Social Stress, Stress Hormones and Neurotoxins

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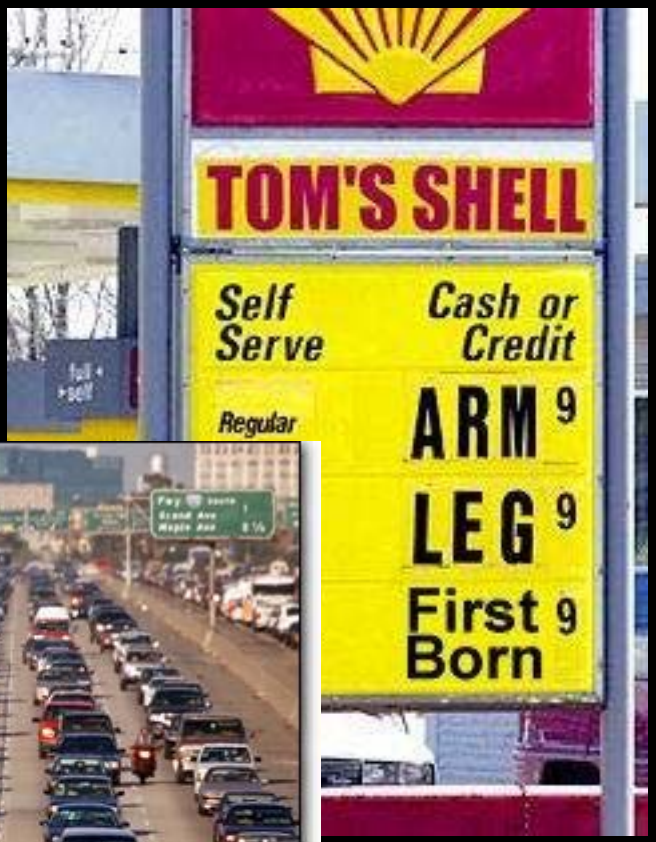
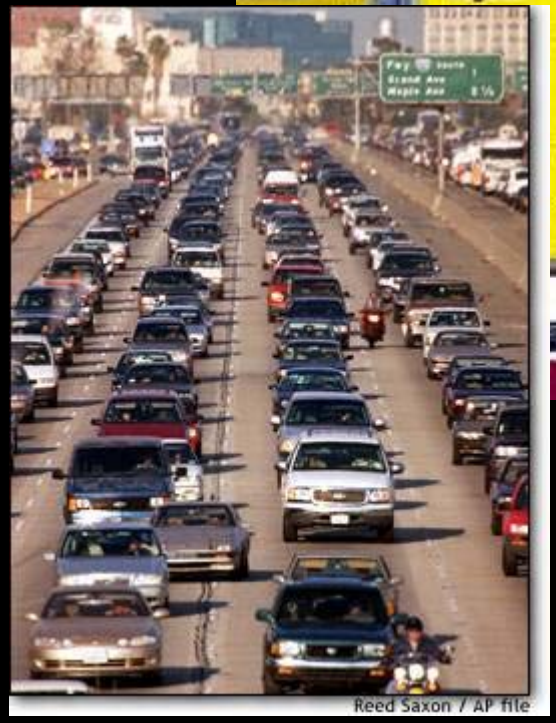

TOM'S SHELL
Self Serve
Cash or Credit
Regular
ARM 9
LEG 9
First 9 Born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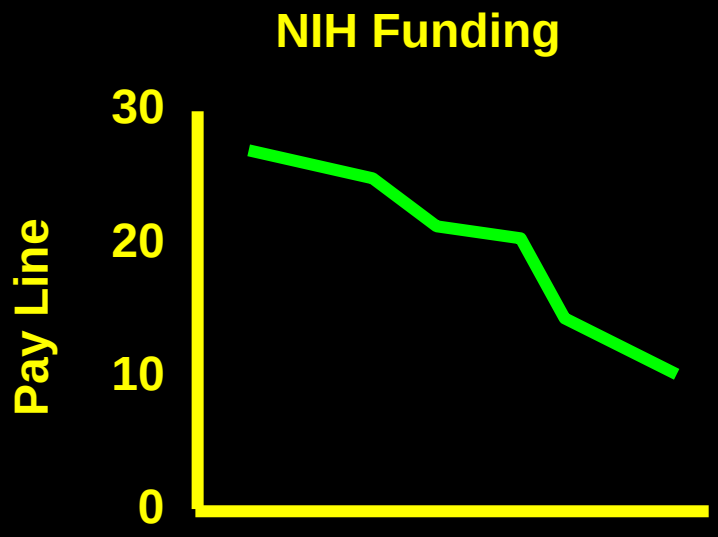
NIH Funding
Pay Line
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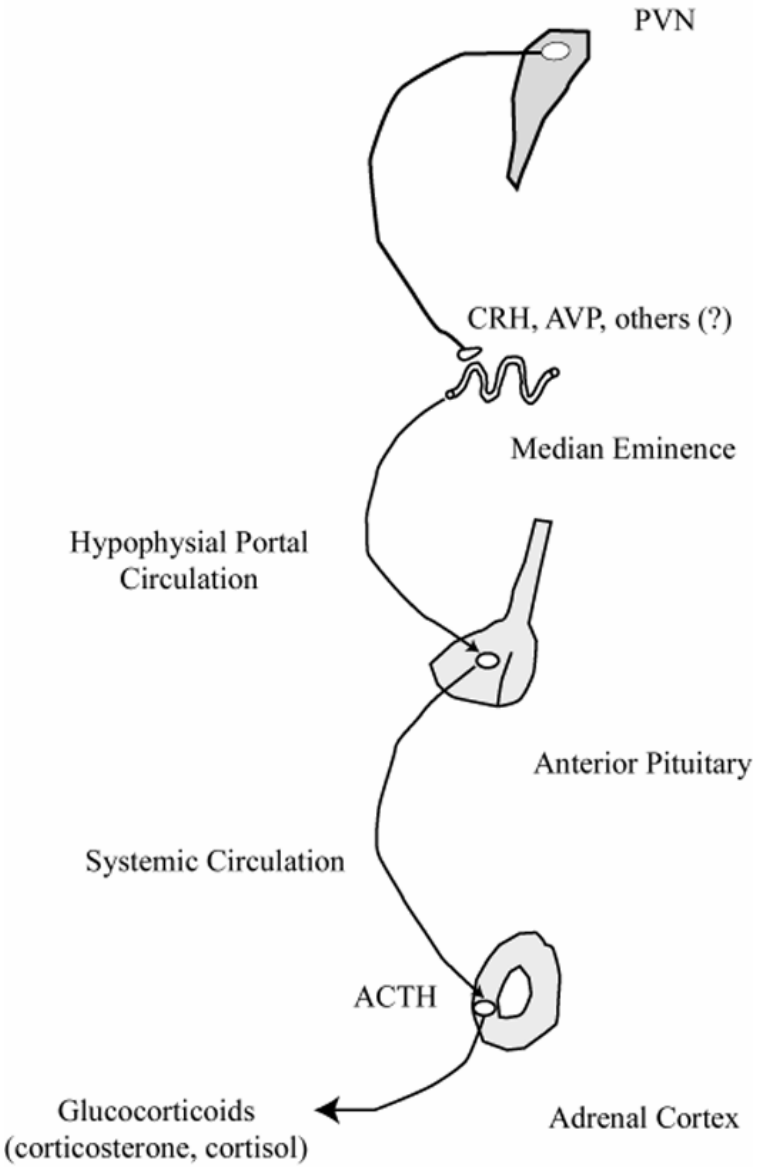
Stress Responses

✓ **Anticipatory in nature:**

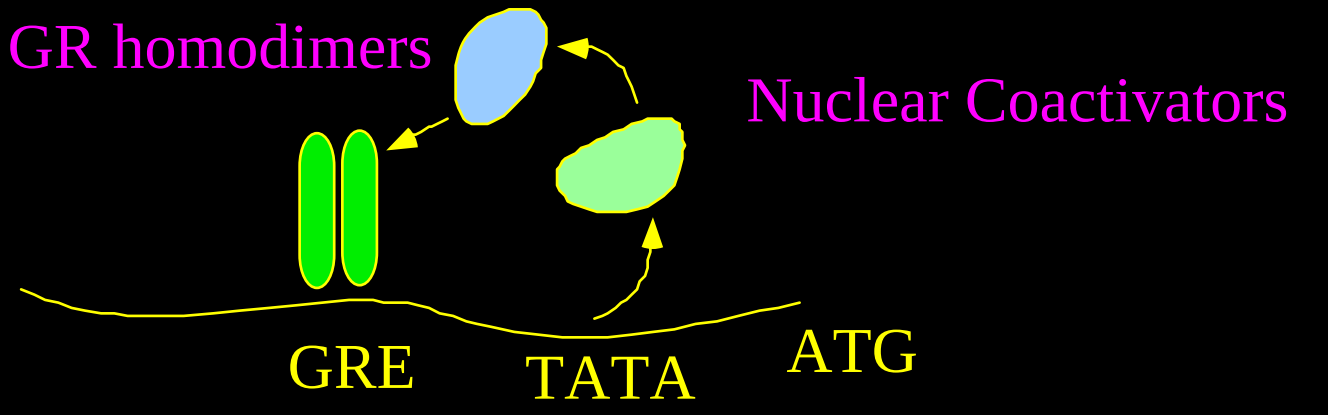
***Caused by possible threat to homeostasis**
***Generated by stimulus comparison**
innate programs
learning

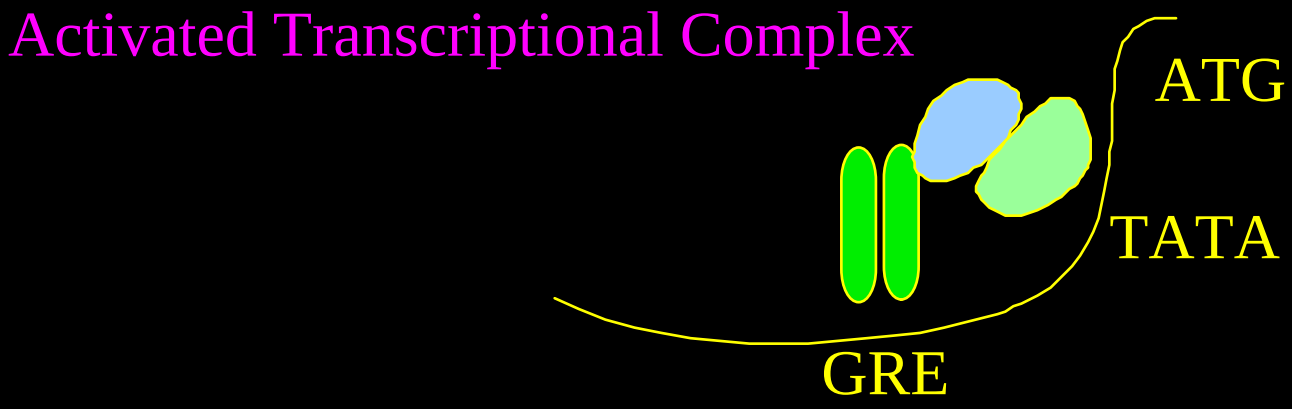
Reactive in nature:

***Caused by direct threat to homeostasis**
***Generated by reflexive pathways**



Herman and Seroogy, Neurol. Clin. 24:641 (2006)


GR homodimers
Nuclear Coactivators
GRE
TATA
ATG


Activated Transcriptional Complex
ATG
TATA
GRE

The HPA Stress Axis and Organismic Homeostasis: Redistribution of Resources

Short-term benefit:

***Energy mobilization**

***Energy diversion**

***Limits immune responses**

***CNS Arousal**

Long-term consequences:

***Metabolic Disease, obesity**

***Musculoskeletal atrophy, HPG problems**

***Immune dysfunction**

***Depression, PTSD(?)**

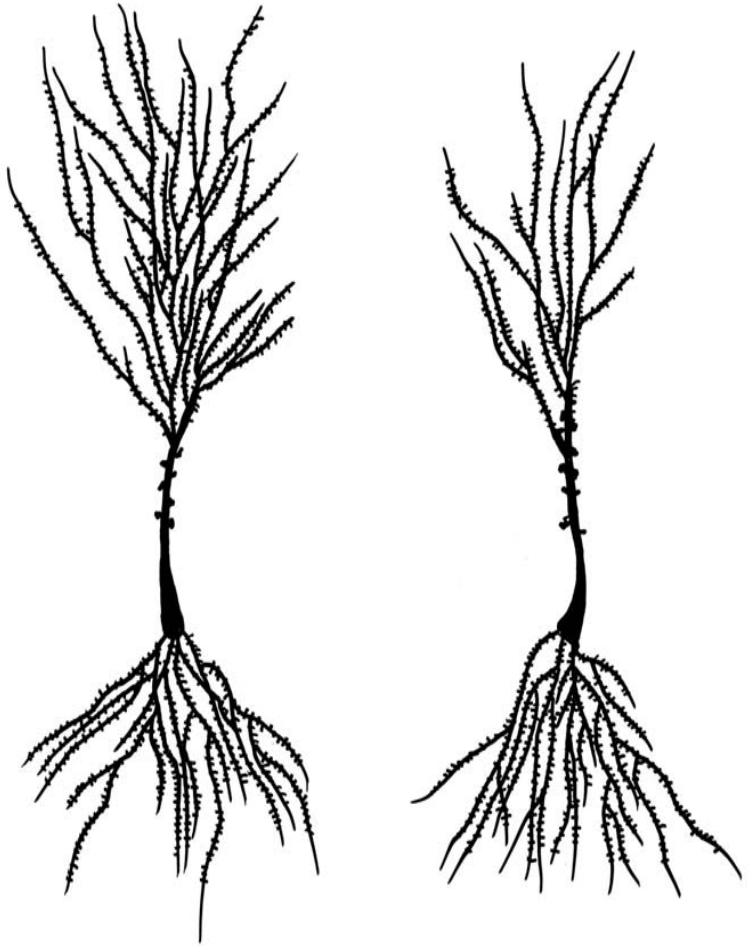
Neurobiological Consequences of Stress

- Stress-related affective disease states (depression, PTSD) affects 10% of the population in any given year
- Stress exacerbates other affective disease states, such as schizophrenia and bipolar disease
- Stress exacerbates other organic disease processes
- Stress hormone secretion can contribute to cell loss/cognitive decline in aging and dementia

Stress, Stress Hormones and (Neuro)toxicity

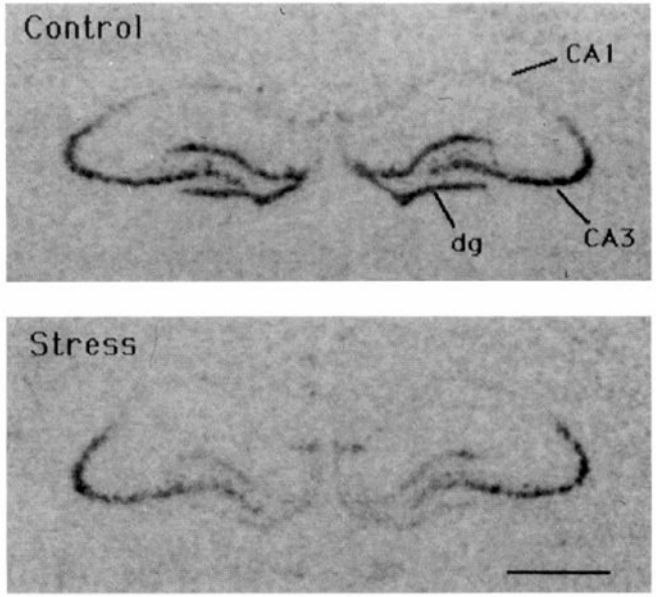
- **Stress and Neuronal Function**
- **Stress as a Predisposing Factor in Neurodegeneration**
- **Stress as a Co-morbid Condition? Implications for Toxicology**

Social Stress Shrinks Dendrites in the Hippocampus



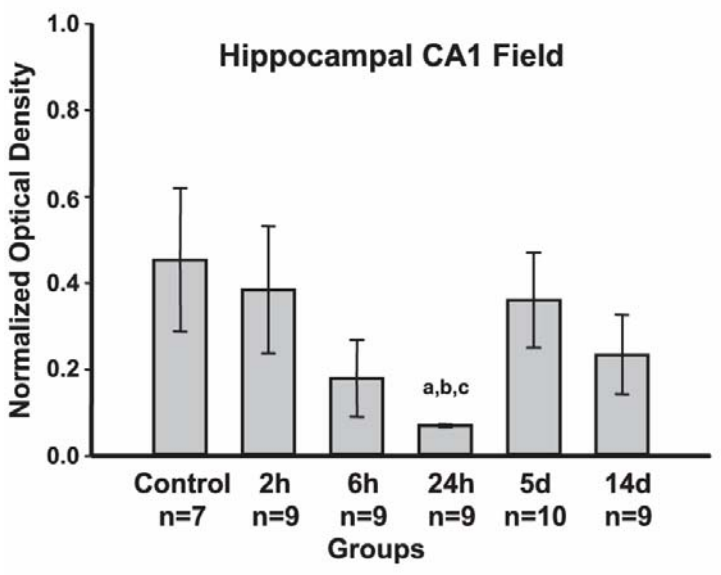
Stress Reduces Neurotrophic Factor Expression in Cortex and Hippocampus

Rats



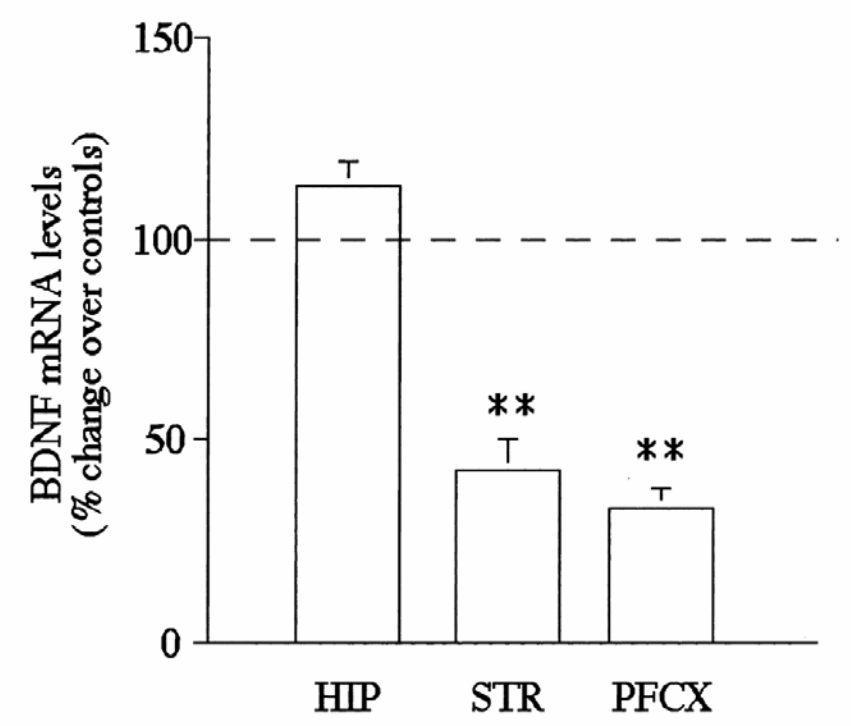
Smith et al, J. Neurosci. 15:1768 (1995)

Mice



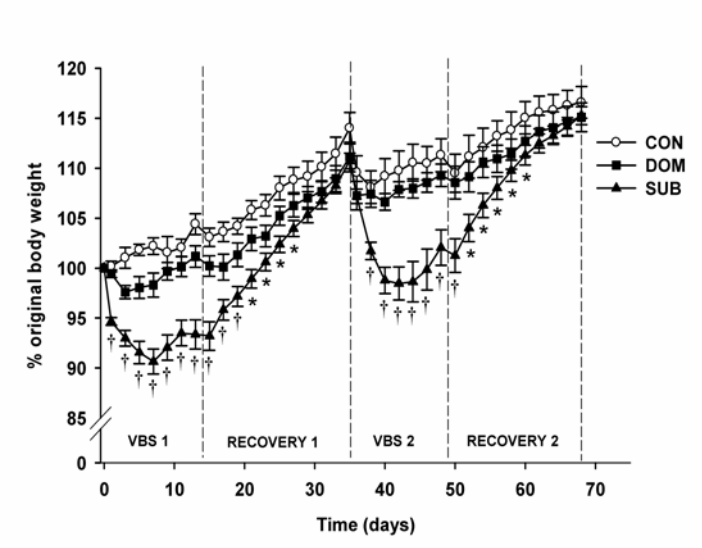
Pizarro et al, Brain Res. 1025:10 (2004)

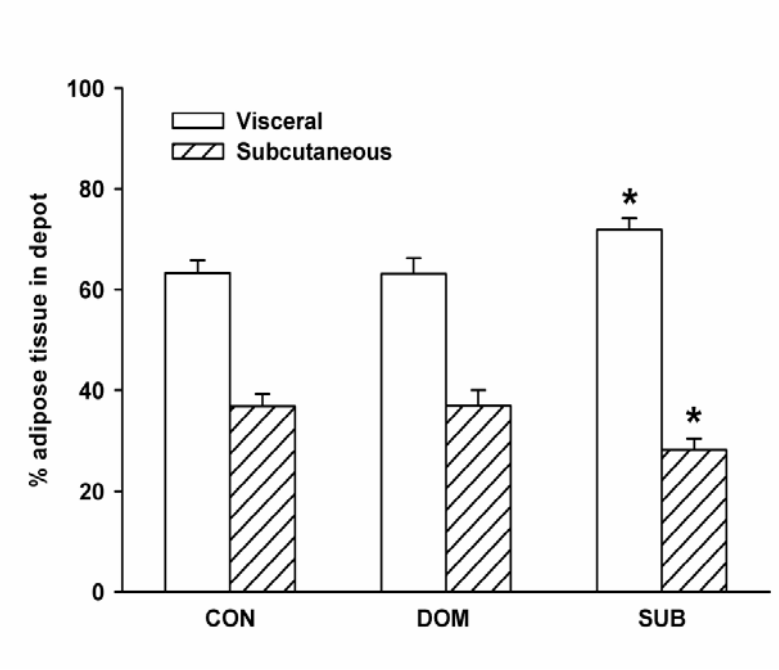
Prenatal Stress Reduces Neurotrophic Factor Expression in Cortex and Striatum



Fumagelli et al, Eur. J. Neurosci 20: 1384 (2004)

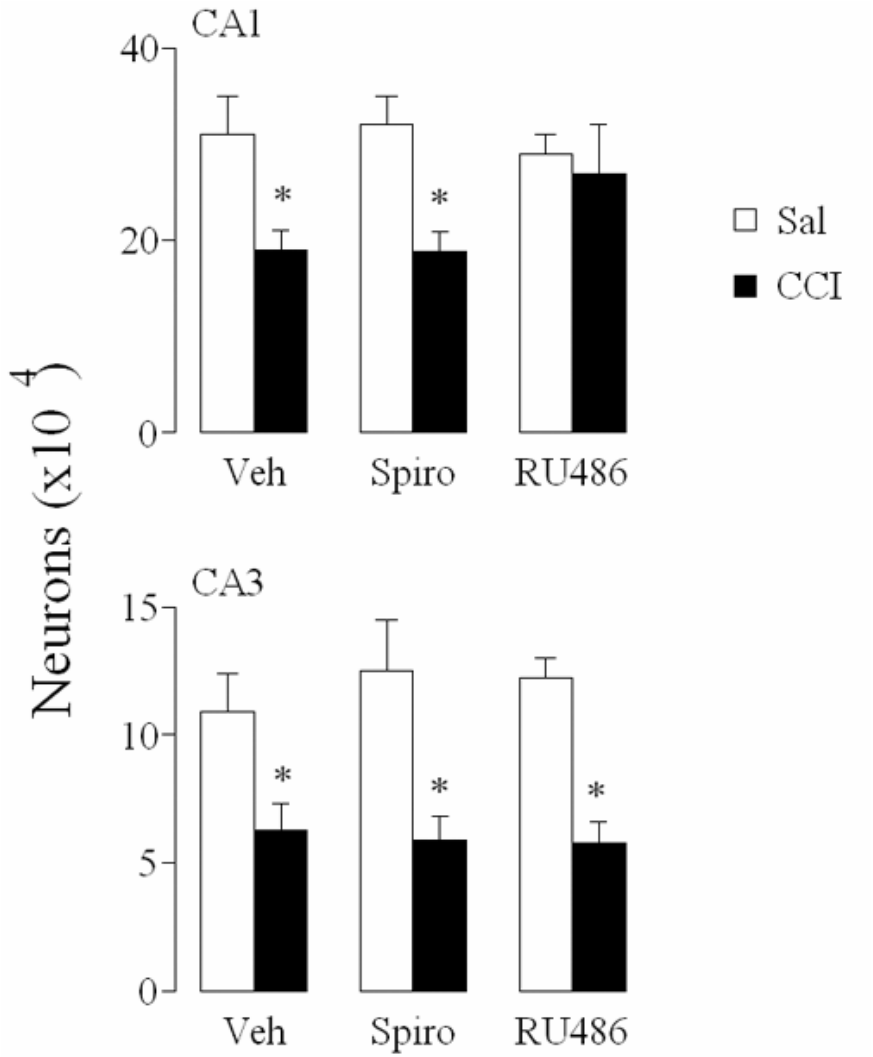
Social Stress Increases Abdominal Fat Accumulation (Obesity)





Tamashiro et al., Amer. J. Physiol. 293: R1864 (2007)

Glucocorticoids Mediate Hippocampal Damage Following Head Trauma

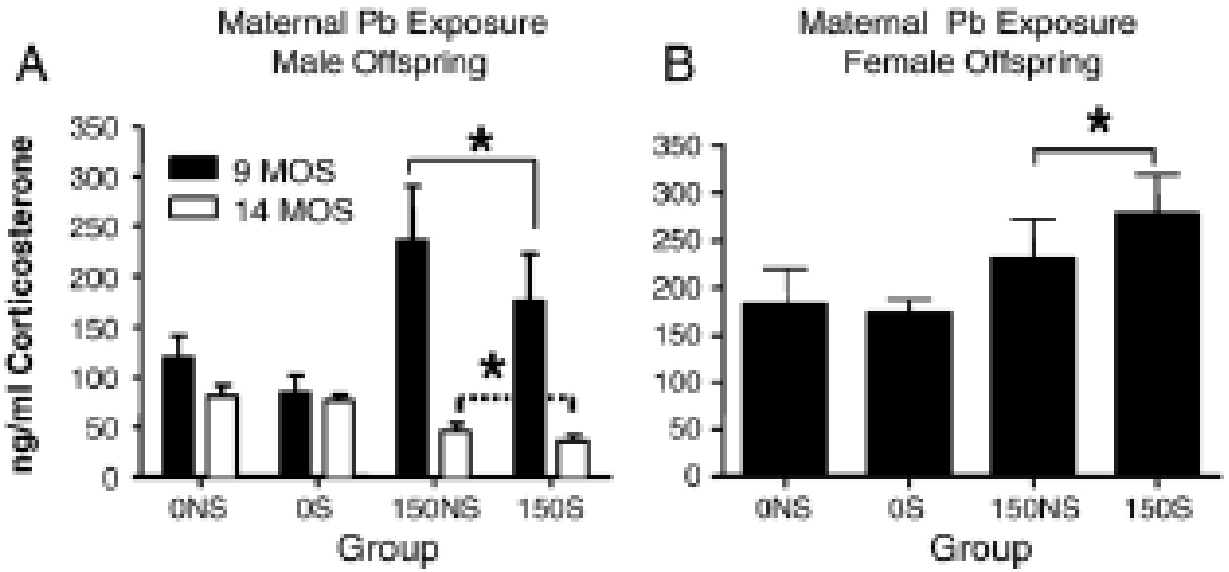


Herman and Seroogy, Neurol. Clin. 24: 461 (2006)

Stress as a Predisposing Factor in Neurodegeneration: Other models

- **Kainate neurotoxicity in hippocampus (epilepsy model)**
- **Infarct size and ischemic cell death (stroke model)**
- **Senescence-related cognitive deficits and neuron loss (aging and Alzheimer's Disease)**

Toxins Alter Stress Axis Function



White et al, Tox. App. Pharm., E-pub

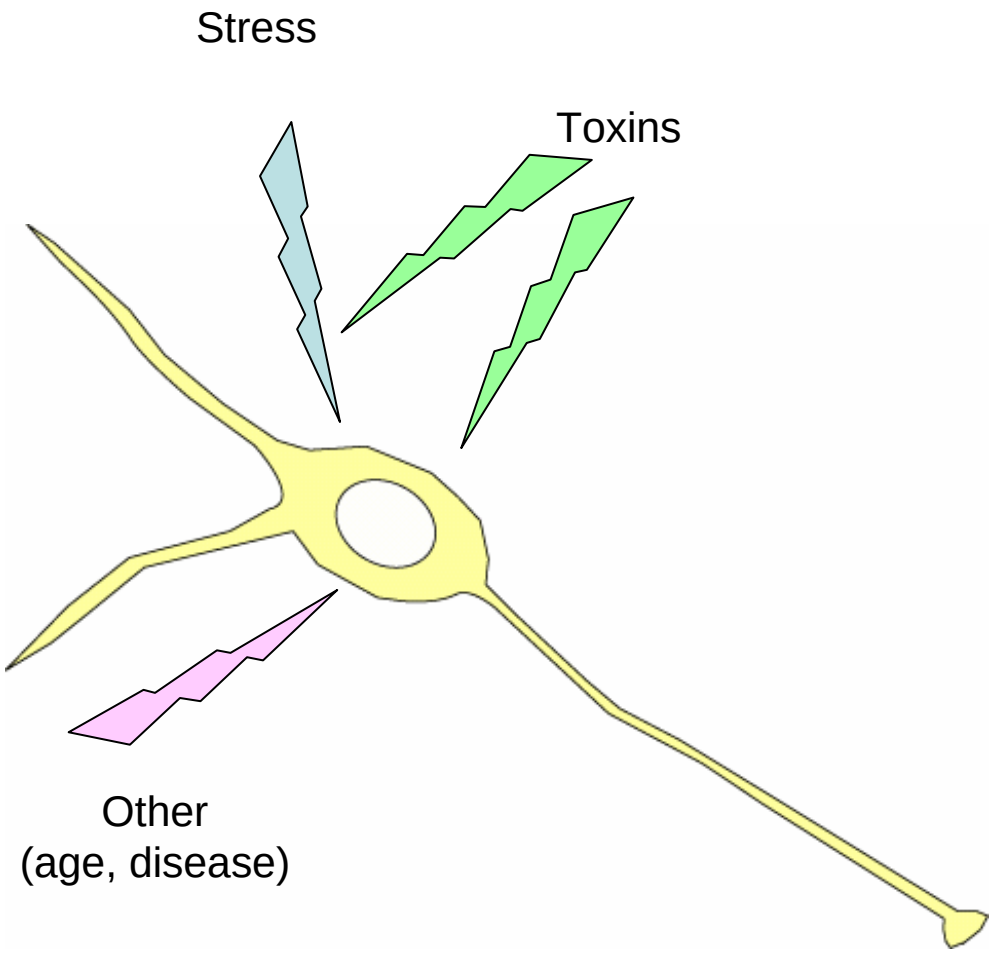
Stress as a Co-morbid Condition? Implications for Toxicology

- **Stress enhances relapse of addictive behaviors (smoking, alcohol, other drugs of abuse)**
- **Social stress promotes abdominal obesity**
- **Prenatal stress interacts with lead exposure to alter brain neurochemistry, behavior and HPA axis drive**
- **Stress: represents one of the 'hits' in the multi-hit hypothesis of toxicity**

Stress as a Co-morbid Condition? Implications for Risk Assessment

- **Substance abuse and obesity are prevalent in lower SES populations**
- **Lower SES groups have disproportionate exposure to some environmental toxicants (e.g., lead)**
- **Environmental toxicants can modulate glucocorticoid secretion**
- **Glucocorticoids enhance neurotoxic processes**

Stress and Cellular Endangerment



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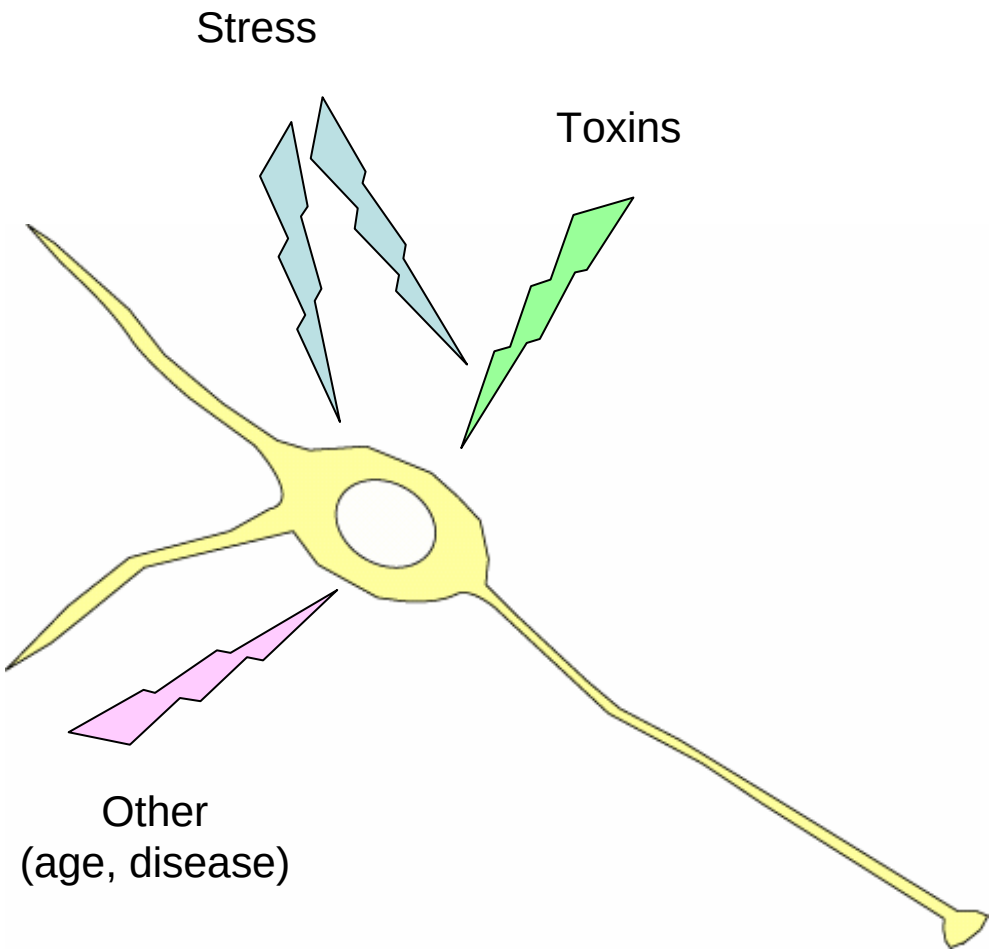

Stress and Cellular Endangerment