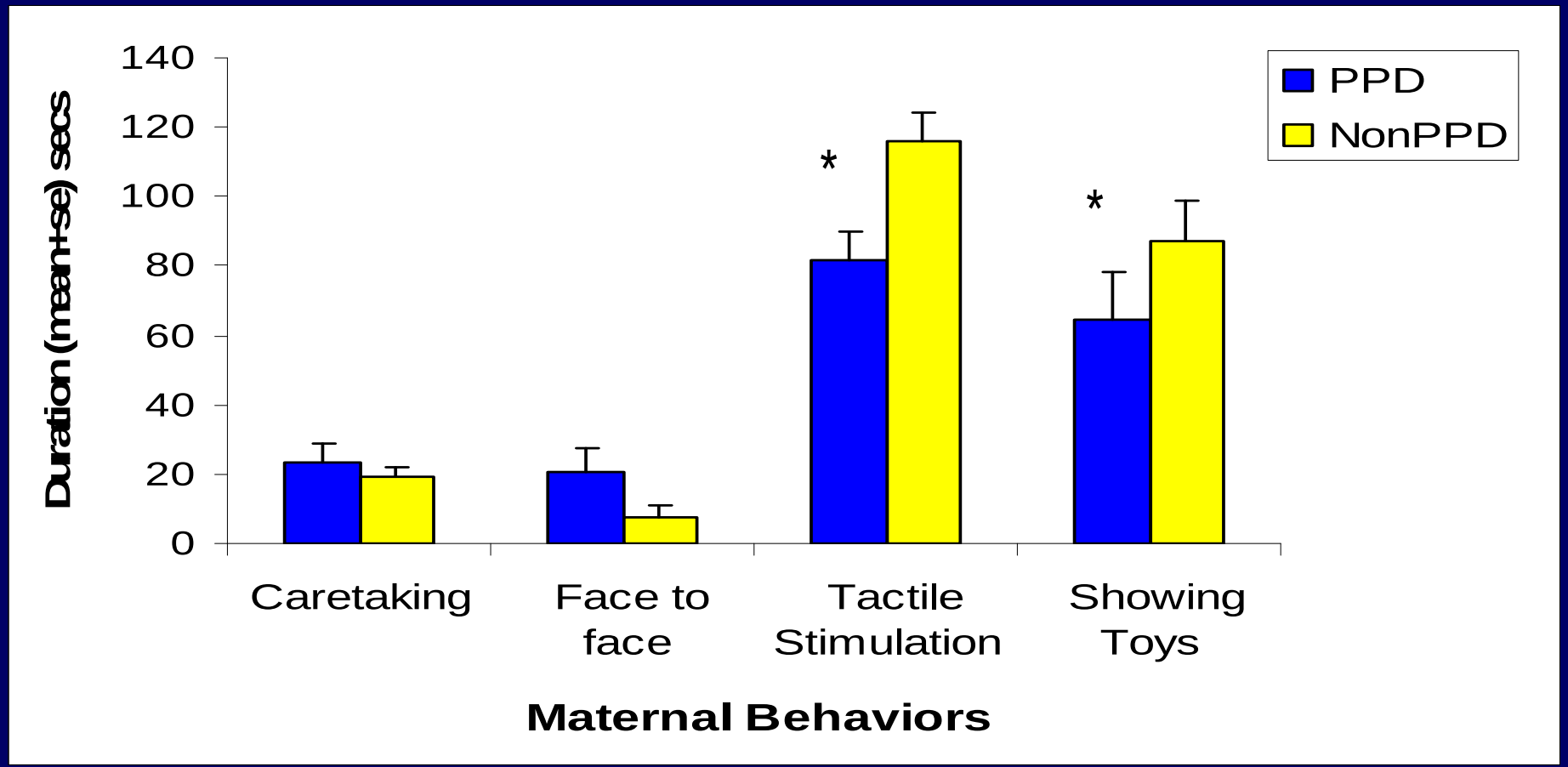
(DON'T WORRY, IT RETURNS IN TIME FOR THE NEXT BABY)



Fleming, Ruble, Flett, & Van Wagner, 1990

New Mothers are often labile and emotional: dysphoria and elation in mothers is associated with variations in mothering behavior

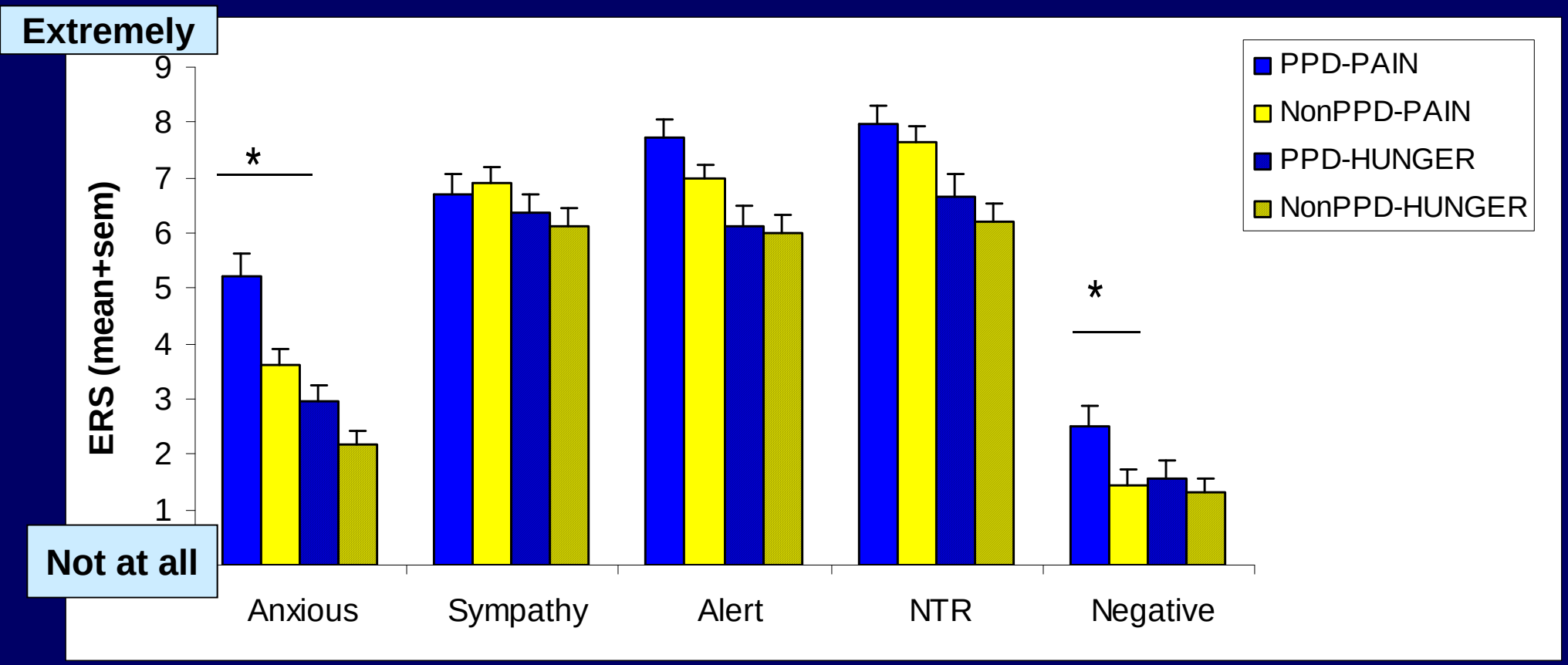
Depressed Mothers at 4-6 mo PP engage in less tactile affection with their babies and play with toys less than non depressed amothers



See also, Tronick & Reck, 2009

Gonzalez et al., in prep

Depressed Mothers Are More Anxious and Negative when Listening to Pain Cries Compared to Non-Depressed Mothers



Gonzalez et al., in prep

New mothers experiencing negative affect post partum who are less maternally responsive have infants who are disengage more

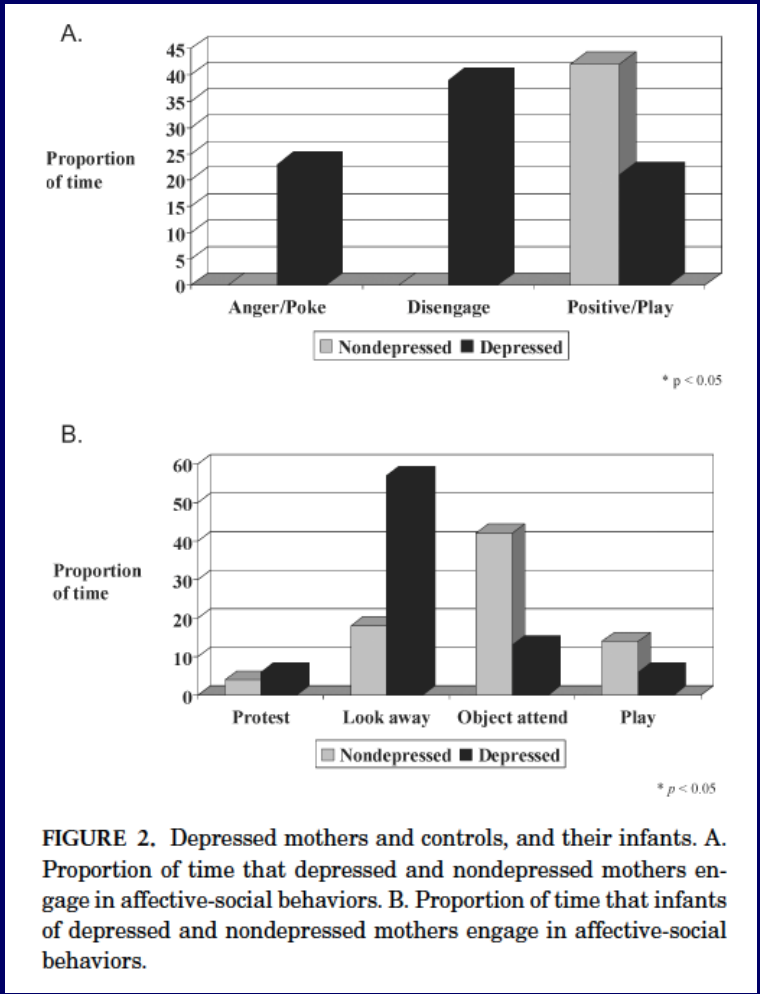


FIGURE 2. Depressed mothers and controls, and their infants. A. Proportion of time that depressed and nondepressed mothers engage in affective-social behaviors. B. Proportion of time that infants of depressed and nondepressed mothers engage in affective-social behaviors.

Tronick & Reck, 2009

The Effects of a Social Support Group on Depression, Maternal Attitudes and Behavior in New Mothers

A. S. Fleming,* E. Klein and C. Corter†

JCPP, 33, 1992

Attention, executive function, and maternal behavior

- Once maternal, the new mother interacts with her baby, engaging in many affectionate and instrumental behaviors.

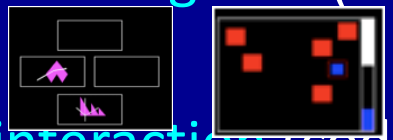
  Normal execution of these behaviors and their sequential and contingent nature requires that mothers have good executive functions: that they can pay attention, easily shift attention, show good working memory, are not impulsive, and so on.

Sensitive mothering involves contingent responding

One representative study:

Neuropsychology and Physiology: Intervening Variables Between Maternal Early Life Experiences and Parenting

- Low-risk community sample of mothers (n=89)
- Tested at 3-6 months PP during 2 home visits
- Measures:
  - Childhood Trauma Questionnaire (Bernstein & Fink, 1998; screening for history of abuse and neglect), Life History Calendar (Caspi et al., 1996; measure of parental separation)
  - Salivary diurnal cortisol
  - Attentional set-shifting task (IED test) and spatial working memory test (CANTAB)



  - Mother-infant interaction (coded 30 minute M-I interaction for maternal sensitivity using Ainsworth scales)

Gonzalez, Jenkins, Steiner, & Fleming, in press

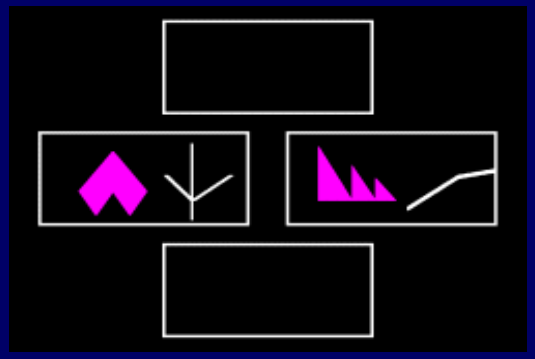
Maternal Behaviour is related to Executive Function:

More sensitive mothers also showed greater attentional flexibility and scored better on the spatial working memory tasks

- Maternal sensitivity & attentional flexibility (ED errors): r = -.26*
- Maternal Sensitivity & spatial working memory: r = - .39*

Mothers who Show Reduced Attention or SPW (on CANTAB: Set-Shifting Task) also Show Reduced Maternal Sensitivity

Attention
ED Shift on CANTAB



-.25

Ainsworth
Sensitivity
Rating Scales

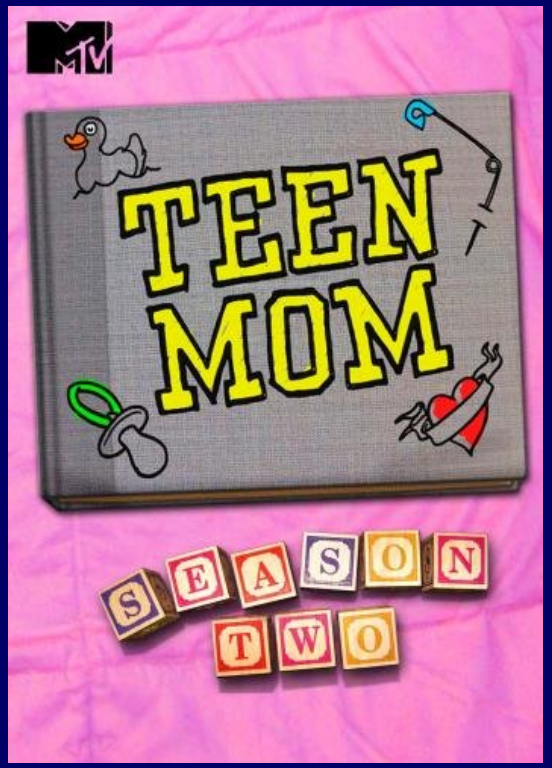
Maternal
Sensitivity

Cambridge Neuropsychological Test Automated Battery
Administered via a touch screen computer
Measures components of executive functioning;

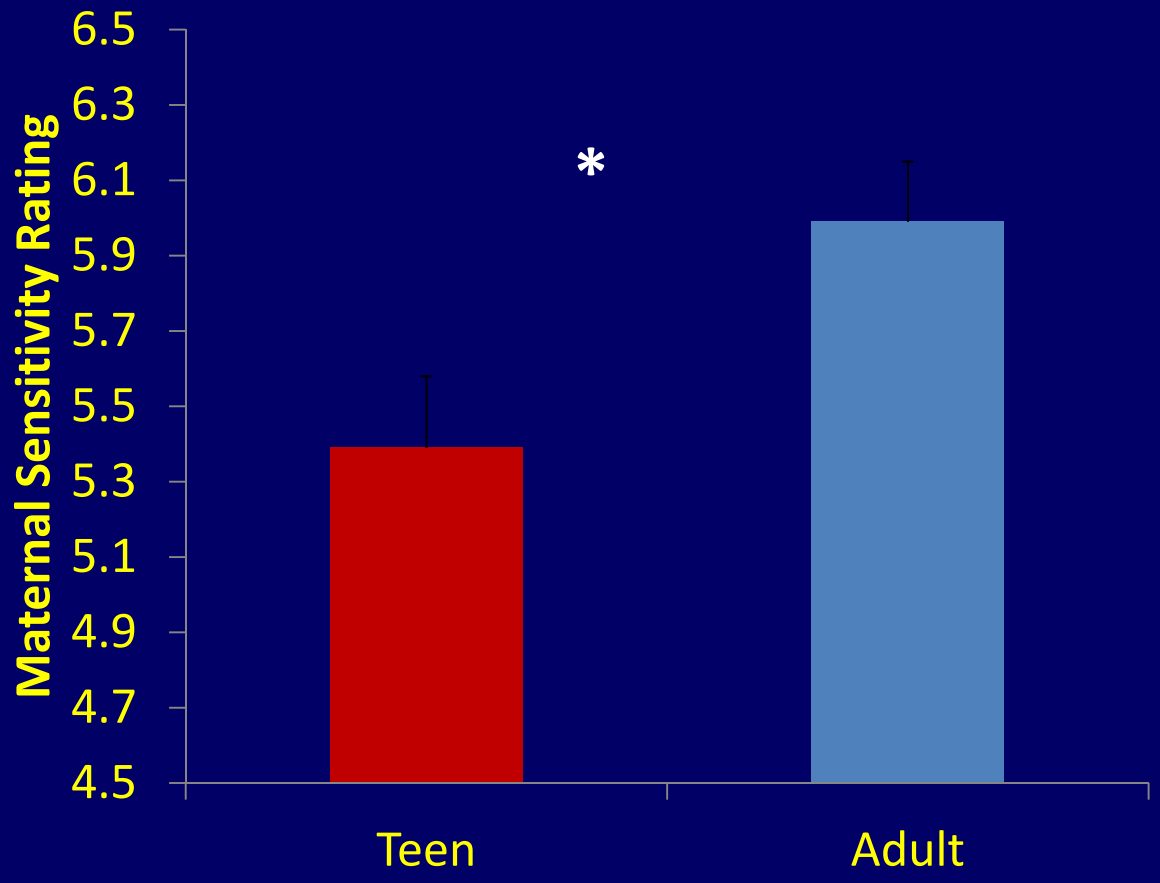
Numbers=stand. β weights

Gonzalez, Jenkins,, Steiner, & Fleming., in pres
Fleming & Gonzalez, 2008

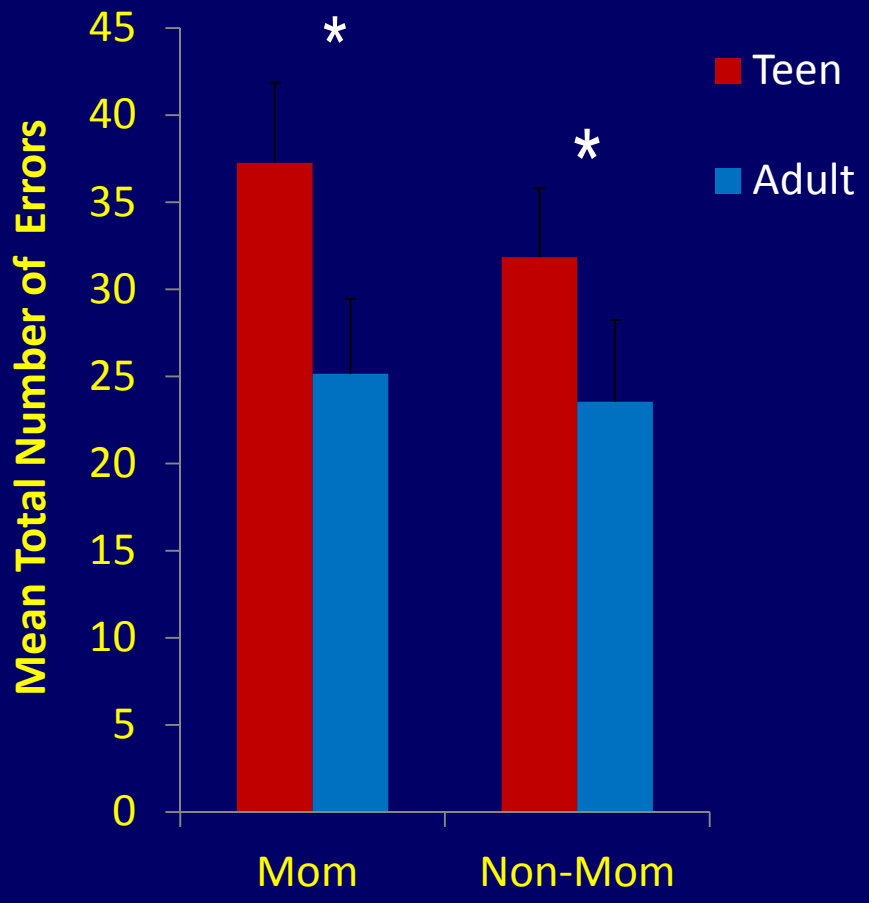
We also see a relation between executive functioning and mothering in a HIGH RISK POPULATION



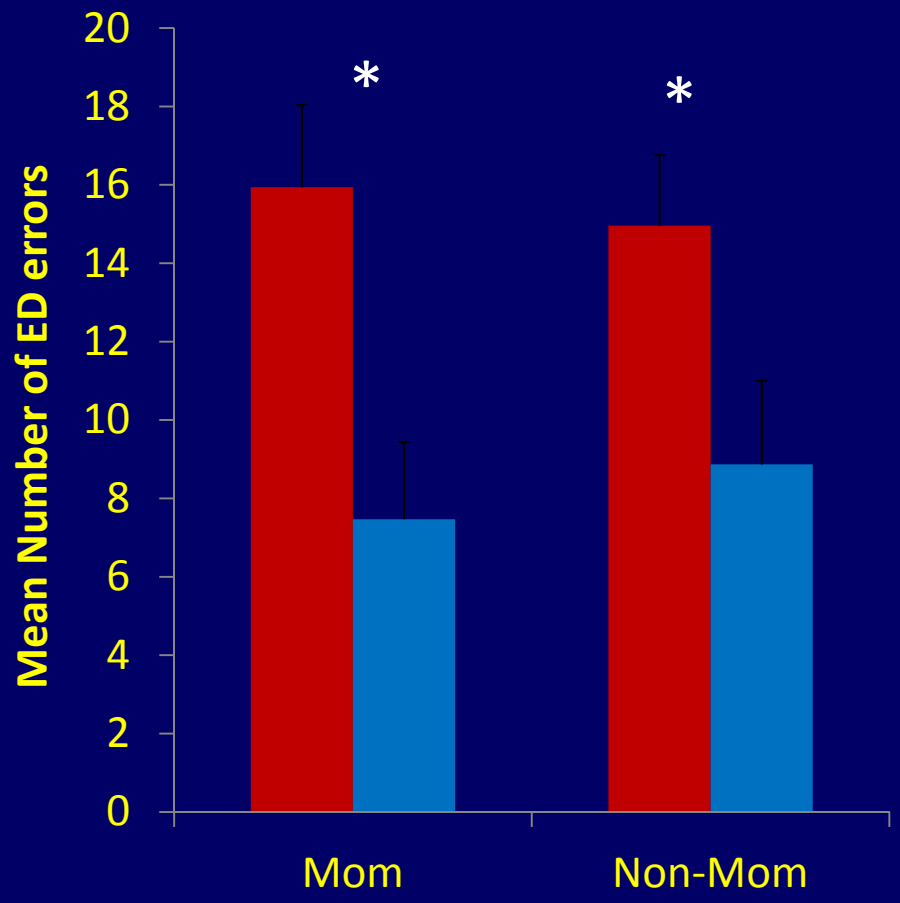
Teens exhibit less maternal sensitivity than adults during interactions with their infants



Teens have poorer attentional flexibility than adults, independent of maternal status

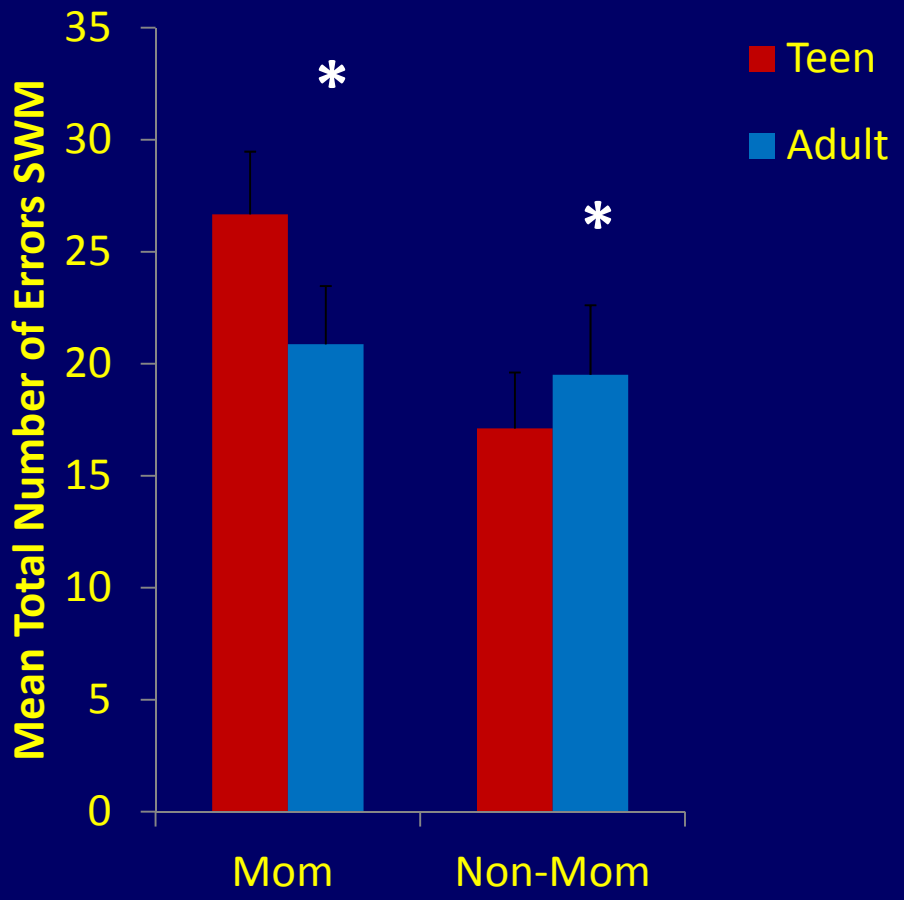


Teen vs. adult $F(1, 113) = 4.44$, $p < .05$

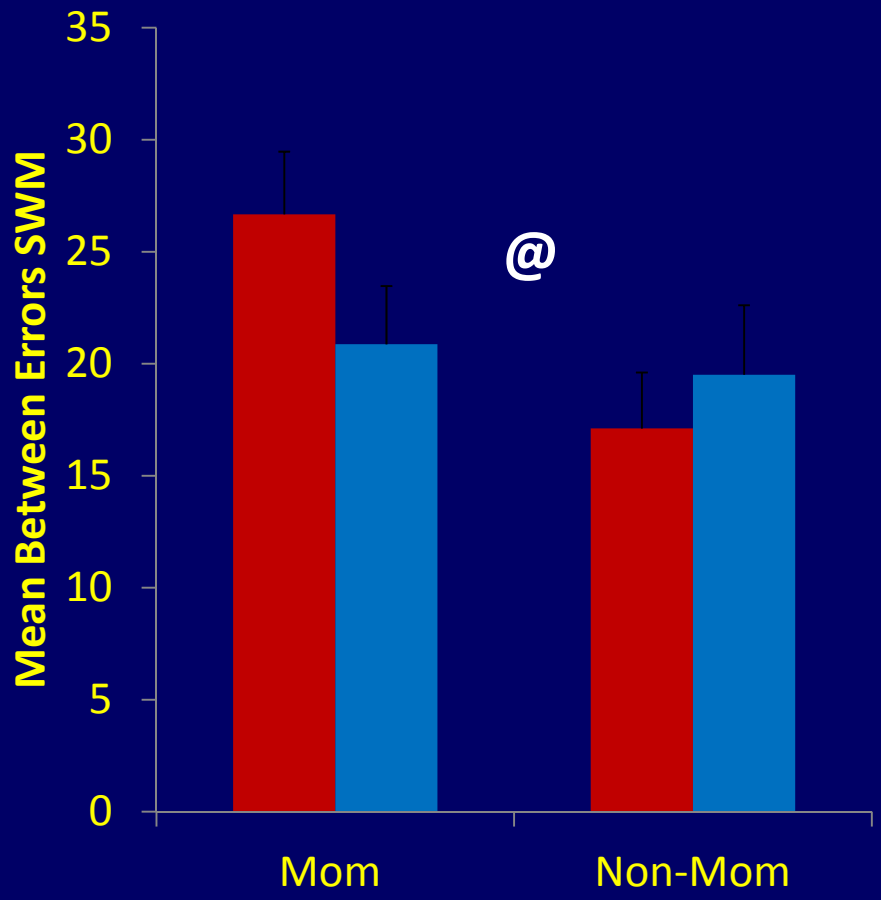


$F (1, 113) = 10.38$, $p < .02$

Teens perform less well on the spatial working memory test; especially teen mothers

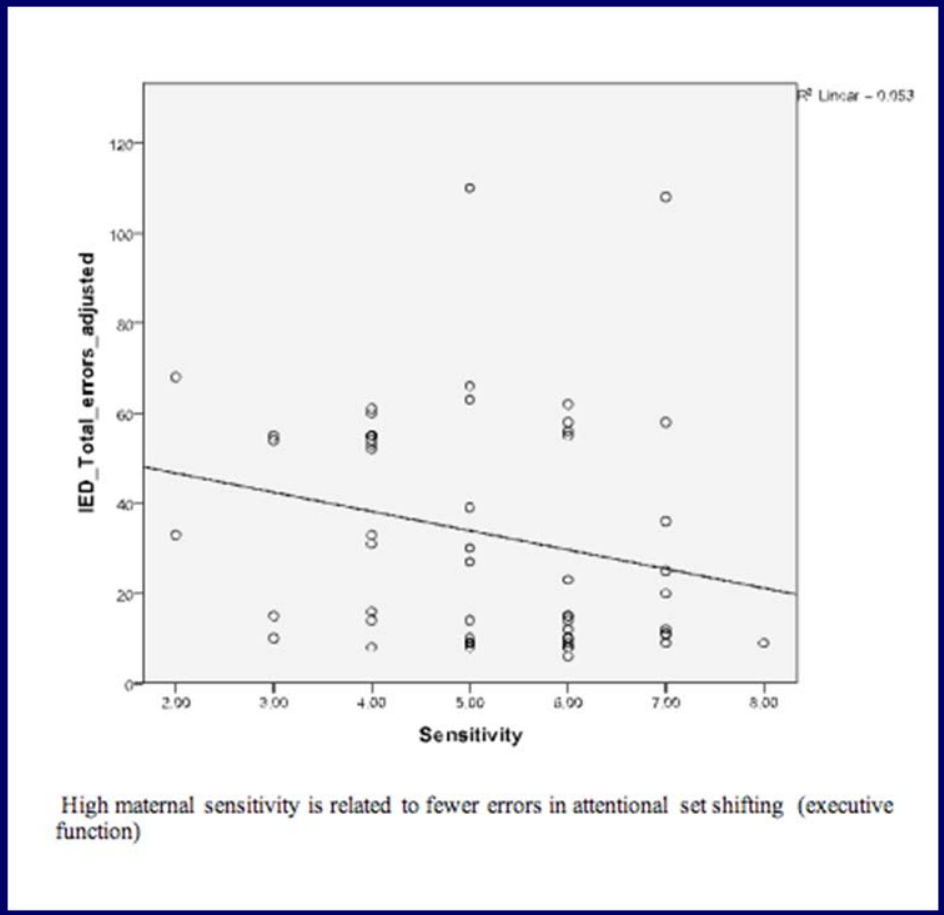


Teen vs. Adult: F (1, 107) = 5.60, $p < .05$

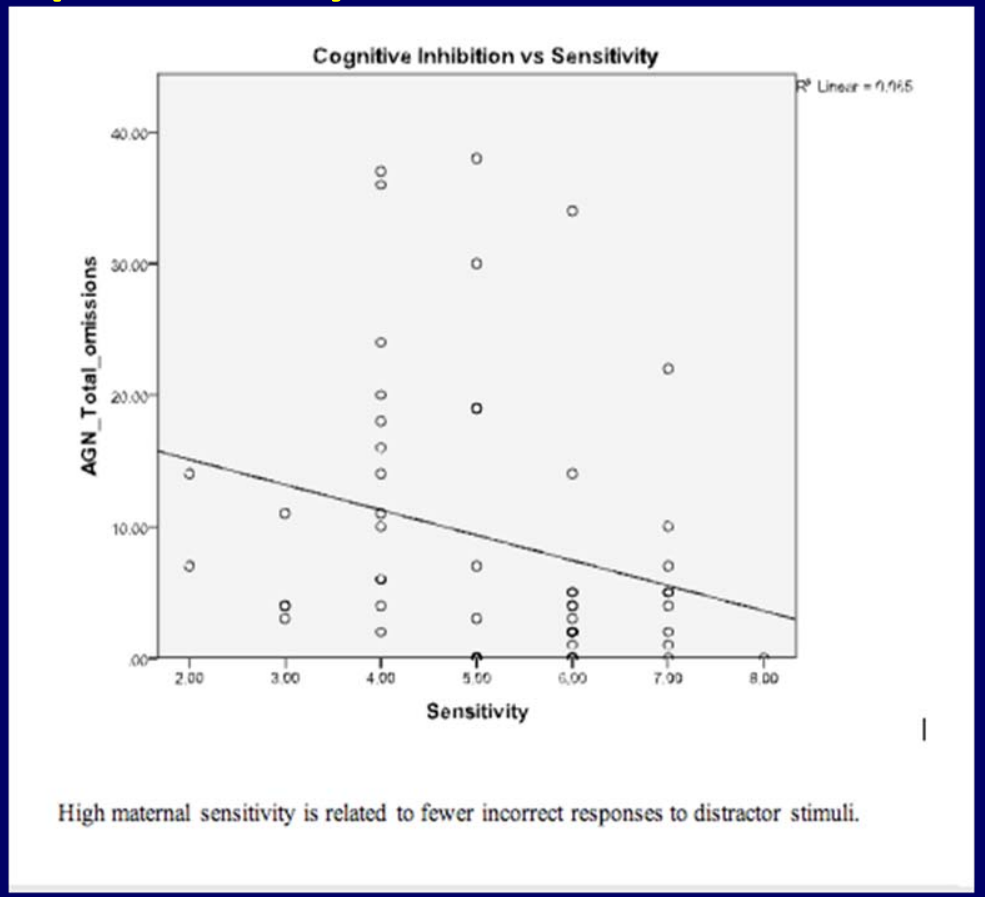


Mom vs. non-mom: F (1, 107) = 3.30 $p = .07$

In teenagers, higher maternal sensitivity is related to reduced attentional errors and reduced impulsivity



High maternal sensitivity is related to fewer errors in attentional set shifting (executive function)



High maternal sensitivity is related to fewer incorrect responses to distractor stimuli.

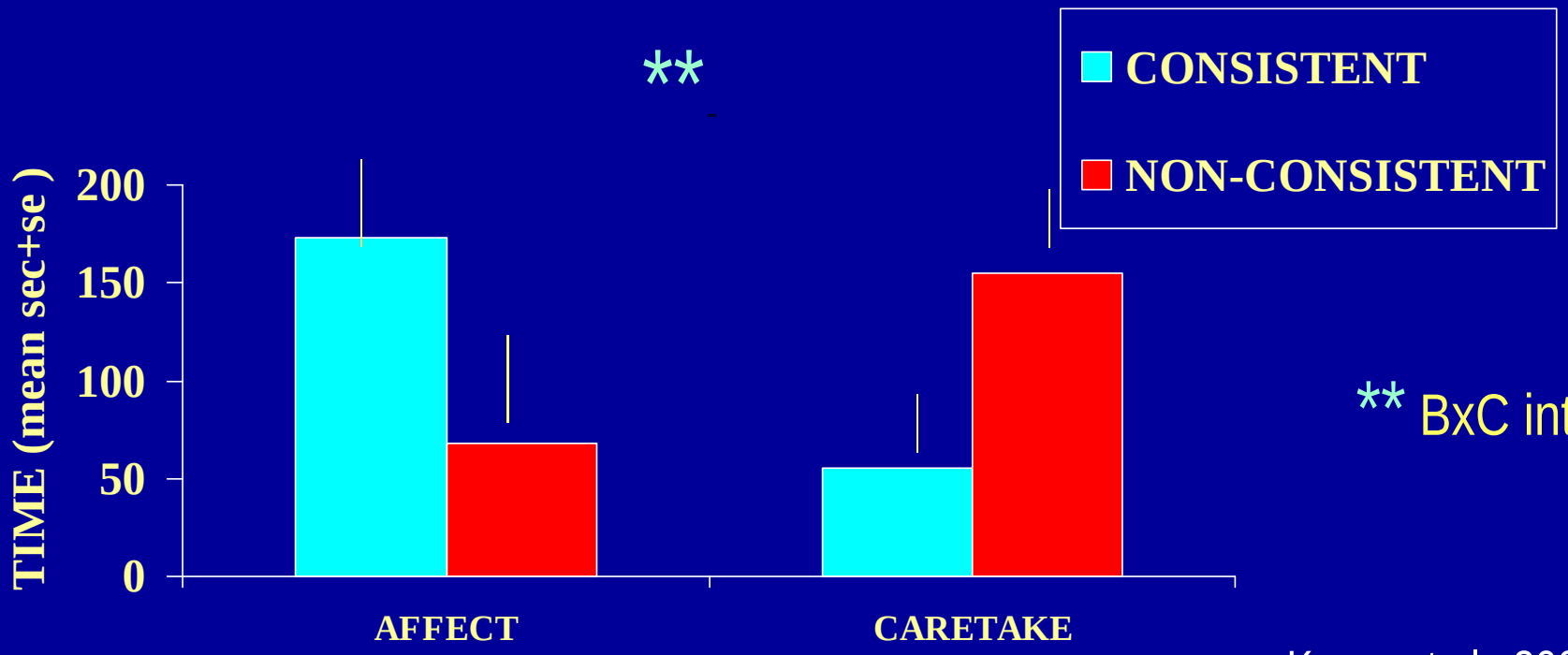
Chico et al., in prep

How does early experiences in family of origin affect maternal behavior and sensitivity at 6 months postpartum?

Early experiences affect mothering

In humans, mothers who grew up in a more adverse early environment show reduced Affectionate Touching and more Instrumental Touching with their Infants; They also attend less to their infants

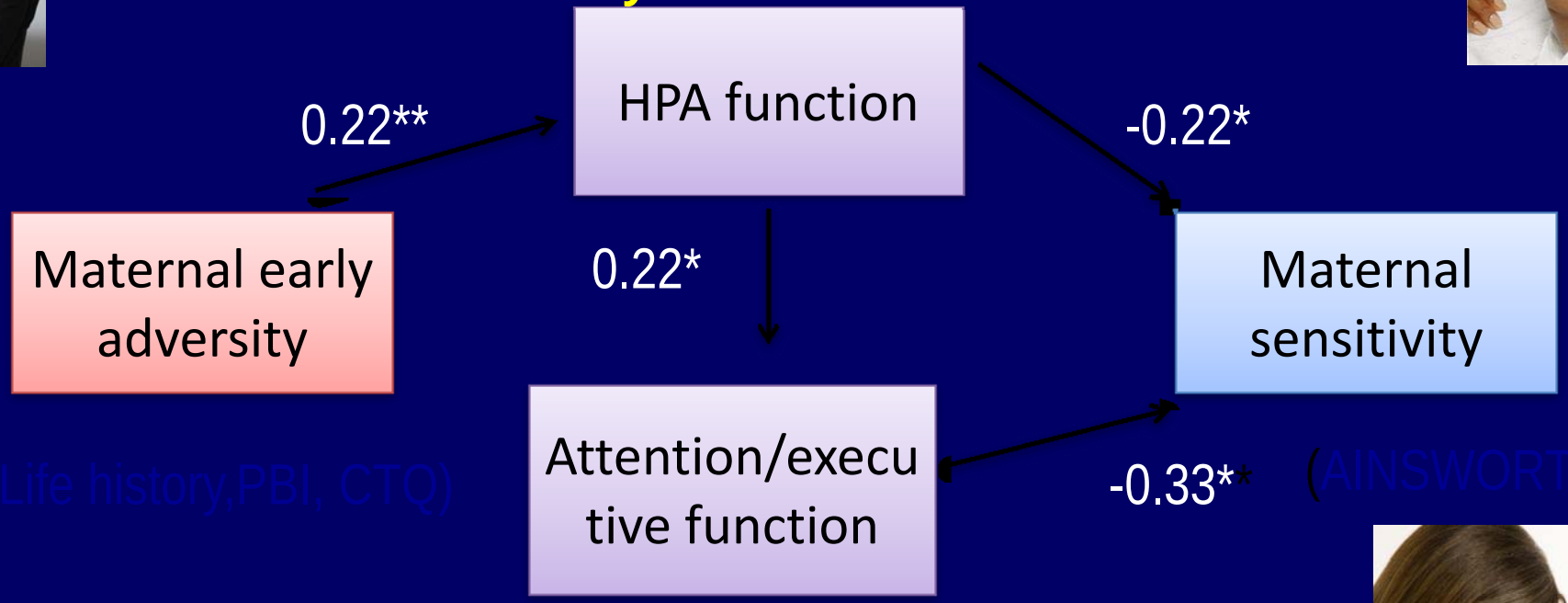
Effects strongest in First time mothers and in Teen mothers



** BxC int

Krpan et al., 2005

In adult mothers those experiencing more early adversity show elevated cortisol levels , which is related to poorer executive function and reduced maternal sensitivity

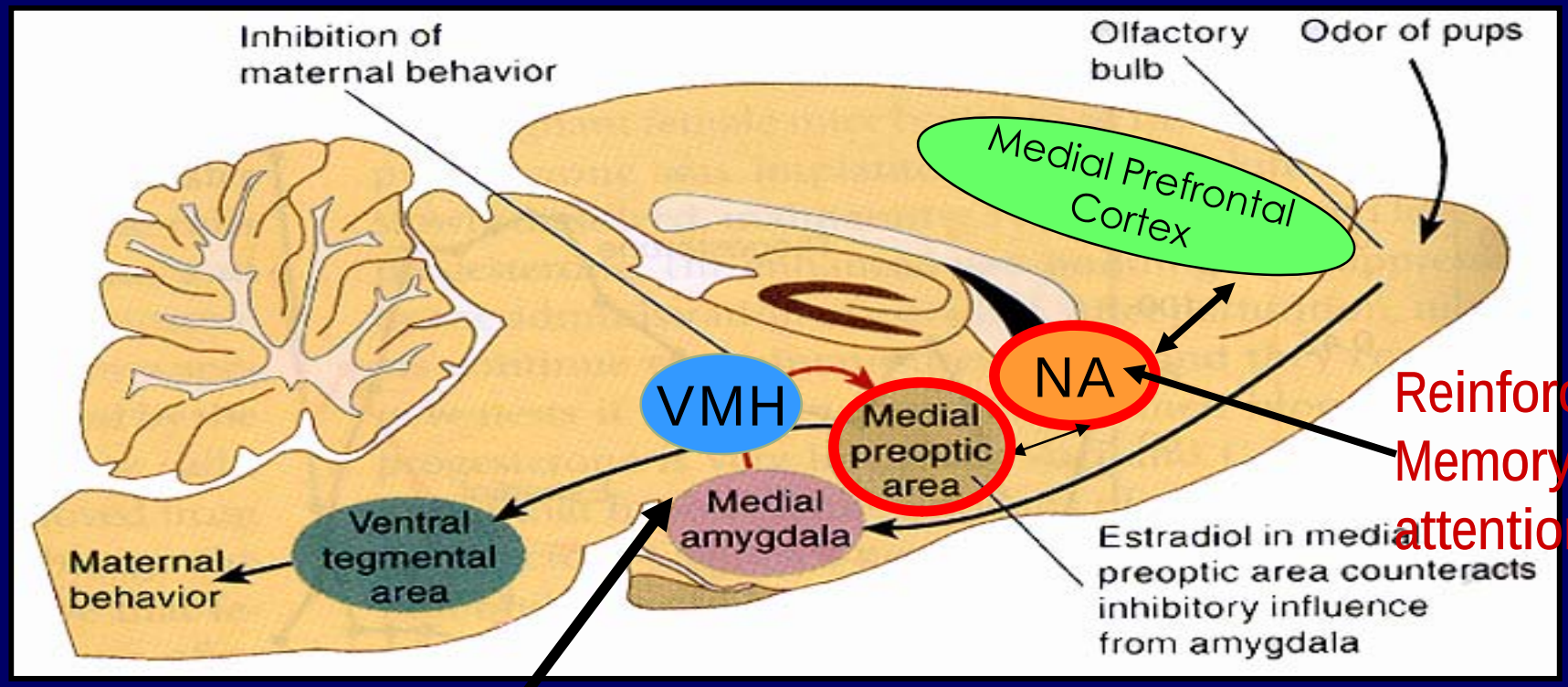


χ^2= 5.53; CFI = .98, RMSEA = .06 *p<.05 **p< .01

Gonzalez, Jenkins, Steiner & Fleming,in press

What is the role of brain in regulating mothering behavior and the associated processes of reward, affect, and attention?

NEURONATOMY: Hormones and Experience act on Multiple systems that intersect with the Maternal Neuroanatomy, : Here focus on AMYGDALA and Nucleus accumbens



Nacc : Stimulus Salience, Rewards,attention

Afonso et al., 2008, 2009, in press; Parada et al., 2009; d”Cunha et al., 2011

Amygdala: Affect

Fleming et al., 1980a,b; 1994, 1999a,b; Li et al., 2003a,b; Numan et al., 2006

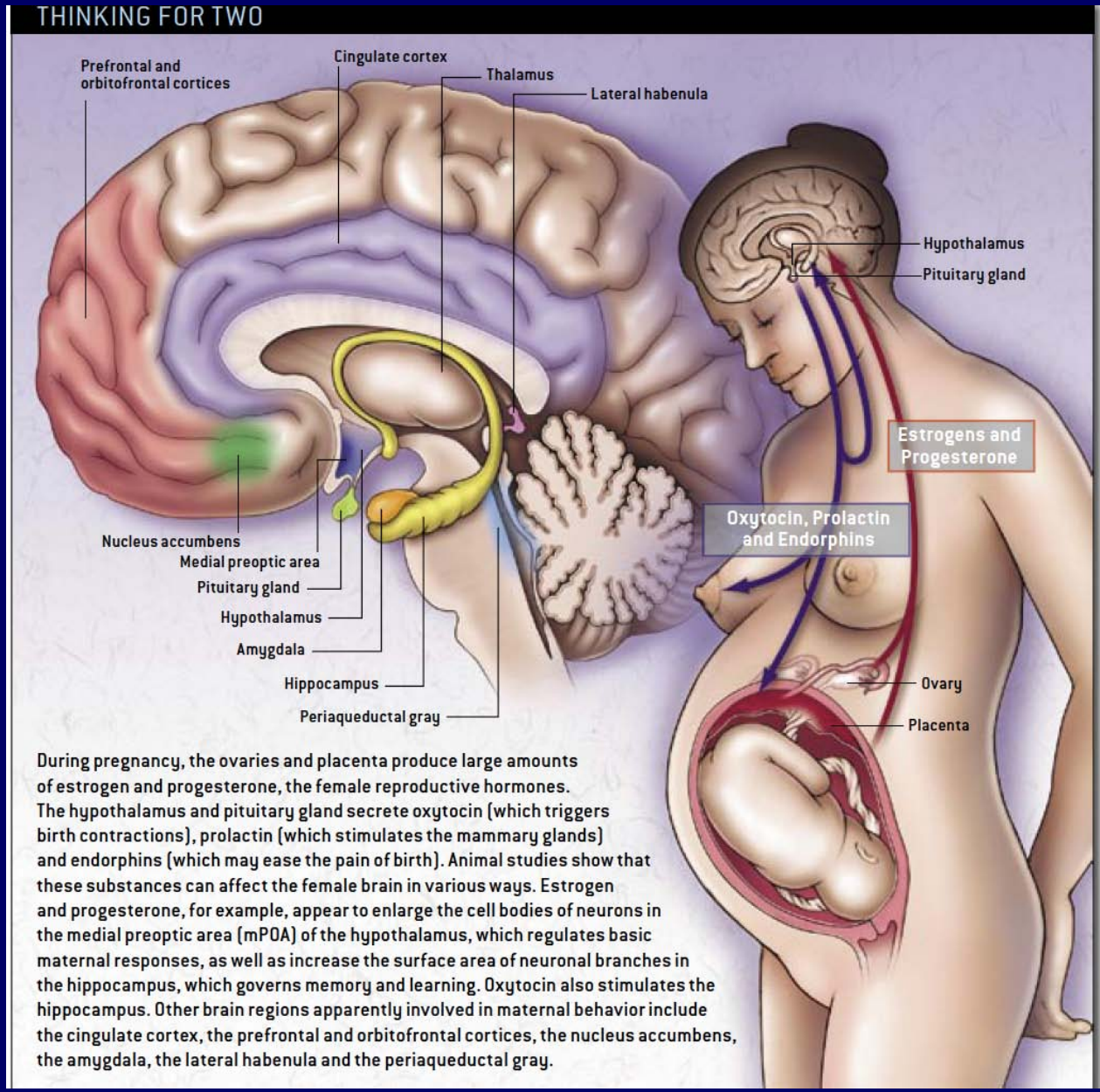
Medial prefrontal cortex: attention, flexibility, working memory

Afonso et al., 2007; Numan et al., 2006

What is the role of the human brain in regulating mothering behavior and the associated processes of reward, affect, and attention?

Similar systems in the human brain have been related to mothering

See Barrett & Fleming, 2011; Kinsley & Lambert, 2009



BRAIN REGIONS THOUGHT TO BE INVOLVED IN HUMAN MATERNAL BEHAVIOR

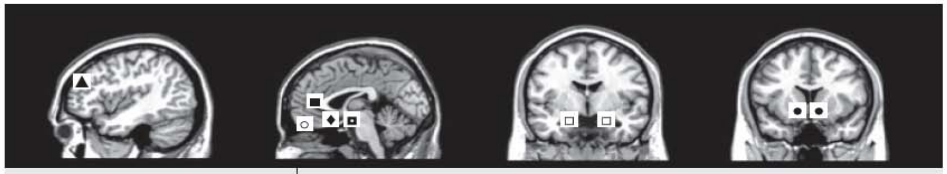
Are also thought to mediate processes of stimulus salience, reward, affect, and cognition

PREFRONTAL CORTEX

HYPOTHAL

AMYGDALA

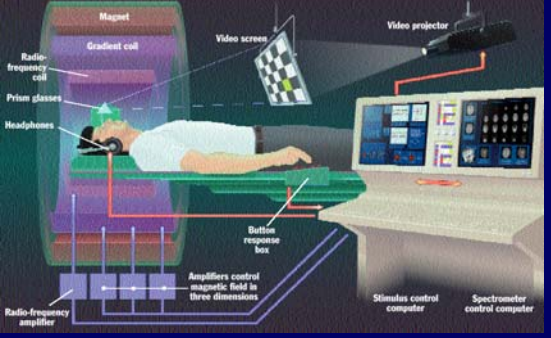
NUCLEUS ACCUMBENS



Brain Region	Location and Function
▲ Dorsolateral prefrontal cortex	•Lateral surface of the frontal lobes, corresponds to Brodmann areas 9, 46 and 9/46 (Petrides & Pandya, 1999) •Top-down control of cognitive and emotional processes,executive function, mood and emotion regulation (Davidson, 2002; Petrides, 2005; Koenigs & Grafman, 2009)
○ Orbitofrontal cortex	•Orbital surface of the frontal lobes, corresponds to Brodmann areas 10, 11 and 47 (Kringelbach, 2005) •Reward, impulsivity and response inhibition, affect/emotion, visceral function (Kringelbach, 2005; Milad & Rauch, 2007; Critchley, 2009; Shoenbaum et al., 2009)
■ Perigenual anterior cingulate cortex	•Medial surface of the frontal lobes, corresponds to Brodmann areas 24 and 32 around the genu of the corpus callosum (Carmichael and Price 1994; Vogt et al. 1995, 2005) •Affect/mood regulation, integrating information from the internal milieu to aid in response generation or behavioral control, social cognition (Paus, 2001; Lam, Batson & Decety, 2007; Drevets & Savitz, 2008; Chaudry et a., 2009; Wang et al., 2009)
♦ Subgenual anterior cingulate cortex	•Medial surface of the frontal lobes, corresponds to Brodmann area 25, 24 and 32, located below the genu of the corpus callosum (Carmichael and Price 1994; Vogt et al. 1995, 2005) •Affect/mood regulation, integrating information from the internal milieu to aid in response generation or behavioral control, anxiety and depression and associated functions (e.g., arousal, stress response) (Paus, 2001; Bremner et al., 2008; Johansen-Berg et al., 2008; Drevets & Savitz, 2008)
◘ Hypothalamus	•Ventral portion of the diencephalon •Motivated behavior, homeostatic and neuroedocrine functions, including blood pressure, heart rate, hunger, thirst, sleep, sexual and maternal behavior, also emotion (Risold et al., 1997; Sewards & Sewards, 2002, 2003)
□ Amygdala	•Medial temporal lobes, at the head of the hippocampus •Stimulus perception, intergration of stimuli with an affective value and organising output to guide affective, autonomic and behavioural responses, also mood/anxiety and stress (Shin, Rauch & Pitman, 2006; Gobbini & Haxby, 2007; Sergerie, Chochol & Armony, 2008; Drevets, Price & Furey, 2008; Dedovic et al., 2009)
● Nucleus Accumbens	•Part of the ventral striatum •Dopamine, integrates information from subcortical regions and prefrontal cortex, involved in motivated behaviors, especially those related to emotion and reward, also addiction and depression (Ikemoto & Panskeep, 1999; Di Chiara, 2002; Goto & Grace, 2005, 2008; Giacobbe, Mayberg & Lozano, 2009)

Brain structures thought to be important in human maternal behaviour. Note that these structures are ed of classic maternal regions such as the hypothalamus, as well as regions whose primary functions are nt to maternal behavior. The top panel illustrates the approximate anatomical location of each region; the able contains a color-coded legend describing each region in terms of location and function

BARRETT & FLEMING, 2011



Have embarked on a series of fMRI studies exploring activation patterns in NAC, AMYG, mPFC,

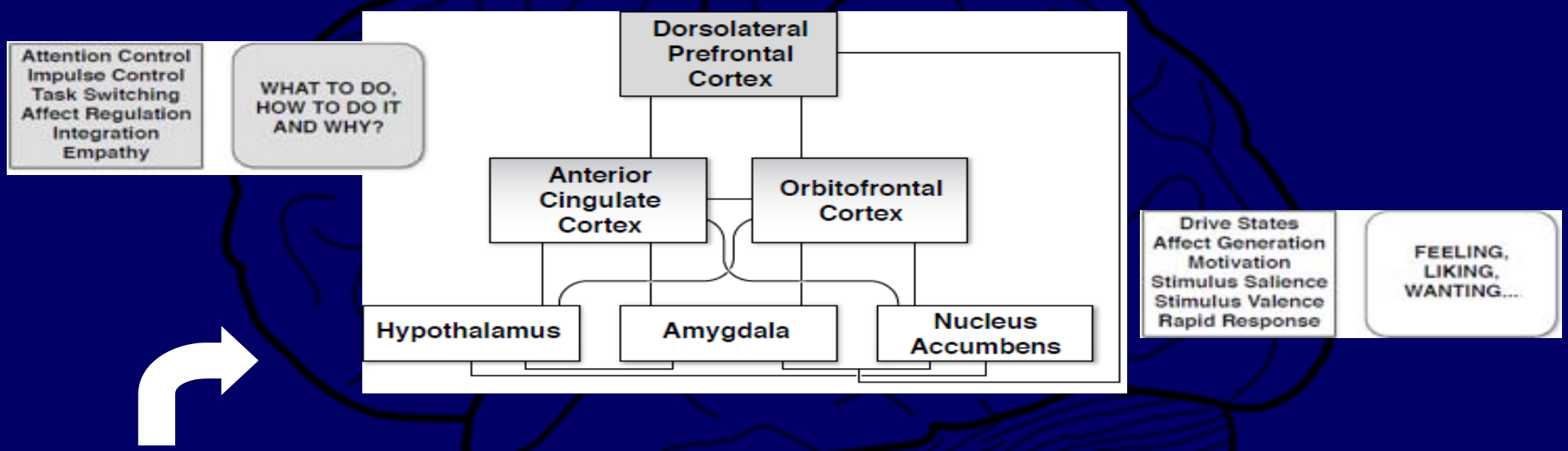
and

other brain sites in the maternal circuit

Study: Maternal affect and quality of parenting experiences are related to amygdala response to infant faces (barrett et al., in press)

Using a whole brain analysis and an ROI approach, we examined mothers' pattern of brain response to visual infant cues varying in emotional valence, familiarity, and as a function of mothers' early life experiences.

Anatomy of Human Maternal Behavior



- Reviewed in Barrett & Fleming, 2011;
- Barrett, Wonch, Hall, Steiner, & Fleming, in press

fMRI Study: Brain response to infant stimuli in new mothers

@3 months

Recruit on maternity ward:

•Moms age 20-40

•Healthy singleton

•No history of DEP

•No involvement of child services

@ 1-2 weeks

Session 1:

1. Photography Session -positive and negative facial expressions

2. Intake and SCID screening

Session 2:

1.fMRI session

2. Questionnaires:
-EPDS
-STAI-T

@ 1-2 weeks

Session 3:

1.Home Visit

2. Questionnaires:
-Parenting Stress
-Maternal Attitudes

Post-processing of pictures: photoshop and ratings

Blood Oxygenation Level Dependent (BOLD) signal
indirect measure of brain activity summ of -postsynaptic poten across ROI)

22 (9 primiparous, 13 multiparous) 3-5 mo.

•Barrett, Wonch, Hall, Steiner, & Fleming, in press

•Own

•>

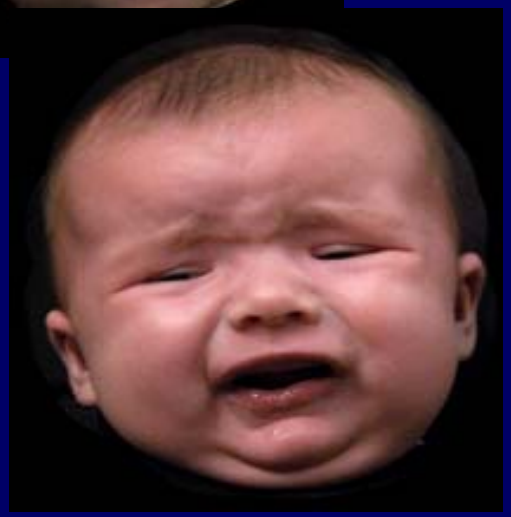
•DLPFC,

• OFC, BA25,

• pACC, HYPO,

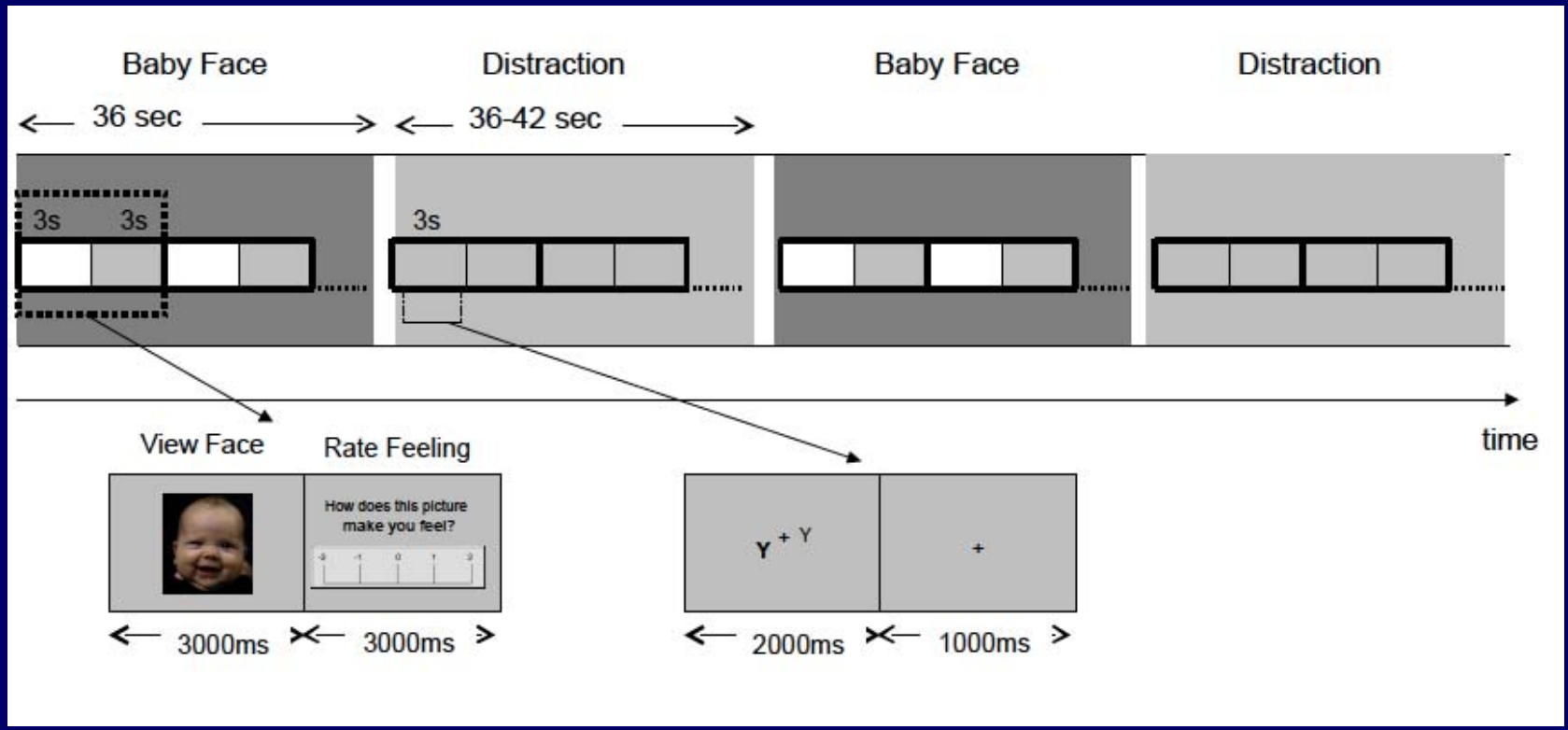
• NAC, AMY

•Unfamiliar



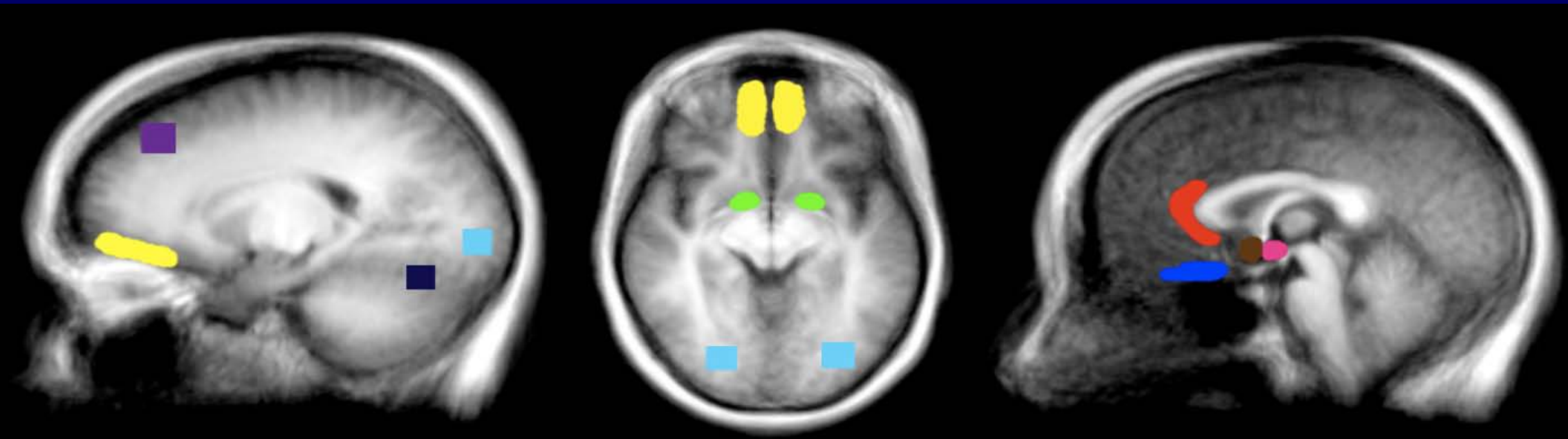
•Prediction: BOLD response in all ROIs will be greater for own

fMRI Protocol: Block design with own and other infant cry and smile faces presented in three runs, with distractor task between



Barrett, Wonch, Hall, Gonzalez, Steiner, & Fleming, in press

Activation of Limbic sites, especially NAC and Amyg by own 'positive' infant picture



Yellow = Orbitofrontal cortex (OFC)

Purple = Dorsolateral prefrontal cortex (DLPFC)

Navy = Fusiform face area (FFA)

Light blue = Occipital face area (OFA)

Pink = Anterior hypothalamus/medial preoptic area (HYPO)

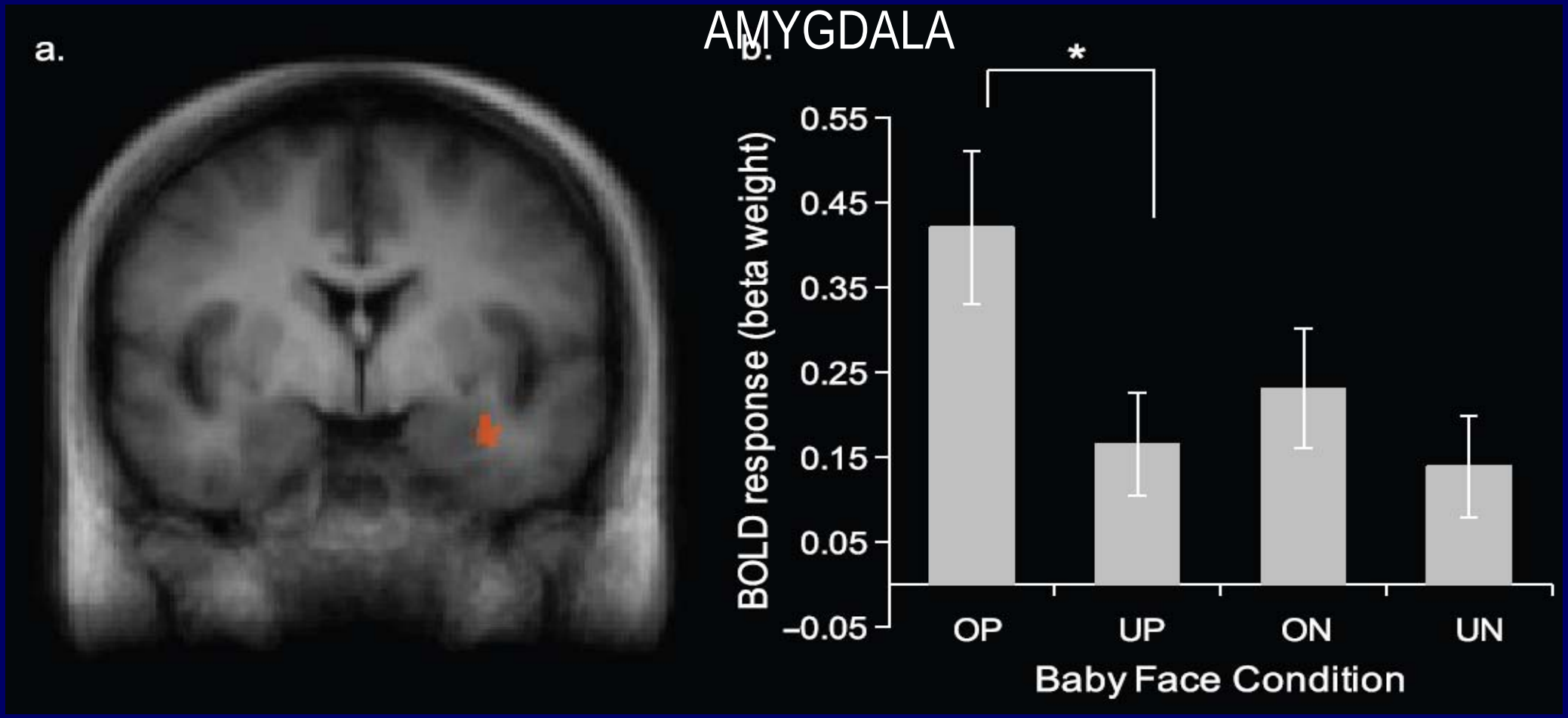
Blue = Subgenual anterior cingulate cortex (sACC)

Red = Perigenual anterior cingulate cortex (pACC

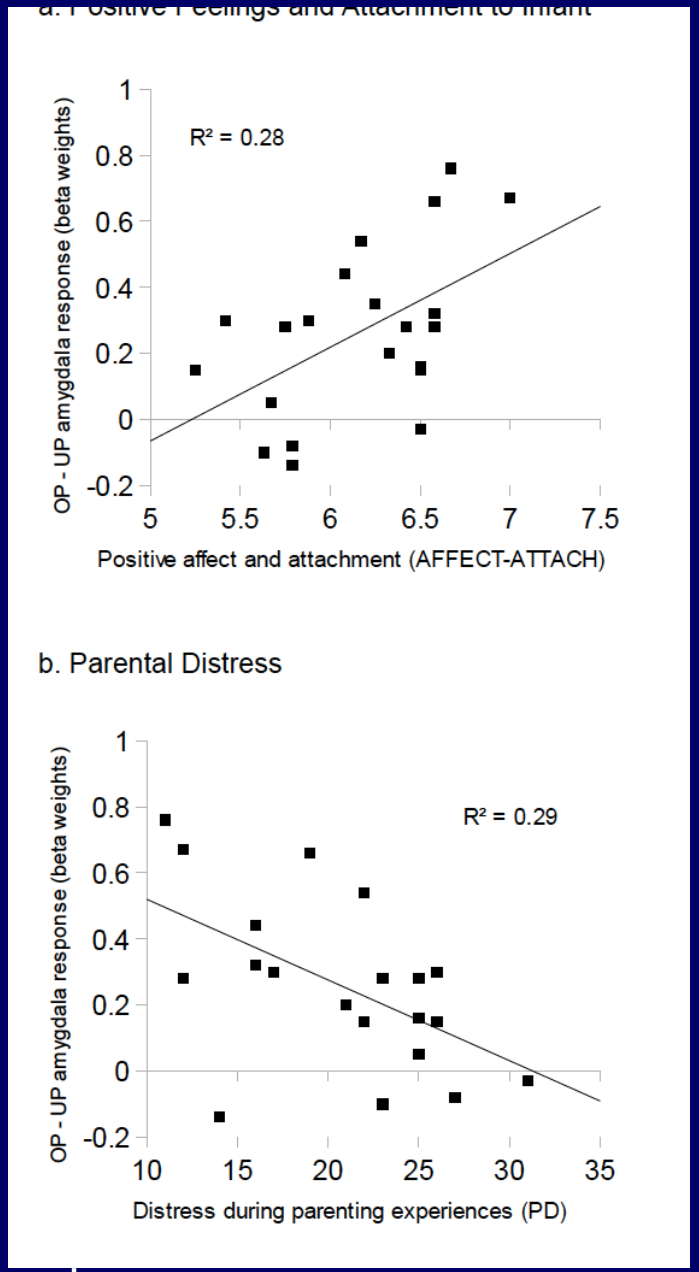
Brown = Nucleus accumbens (NAC)

Green = Amygdala (AMY)

Greater BOLD response to own positive infant faces over other positive infant faces in Amygdala and nucleus accumbens (not shown) (not true of many control sites)



Mothers showing higher BOLD responses in AMYGDALA to own positive vs other infant pictures feel more nurturant towards their infants and experience reduced reported parental stress

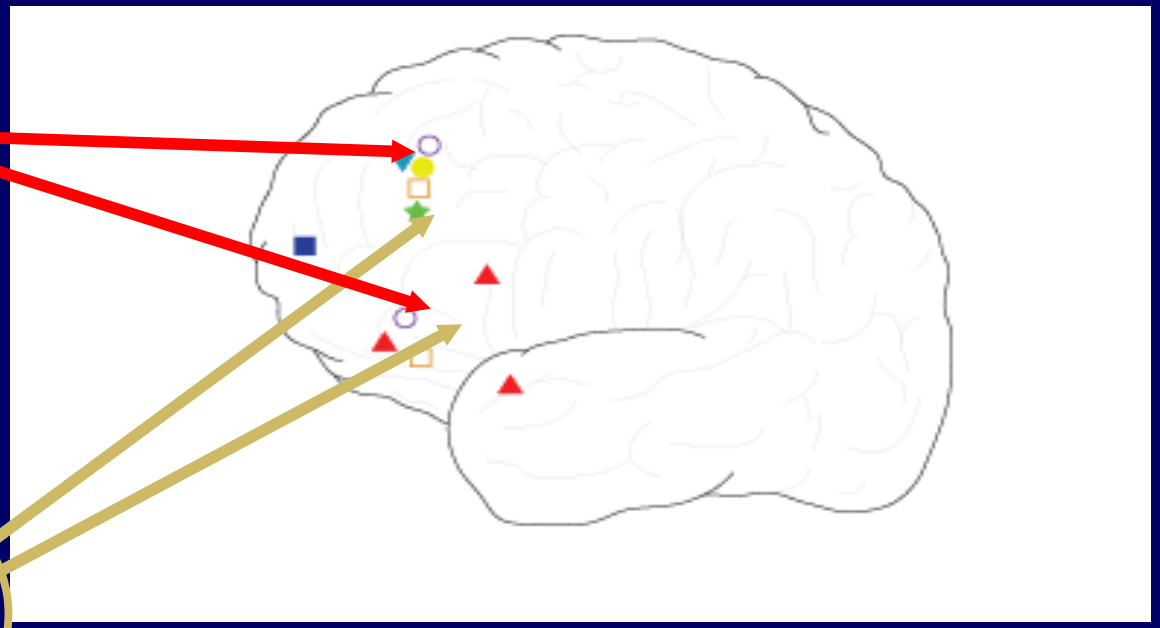


Barrett, Wonch, Hall, Steiner, Gonzalez, & Fleming, in press

A summary of the fMRI studies shows that regions of the cortex that are activated during An executive function task overlap with areas that are activated by infant stimuli in the magn

Associated with infant cues

With performance on tasks of executive function



- activation - Empathy (Völlm et al., 2006)
- activation on Theory of Mind Tasks (Beer and Oschner, 2006; Decety and Sommerville, 2003; Frith and Frith, 2006; Lieberman, 2007; Völlm et al., 2006)
- activation on spatial working memory tasks (Cabeza and Nyberg, 2000; Owen et al., 1996; 1998)
- activation on tasks cognitive and flexibility (ID/ED and WCST), (Alvarez and Emory, 2006; Barcelo, 2000; Hampshire and Owen, 2006; Rogers et al., 2000)
- deactivation in mothers in response to infant cues (cries and pictures)
- activation in mothers in response to infant cues (cries and pictures) Bartels and Zeki, 2004; Lorberbaum et al., 2002; Nitschke et al., 2004; Popeski et al. in prep.; Seifritz et al., 2003; Strathearn and McClure, 2002; Swain et al., 2007)
- related to both empathy and cognitive flexibility (Shamay-Tsoory et al., 2003)

Gonzalez, Atkinson, & Fleming, 2009

Summary

- Due to hormones, mothers change from animals that are neophobic and ‘timid’ to animals that will approach novel stimuli and pups.

- Young are first attractive, then rewarding, to the new mother as a result of both hormones and experience

- Rewarding and salient young regulate mothers’ approach to and contact with the young. They enhance her motivation to mother.

Summary, cont'd

- Attraction to young pp is mediated by the 'reward' dopamine system, especially nucleus accumbens or mesolimbic DA system
- Altered emotional state pp is mediated by the amygdala system
- Altered attention pp is mediated by the mPFC system

Summary, cont'd again

- These brain systems interface with the final common path for the expression of mothering, the MPOA

- And their development is mediated by previous experiences and by genetics (ANOTHER STORY, ANOTHER TIME)

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