



Addiction and Disordered Attachment

What leads to what?

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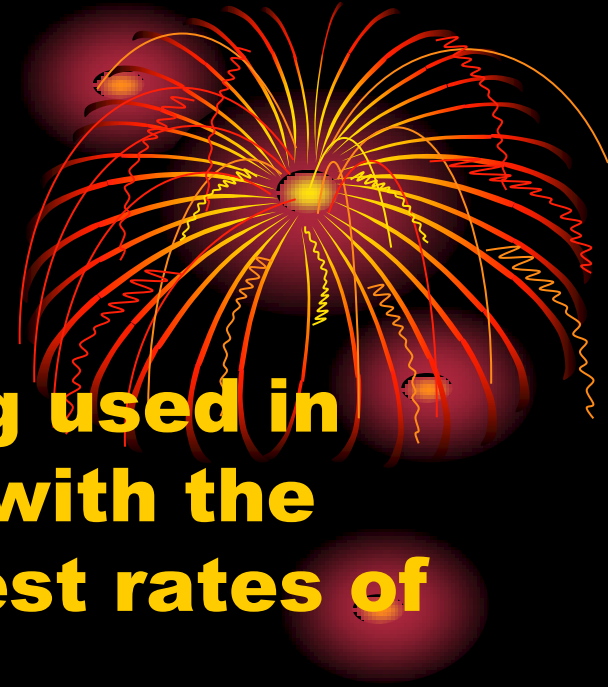
Addiction and maternal care



- **Addiction severely impairs a mother's ability to care for her infant**
- ***But* does impaired early childhood caregiving also increased one's vulnerability to addiction?**

Cocaine

- **2nd most popular illicit drug used in Europe (2nd to marijuana), with the UK having one of the highest rates of use**
- **~12 million Europeans (3.6%) have used cocaine at least once, 4 million (1.2%) in the last year, and 2 million in the last month (0.5%)**
- **Cocaine addiction is on the increase in the UK, especially London and the south-east**



Cocaine



- **Usually snorted but sometimes injected**
- **Crack cocaine**
 - **more volatile base form produced by heating powder with baking soda and water**
 - **usually smoked but sometimes injected.**
- **Results in a “high” followed by a “come down”**
- **Almost 90% of those who used in the last year are young adults (15–34 years old)**
- **One in three users are female**

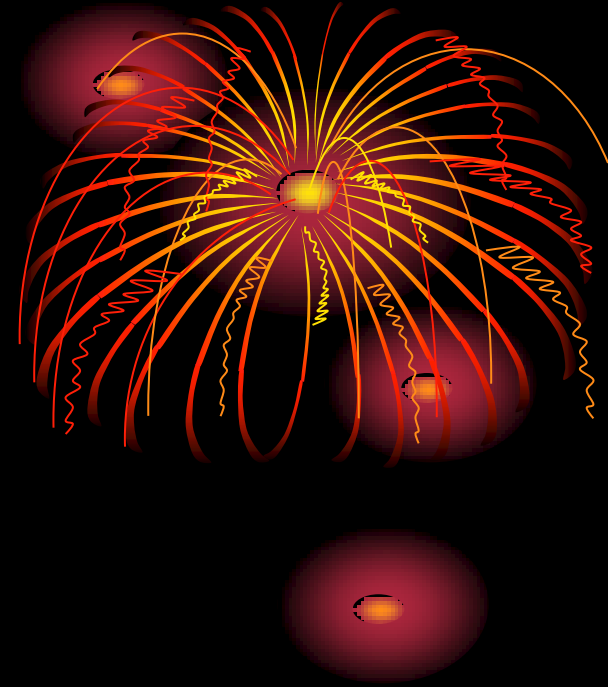
Maternal Addiction



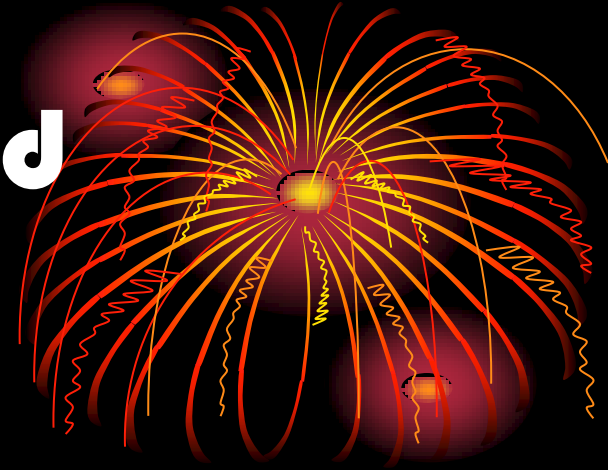
- **Data unknown in the UK**
- **In the US, 5.2% of pregnant women report using illicit substances during the past month**
- **In the US, there are 750,000 drug exposed births annually**
- **High rates of reported child maltreatment and foster care placement**

Maternal Addiction

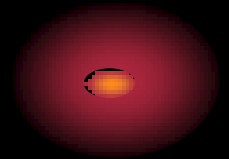
- **Addicted mothers are**
 - **More harsh and threatening**
 - **More overly involved**
 - **More authoritarian**
 - **More permissive and neglectful**
 - **Show role-reversal with child**
 - **Less tolerant of child's demands**
- **Infants are**
 - **More stressed to novelty**
 - **Less interactive and show less pleasure**



The maternal brain and cocaine abuse



- **Cocaine co-opts similar neural circuitry involved in maternal behavior**
 - **Mesocorticolimbic and nigrostriatal dopamine circuits**
 - **Oxytocinergic system**
 - **Stress system**

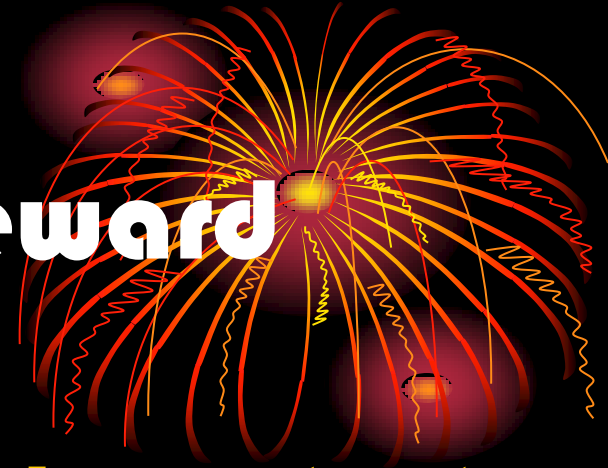


Possible Neuroendocrine Systems Involved in Attachment Behavior



- 1. Dopamine (DA)**
- 2. Oxytocin (OT)**
- 3. Corticotrophin releasing factor (CRF)**

Dopamine – drug of reward

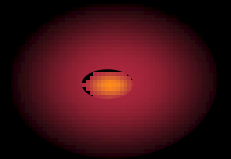


- **Brain neurotransmitter important in:**
 - **Maintenance of maternal behavior (released during mother-pup interaction in rats)**
 - **Reward learning / reinforcement behavior**
 - **Prediction of temporal differences / errors**

Dopamine – drug of reward



- **Implicated in the following disorders:**
 - **Drug addiction**
 - **Attention deficit hyperactivity disorder**
 - **Compulsive gambling**
 - **Schizophrenia**



Oxytocin – drug of affiliation



- **Blood hormone important for**
 - **Initiation of labor**
 - **Breastfeeding**
- **Brain neuromodulator critical for**
 - **Onset of maternal behavior**
 - **Sexual behavior (orgasm, penile erection)**
 - **Reduction in anxiety/fear responses**
 - **Learning and social memory**
 - **Trust**

CRF (Corticotrophin Releasing factor) – Drug of Stress



- **Stimulates release of a cascade of stress-related hormones**
- **Receives negative feedback from cortisol, via the glucocorticoid receptor**
- **Maternal care alters the expression of this receptor via epigenetic mechanisms**

Model: Maternal Brain Responses



**Mesocorticolimbic
Dopamine
Pathway: “Reward”**

**Nigrostriatal
Dopamine Pathway:
“Action
Contingencies”**

**MEDIAL
PREFRONTAL
CORTEX
(mPFC)**

**DORSOLATERAL
PREFRONTAL
CORTEX (DLPFC)**

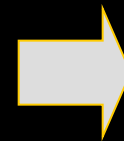
**SENSORY
INPUT**
(e.g. infant face
cues)



**VENTRAL
STRIATUM**

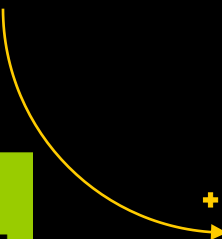
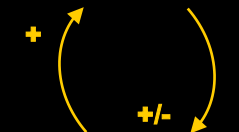
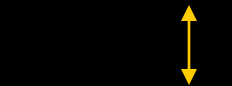
**DORSAL
STRIATUM**

**MOTOR
OUTPUT**
(e.g. caregiving
behavior)



**VENTRAL
TEGMENTAL
AREA (VTA)**

**SUBSTANTIA
NIGRA
(SN)**



Model: Cocaine and Maternal Responses

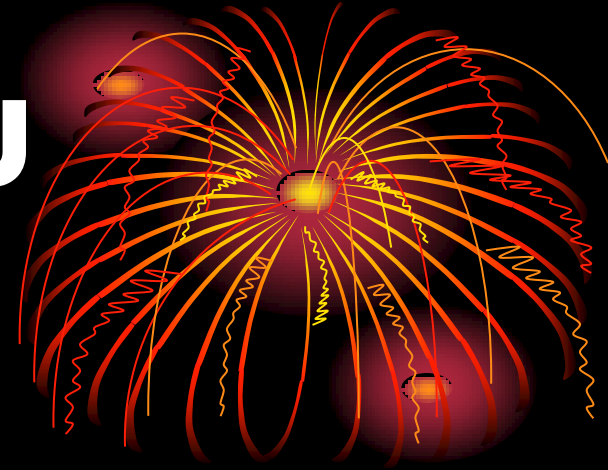
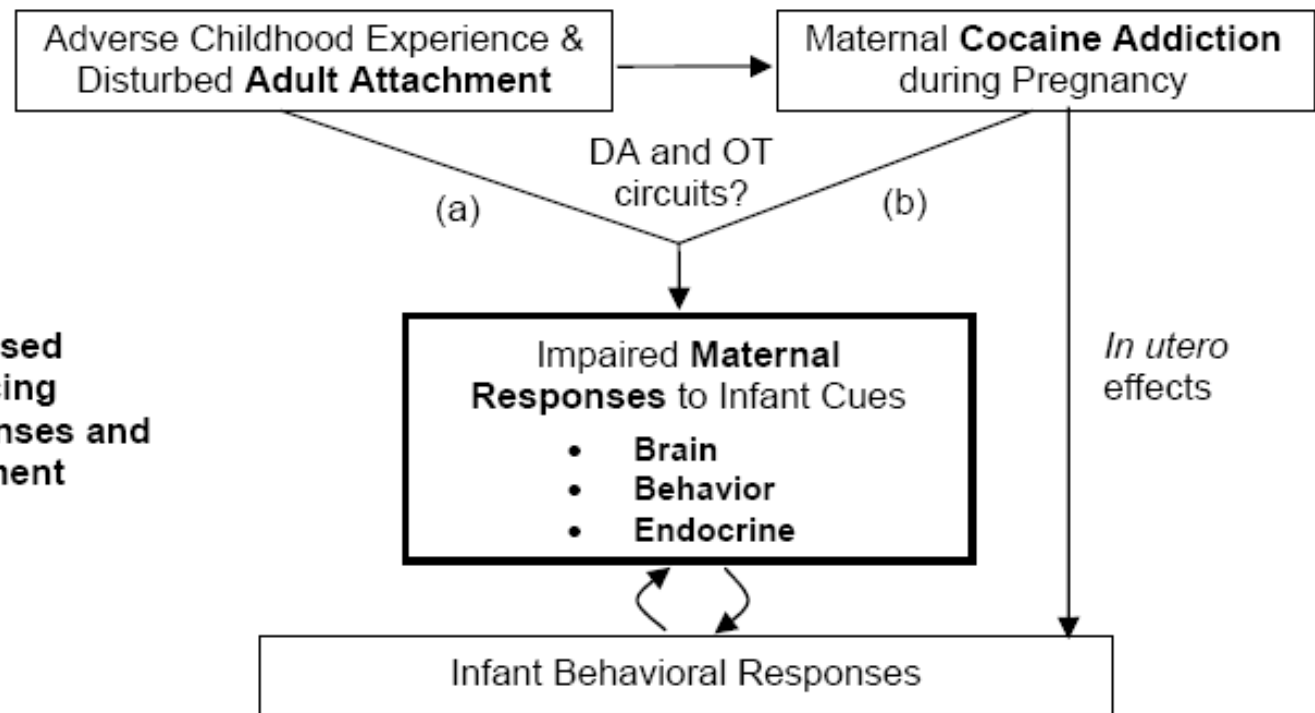


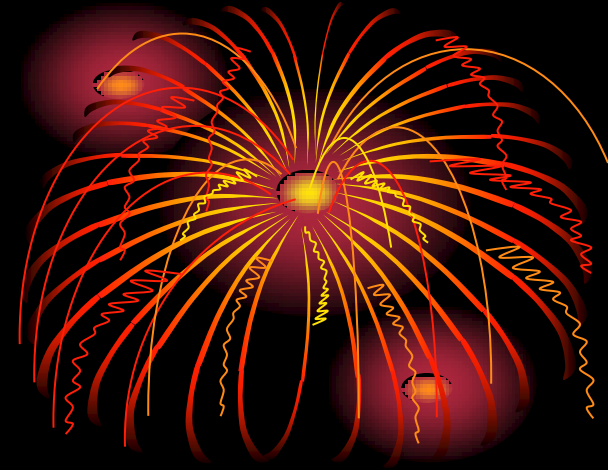
Figure 1: Proposed factors influencing maternal responses and infant development

DA, dopamine

OT, oxytocin



Pilot Study of Cocaine Exposed Mothers



- **Visit 1: Mothers of 3-6 month old infants from Santa Maria Hostel, a residential treatment program**
 - **Addiction Severity Index**
 - **Videotaped mother-infant interaction**
- **Visit 2: 2 weeks later**
 - **Parent Development Interview**
 - **Functional MRI: maternal responses to infant facial cues – Happy/Neutral/Sad**



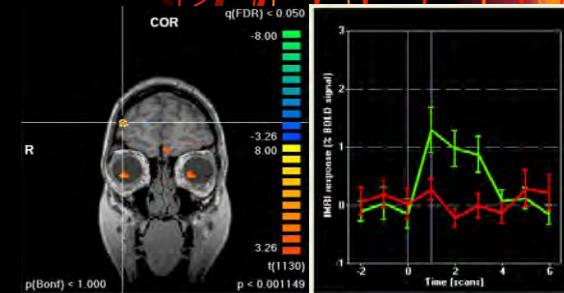
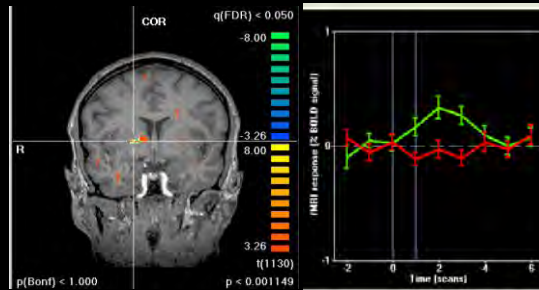
MATERNAL BRAIN RESPONSES TO OWN VS. UNKNOWN HAPPY BABY FACE

($p < 0.005$, Fixed Effects Analysis)

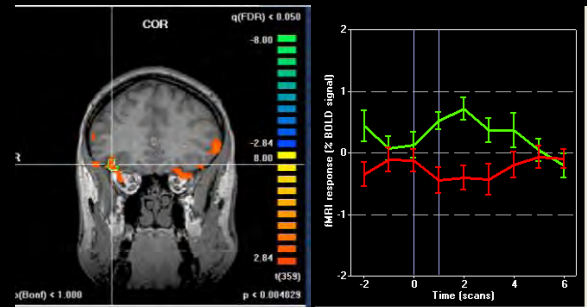
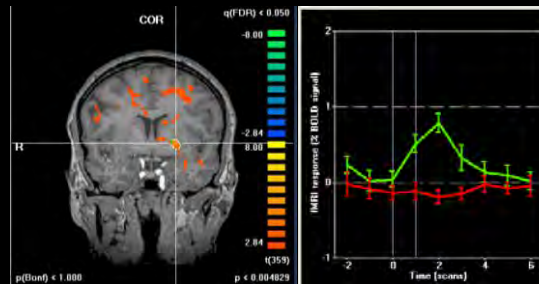
PREFRONTAL
CORTEX

Normal Control
(secure attachment)
($n=6$)

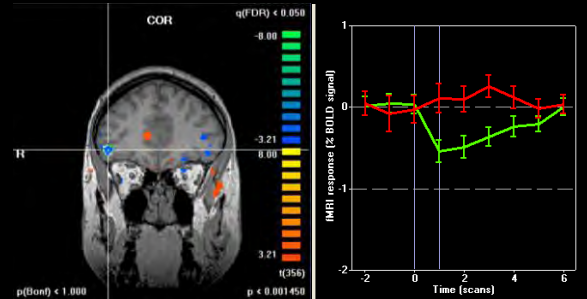
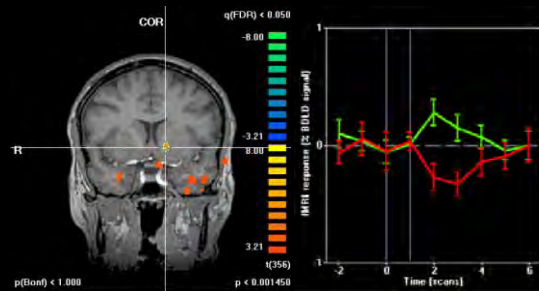
VENTRAL STRIATUM

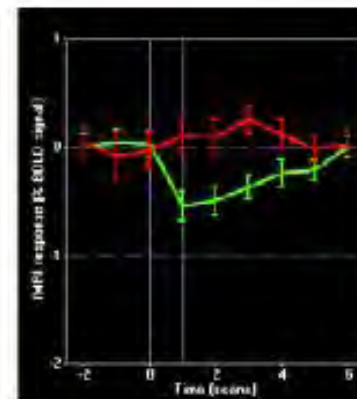
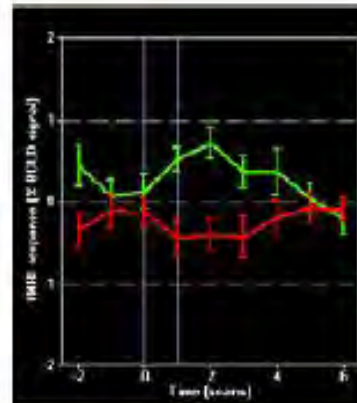


**Residential
Treatment
Control ($n=2$)**



**Chronic
Multi-drug
Abuse ($n=2$)**





p<0.005,
FDR corrected p<0.05;
Fixed Effects Analysis

Implications for Maternal Care

- **Cocaine addicted mothers appear to show normal ventral striatum responses to happy infant face cues**
- **However, there appears to be a marked deficit in prefrontal cortex response, with de-activation seen in chronically abusing mothers**
- **This may be related to impaired judgment in responding to infant cues, which may predispose to child neglect or abuse.**

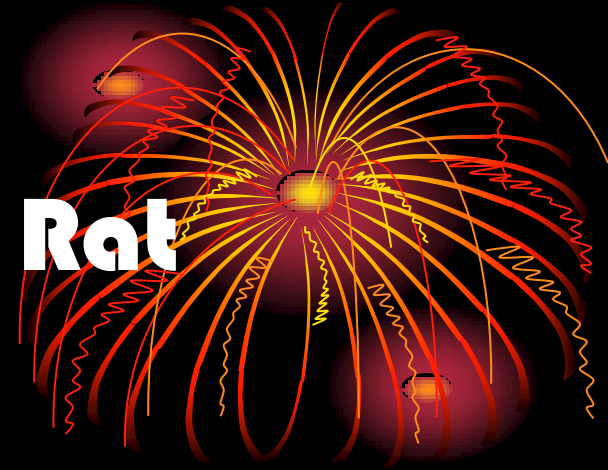


Implications for Infant Development



- **Drugs such as cocaine may have a direct in utero effect on infant behavior and development**
- **But, may also effect infant development via changes in maternal caregiving**

Maternal Behavior in the Rat



- **Pup vocalization**
- **Licking and grooming**
- **Arched-back nursing**

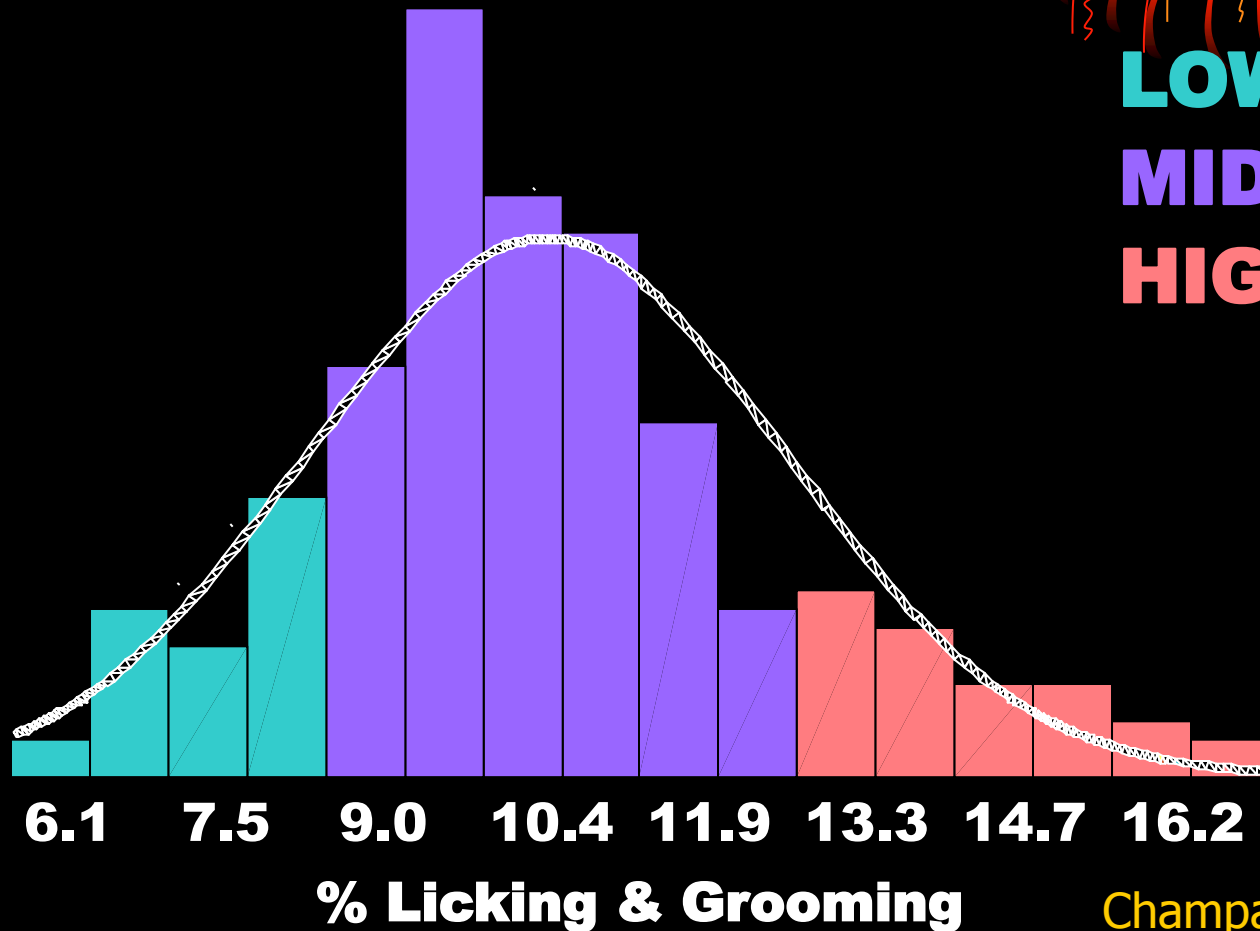


Champagne, 2003

Frequency Distribution of Time Spent licking/ Grooming by lactating Mothers

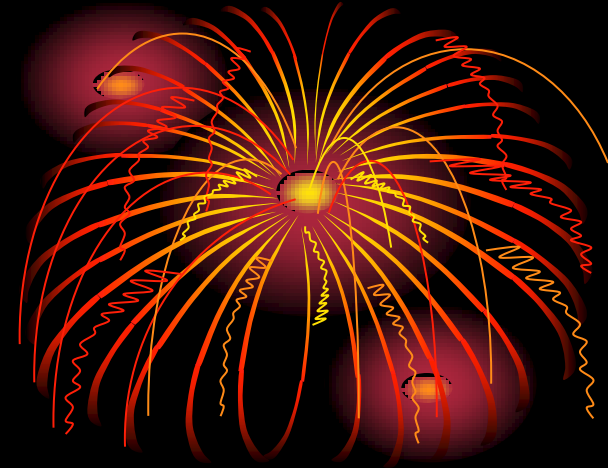


LOW
MID
HIGH



Champagne, 2003

Offspring of low vs. High Licking/Grooming Mothers



1. Cognition

- **Decreased hippocampal synaptogenesis**
- **Decreased neurotrophic factors (e.g. NGF, BDNF)**
- **Altered NMDA glutamate receptor expression**
- **Decreased dopamine production in the nucleus accumbens** J Neurosc 2004 24:4113
- **Reduced spatial memory and learning**

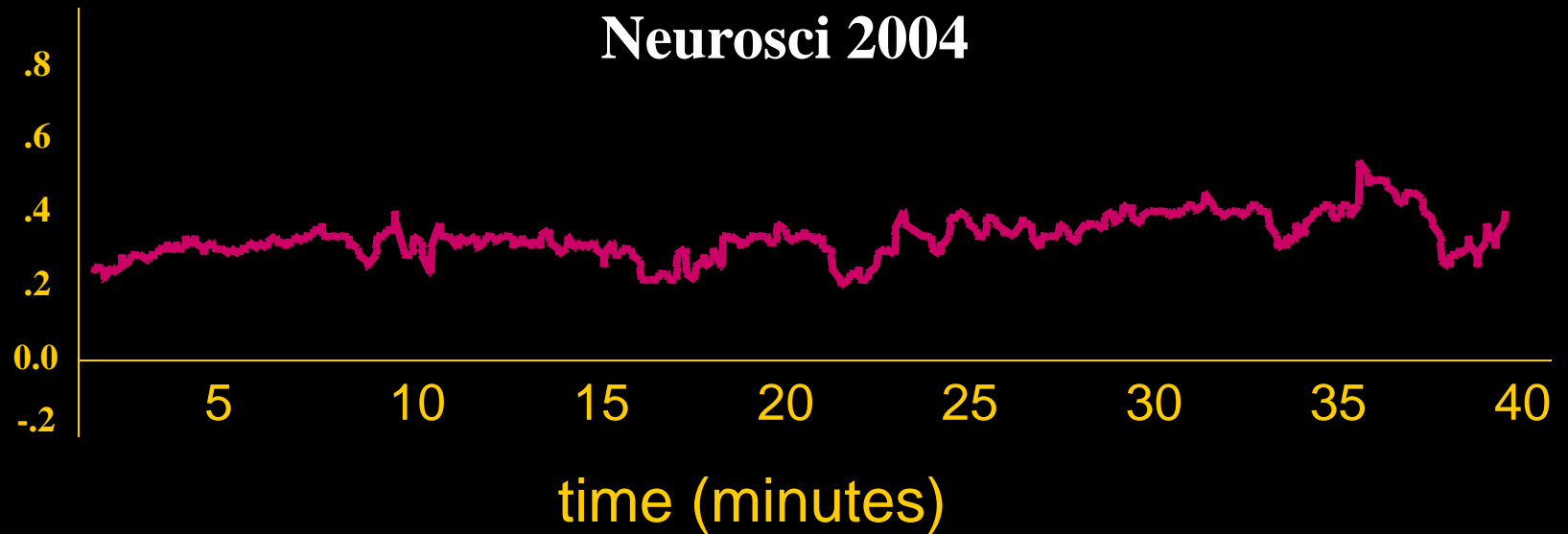


Champagne, 2003



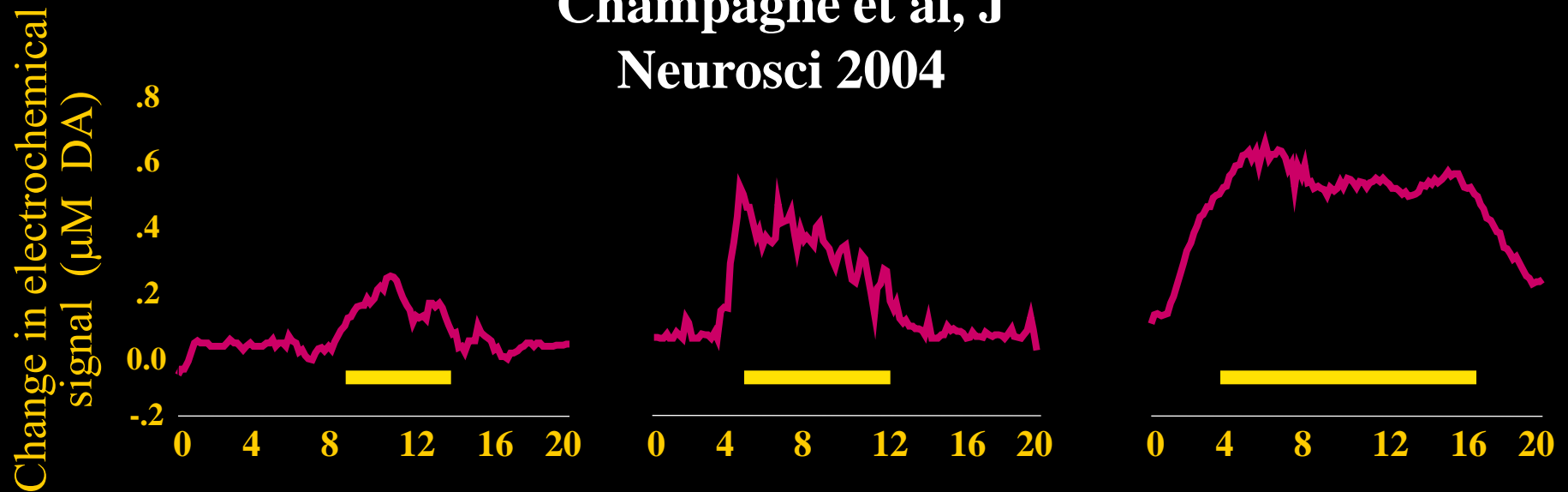
Champagne et al, J
Neurosci 2004

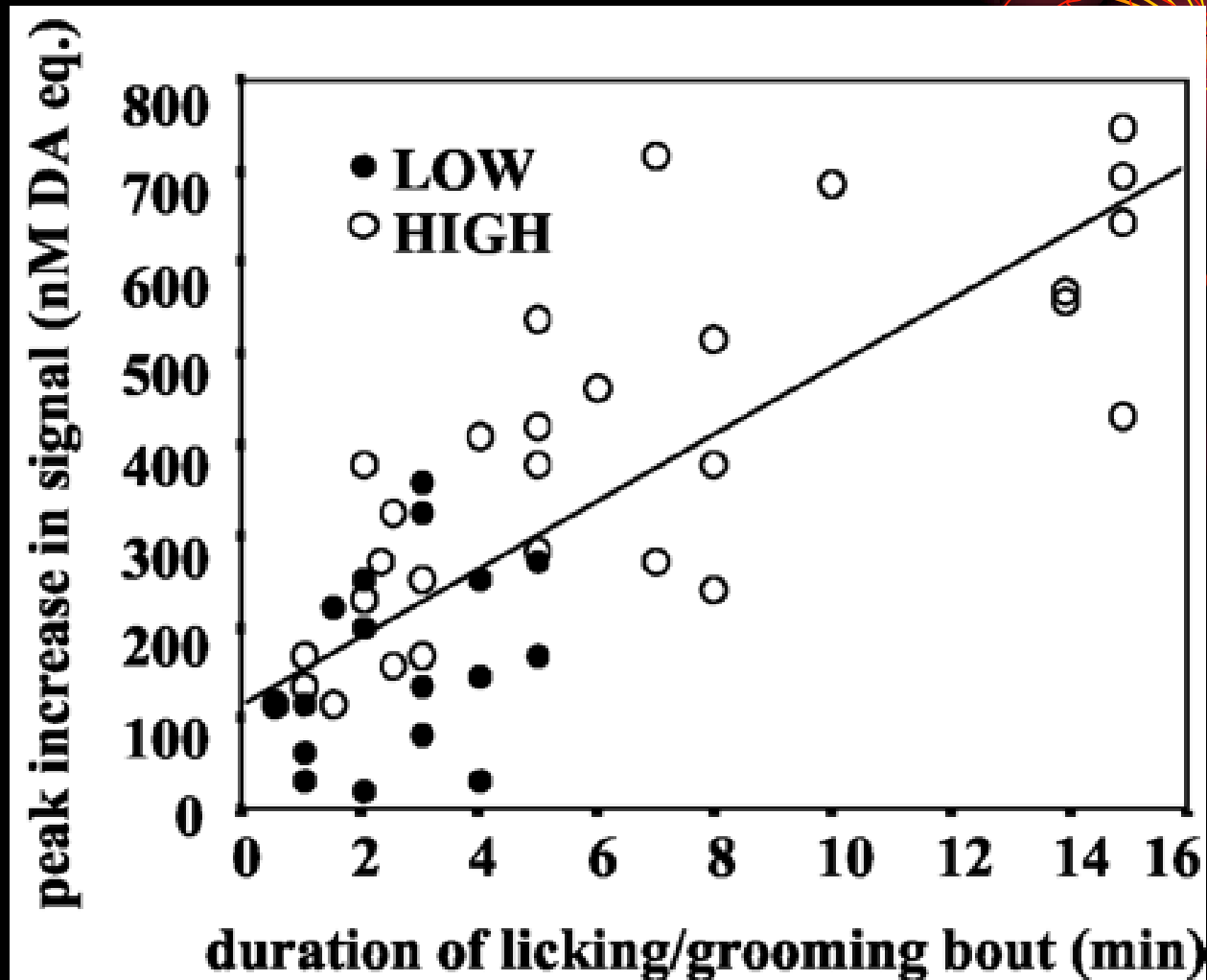
Change in electrochemical
signal ($\mu\text{M DA}$)



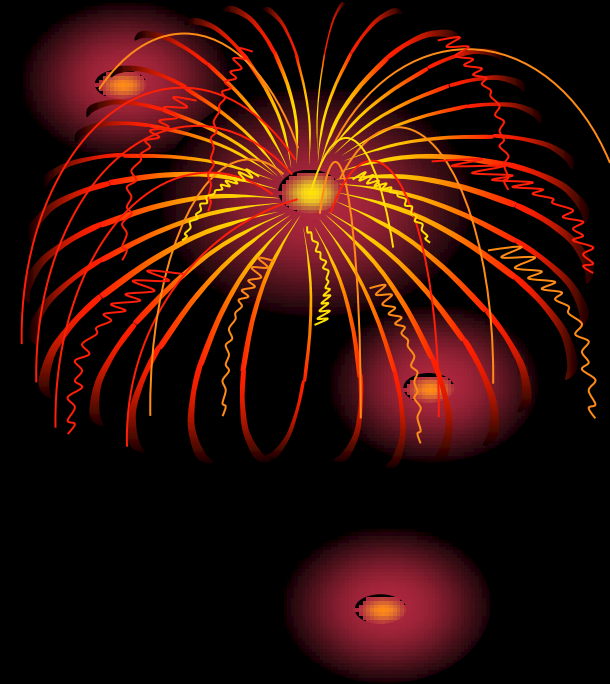
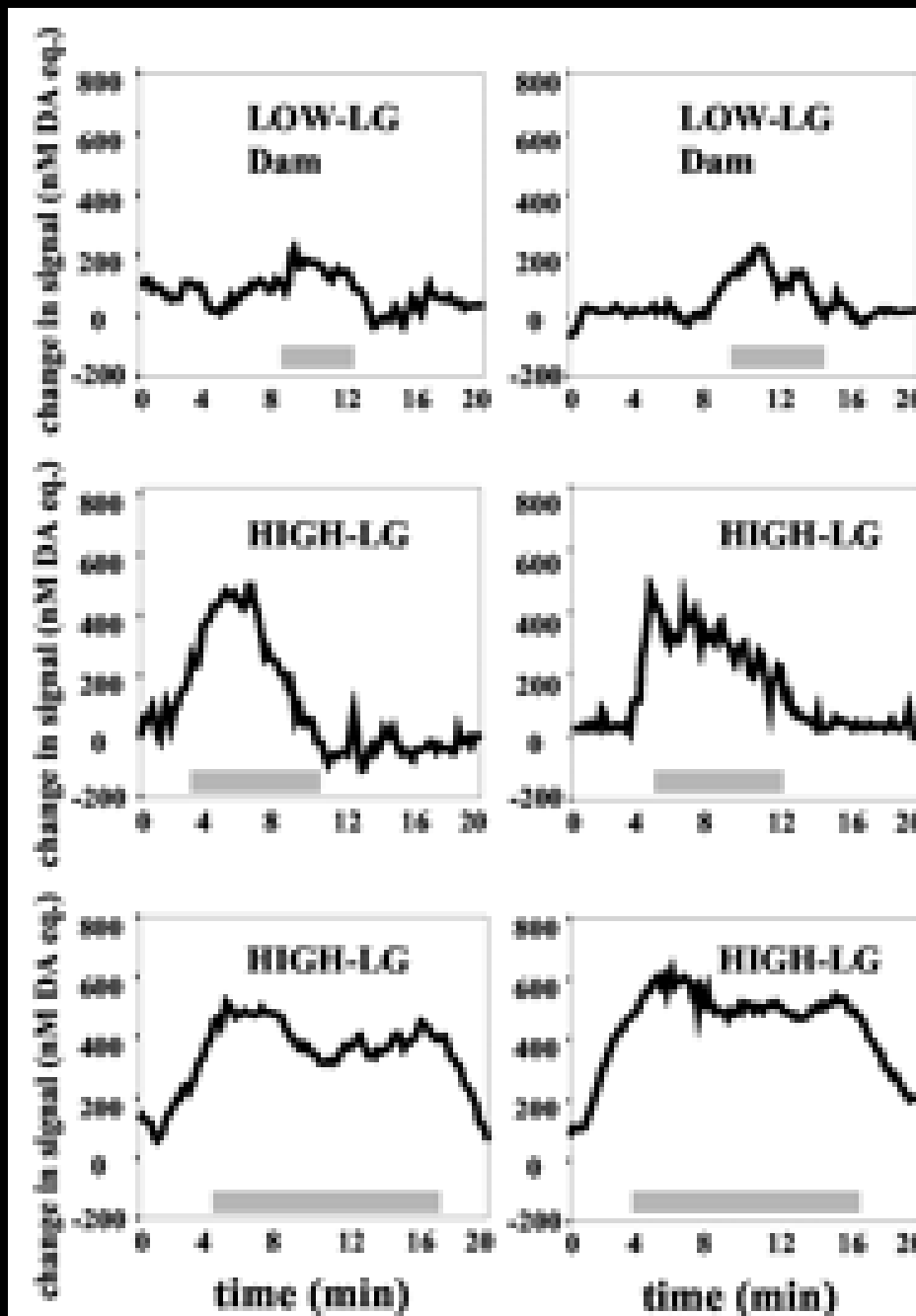


Champagne et al, J
Neurosci 2004



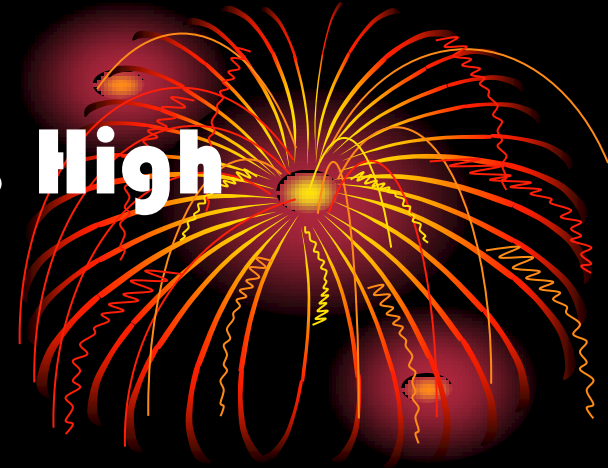


**Champagne et al, J
Neurosci 2004**



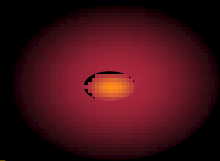
**Champagne et al, J
Neurosci 2004**

Female Offspring of low vs. High Licking/Grooming Mothers

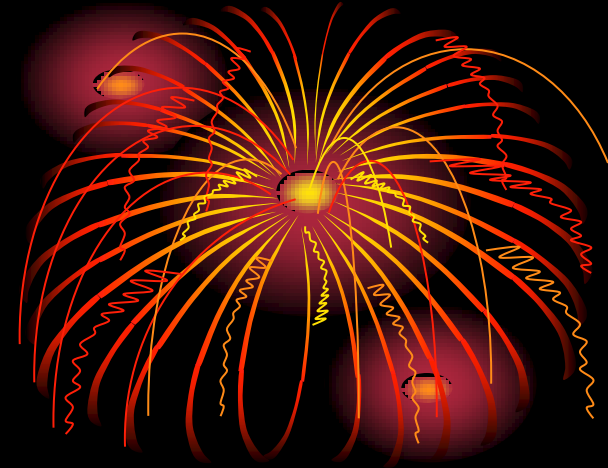


2. Maternal Behavior

- **Decreased oxytocin receptor expression (BNST, amygdala, PVN, MPOA, lateral septum)**
Proc.Natl.Acad.Sci.U.S.A 2001 98:12736
- **Decreased levels of licking/grooming, arched back nursing and other maternal behaviors**
Science 1999 286:1155

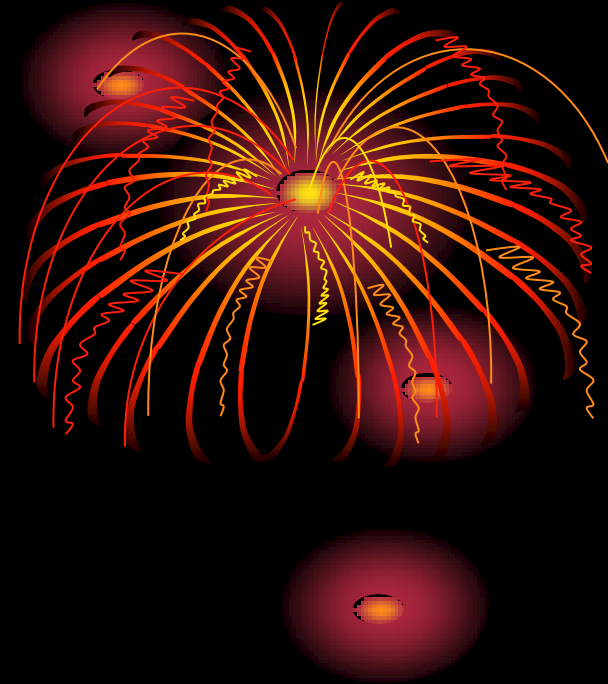
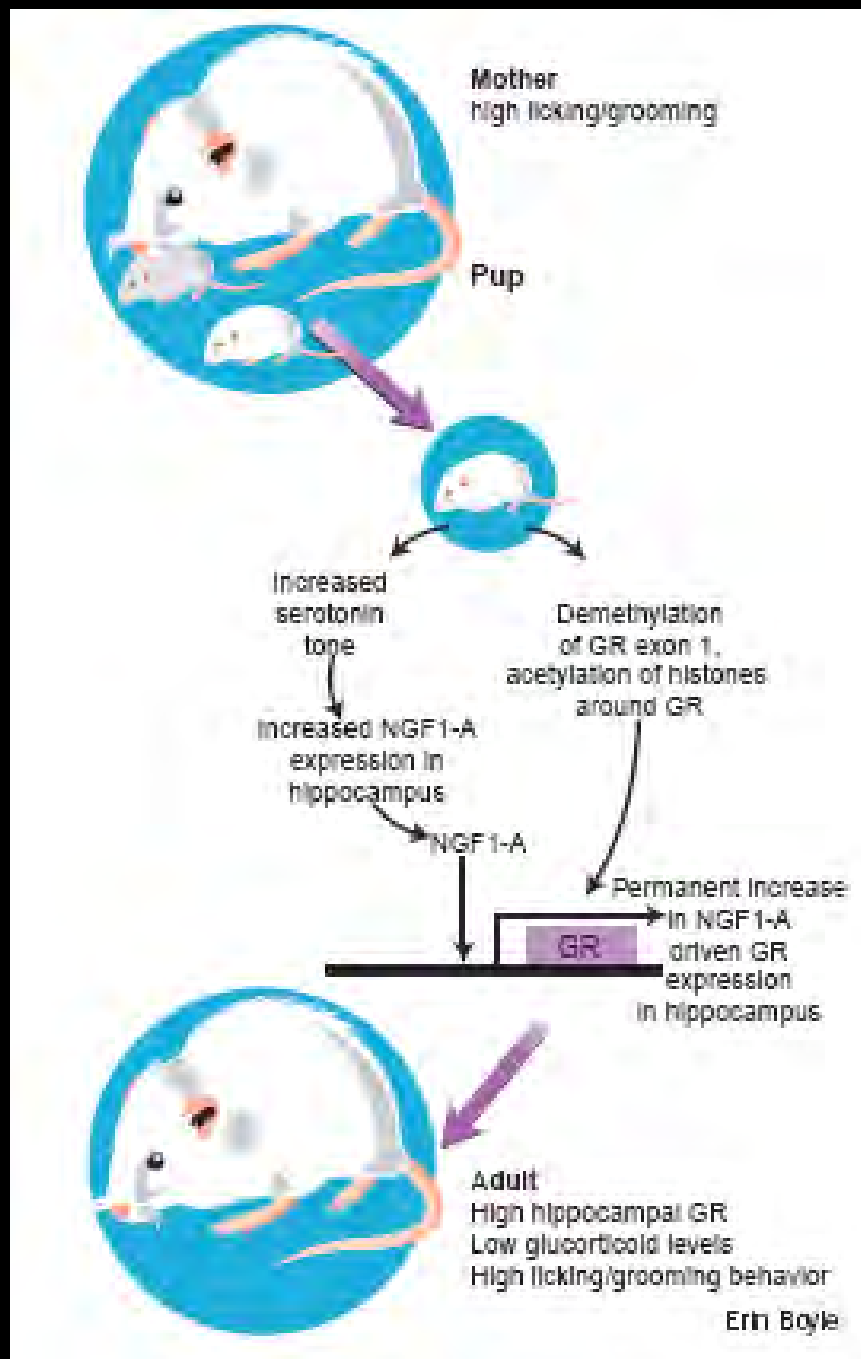


Offspring of low vs. High Licking/Grooming Mothers



3. Stress Reactivity

- **Decreased GR mRNA in the hippocampus (with DNA methylation of GR promoter)** Nat Neurosc 2004 7:847
- **Increased CRF mRNA**
- **Increased glucocorticoid and ACTH production in response to stress** Science 1997 277:1659
- **Impaired BZD receptor expression**
- **Reduced open field exploration (increased anxiety)**



Sapolsky, *Nat Neurosci* 7:791

Model: Cocaine and Maternal Responses

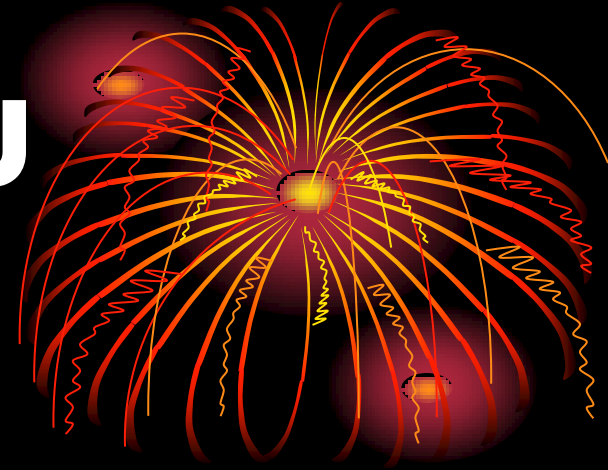


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