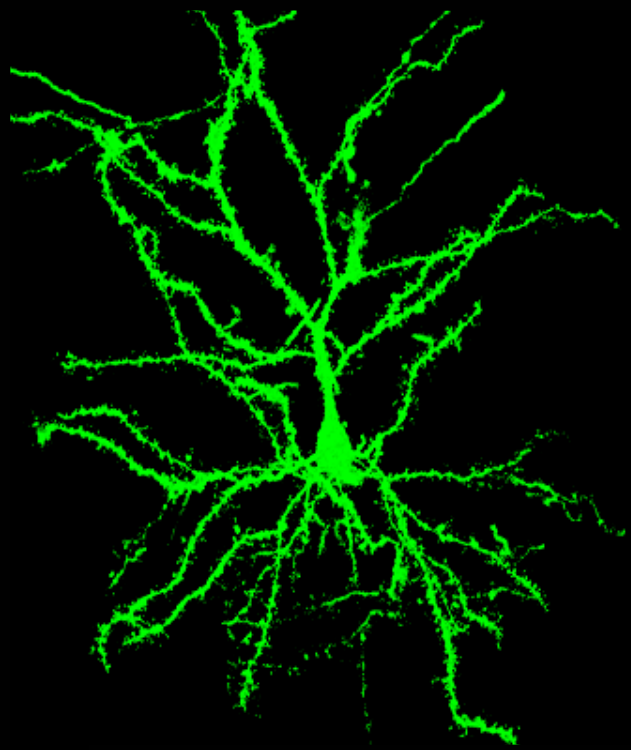
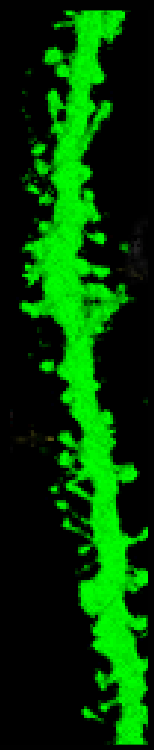
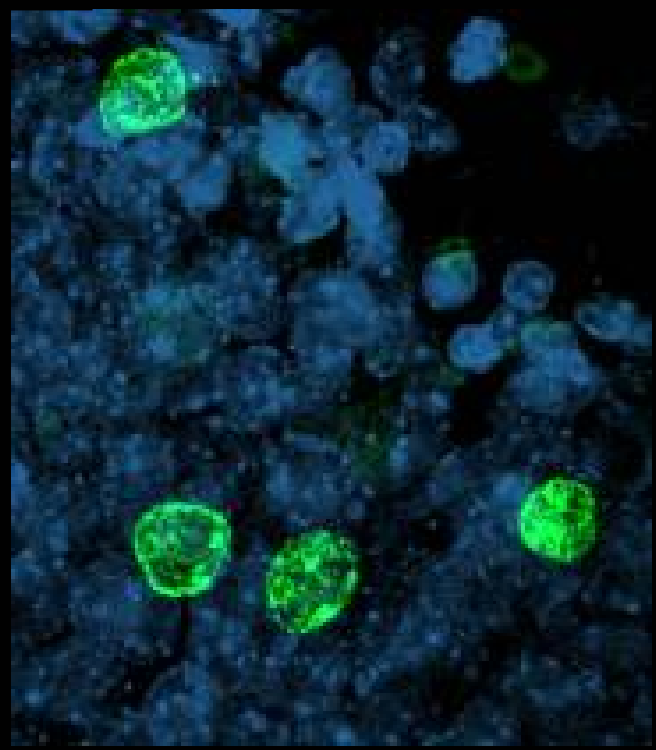
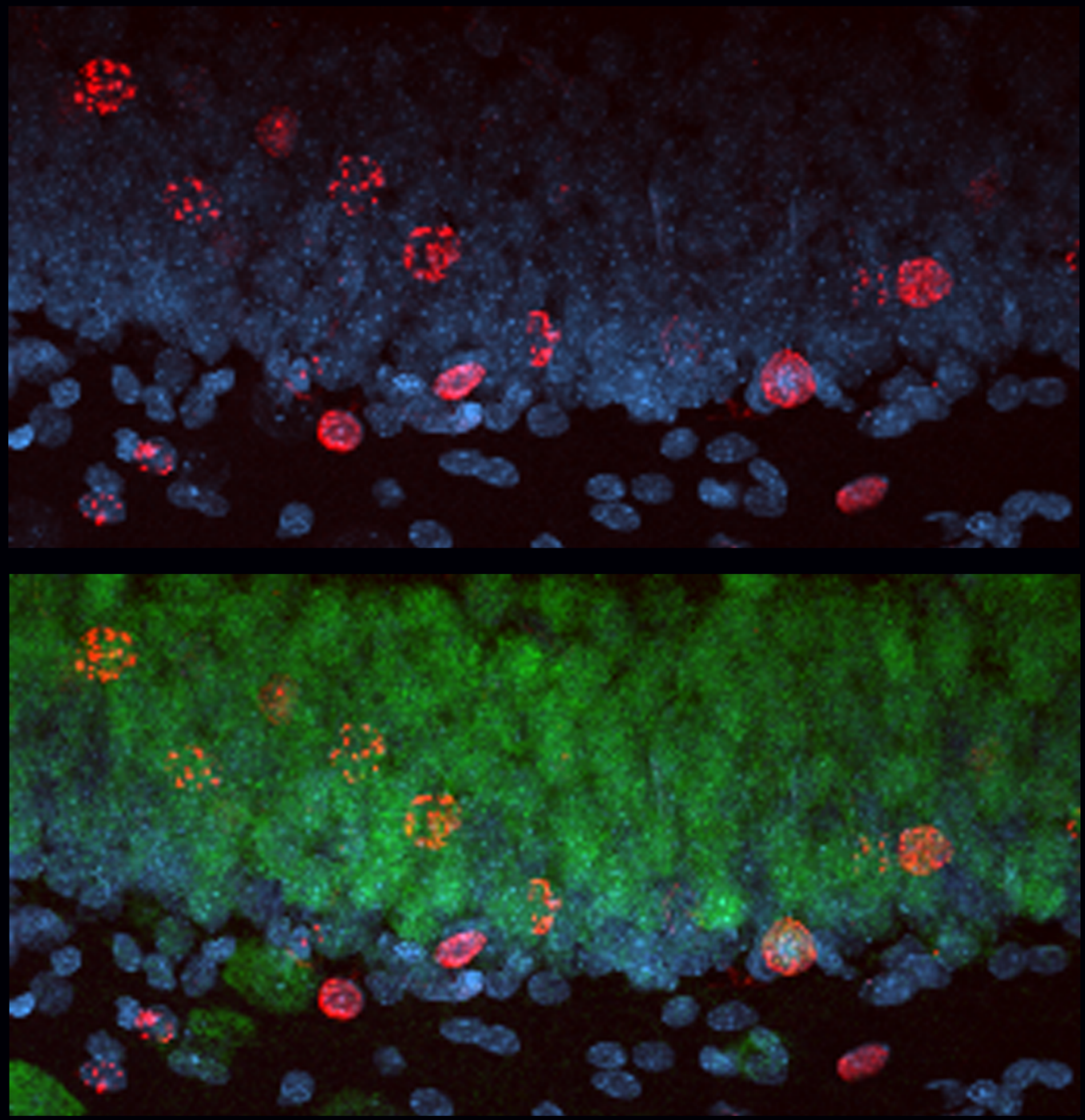
Positive and negative stress alter brain structure

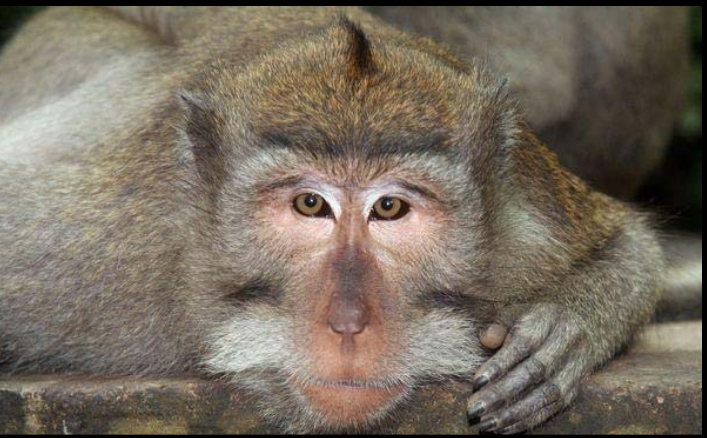






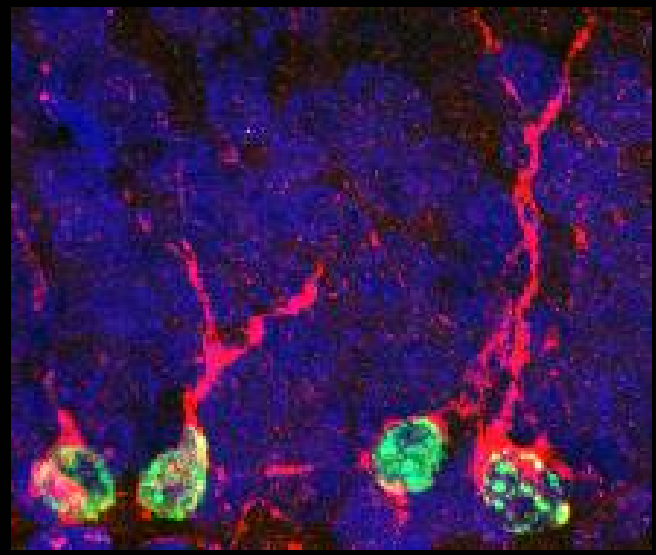


Adult neurogenesis in the hippocampus

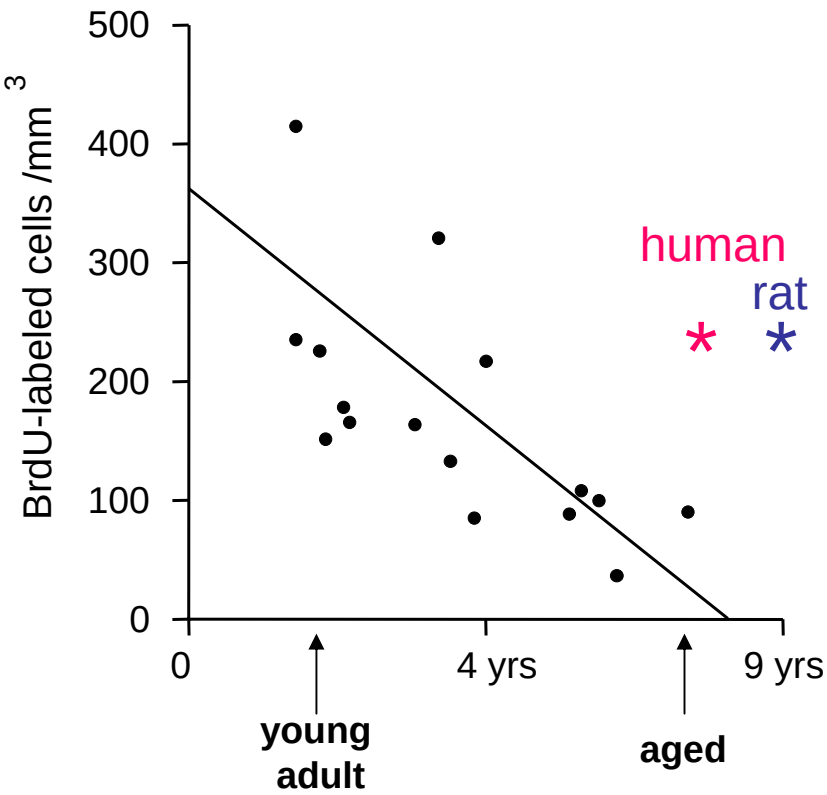


Evidence for new neurons in the hippocampus

- Synapses on cell bodies and dendrites
- Extend dendrites and axons
- Generate action potentials
- Express neuronal-specific proteins

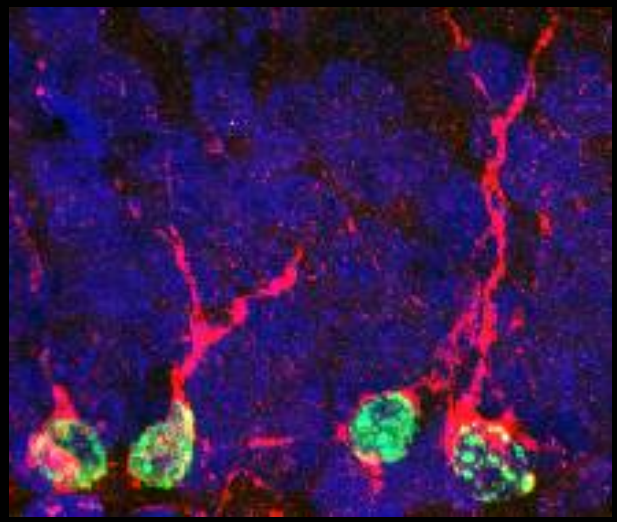


Adult neurogenesis in the hippocampus of marmosets declines with age

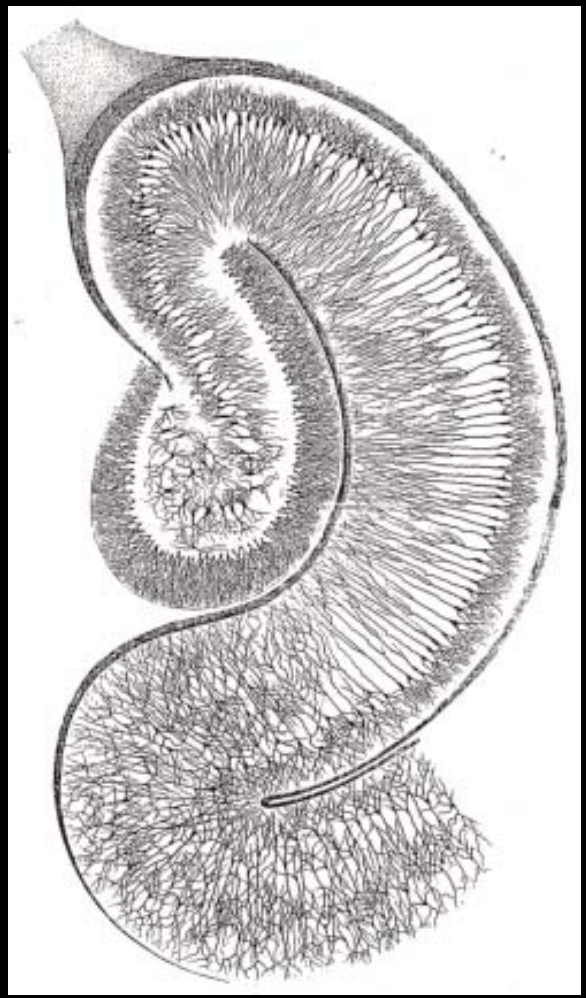


How many new neurons?

>9,000 per day – 250,000 per month
in the young adult rat (Cameron & McKay, 2001)



The hippocampus



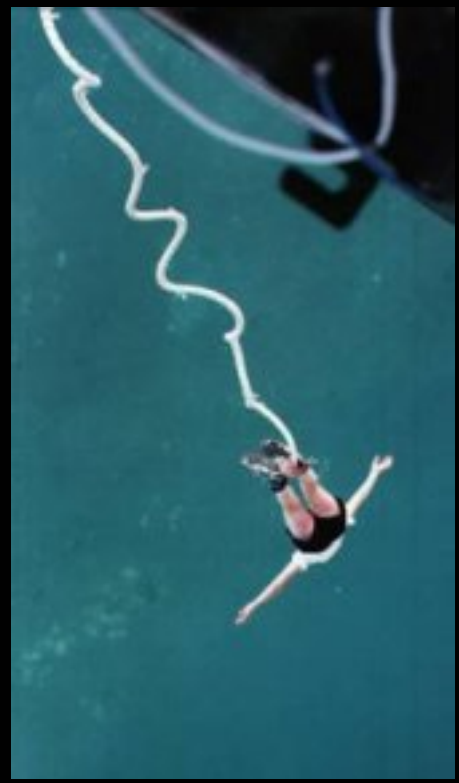
- Learning and memory
- Anxiety
- Stress

Experience modulates adult neurogenesis

- Stress (Gould et al., 1997; 1998; Tanapat et al., 2001)
- Social dominance (Kozorovitskiy & Gould, 2004; Pravosudov & Omanska, 2005)
- Physical exercise (van Praag et al., 1999; Stranahan et al., 2006)
- Environmental complexity (Kempermann et al., 1997; Nilsson et al., 1999)
- Learning (Gould et al., 1999; Leuner et al., 2004; 2006)
- Parenting (Leuner et al., 2007; Pavlic & Kozorovitskiy, unpub)

Individual differences in response to stress

- Some individuals respond to stress by developing psychopathology (depression, anxiety disorders)
- Others respond to stress with resilience
- Still others thrive on “stressful” experiences



What determines individual responses to stress?

- Psychological variables – controllability, predictability
- Emotional valence of the stressor
- Social context
- Developmental history

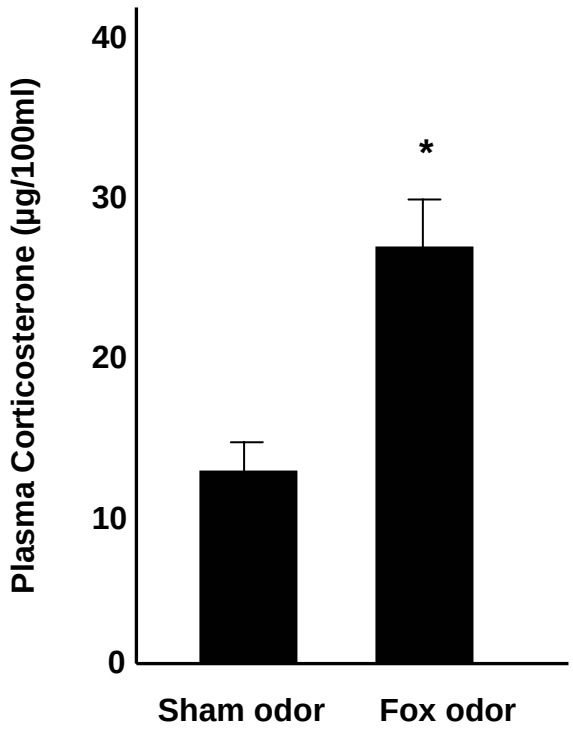
Experiences that activate the HPA axis

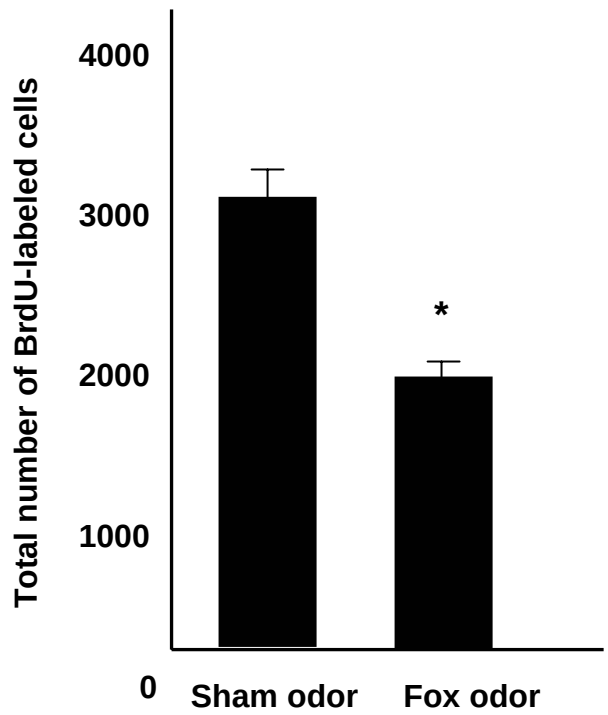
Negative stress (Punishing, aversive)	Positive stress (Rewarding, motivating)
Social subordination	Sexual behavior
Physical pain	Eating
Restraint	Running
Predator odor exposure	

Negative stressors that inhibit adult neurogenesis in the dentate gyrus

- Predator odor
- Subordination
- Restraint
- Electric shock
- Sleep deprivation

Exposure to predator odor elevates glucocorticoid levels and inhibits adult neurogenesis in rats



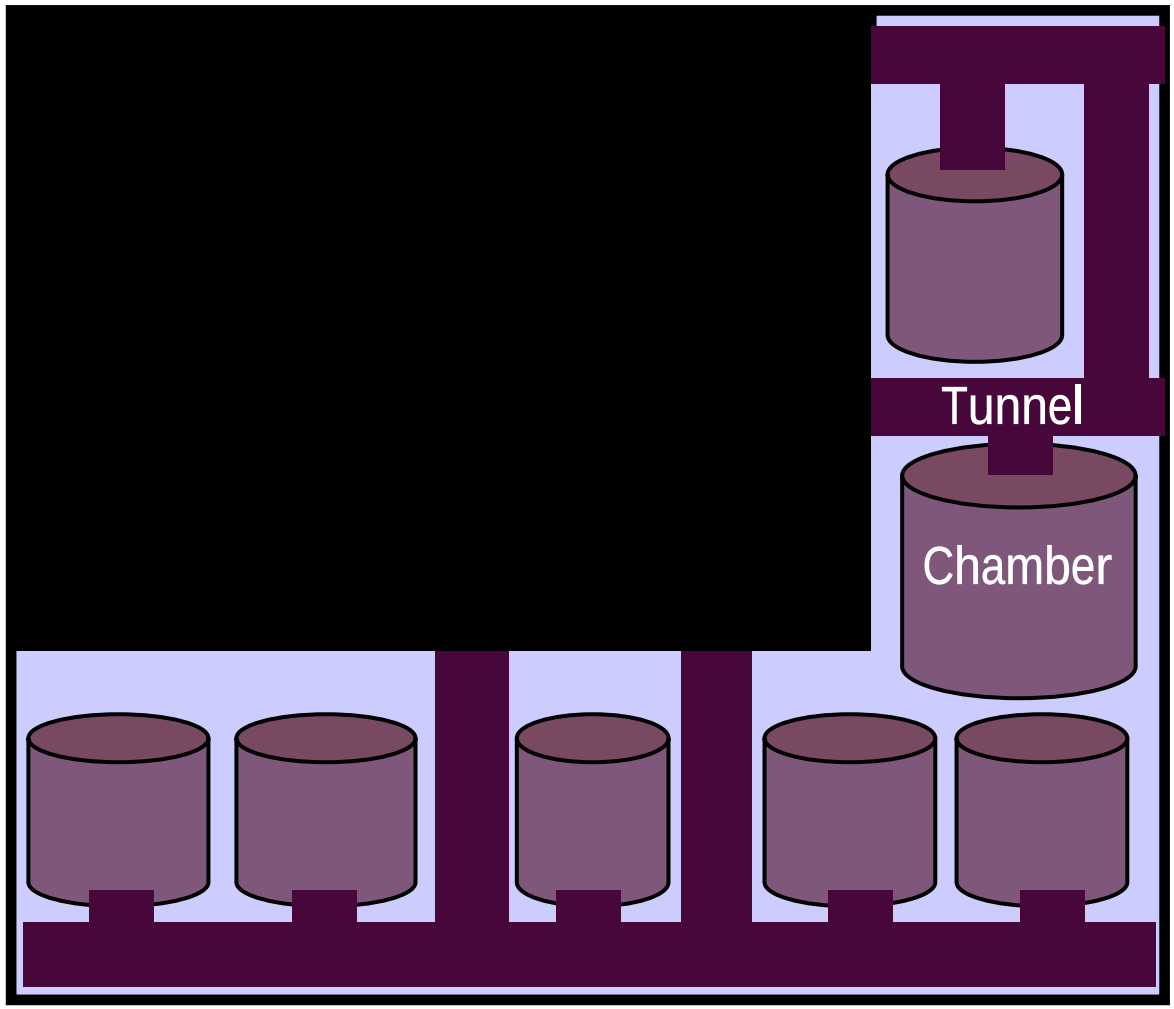


Similar effect with other aversive stressors and in other species

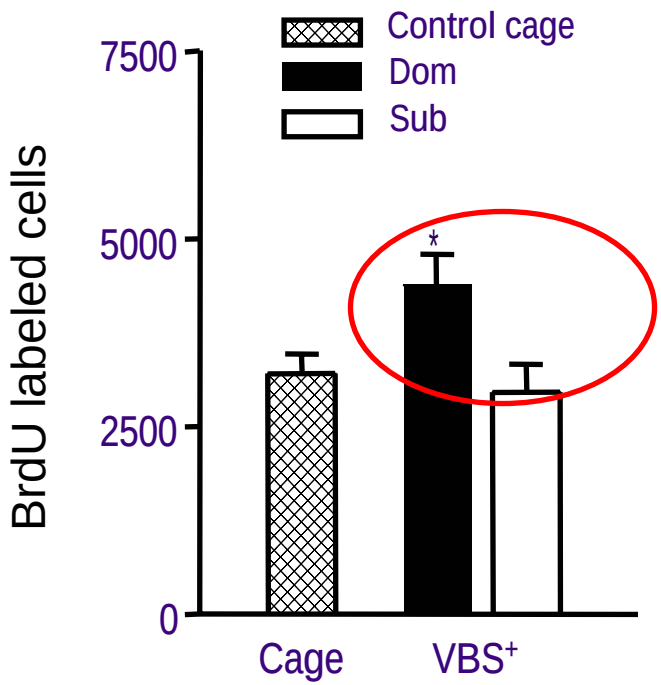
Visible Burrow System (VBS)

H2O

FOOD

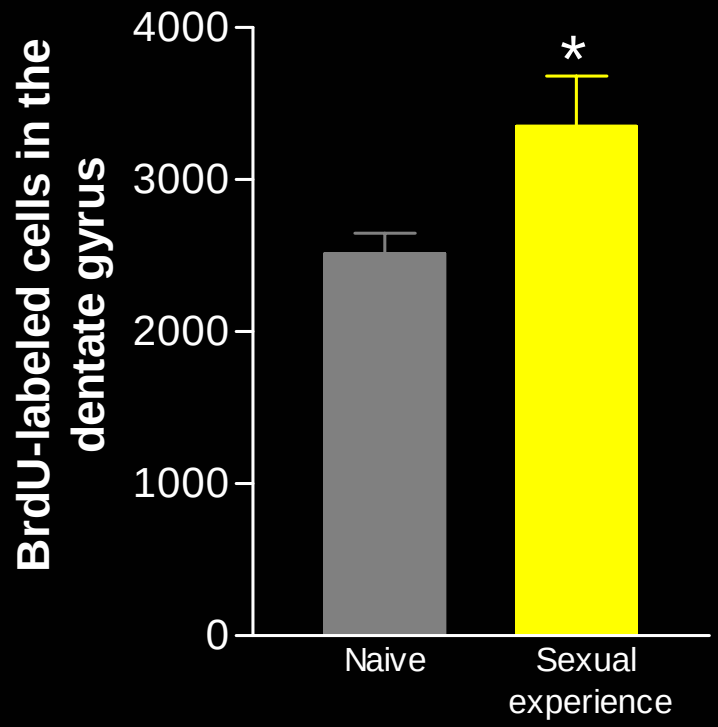


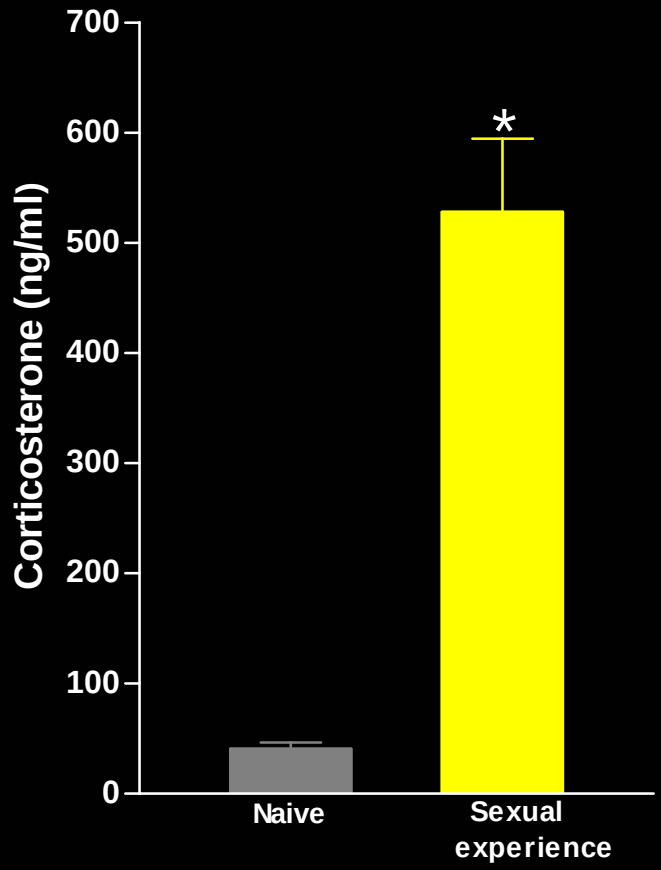
Dominants have more new neurons than subordinates or controls



Kozorovitskiy & Gould (2004)
J Neurosci

Sexual experience enhances adult neurogenesis despite elevated stress hormones



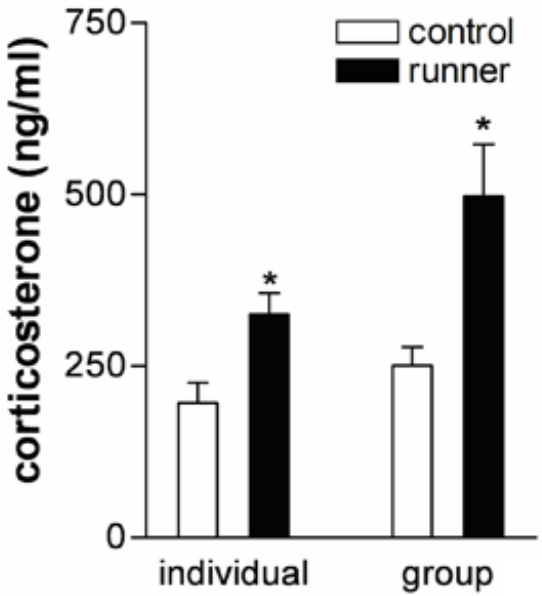


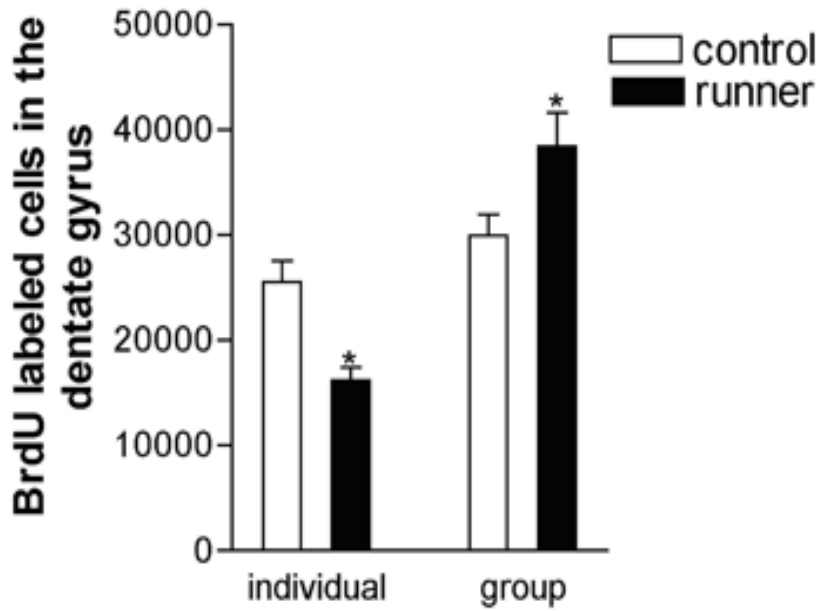
Running is a universally motivating behavior (for rodents)

- Healthy rats will run several km a night if given access to a running wheel
- Rats will develop a place preference for a running wheel
- Rats will readily learn to bar press for access to a running wheel

- Running activates the HPA axis
- Running enhances adult neurogenesis

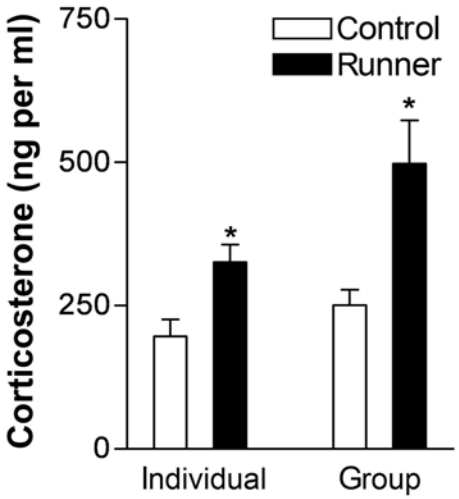
Does social housing affect the response to a positive stressor?



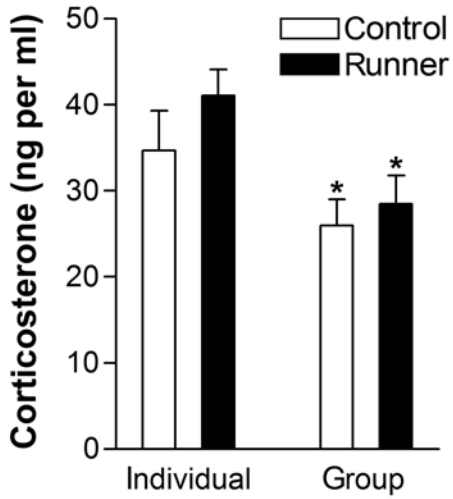


Social housing alters the corticosterone response to stress

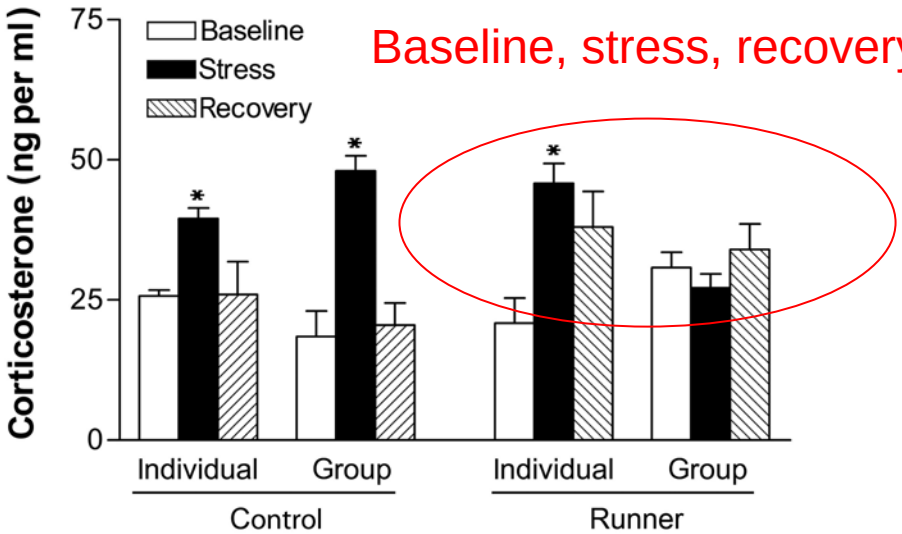
Baseline - 7PM



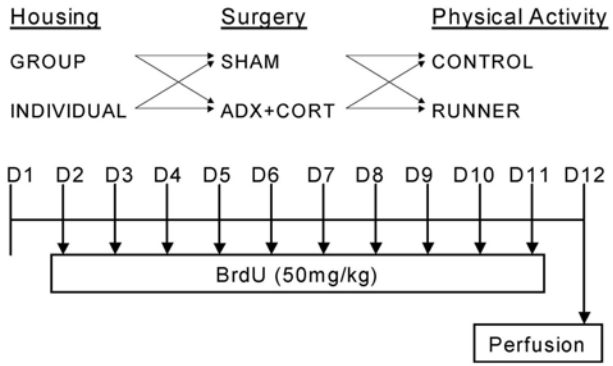
Baseline - 11PM

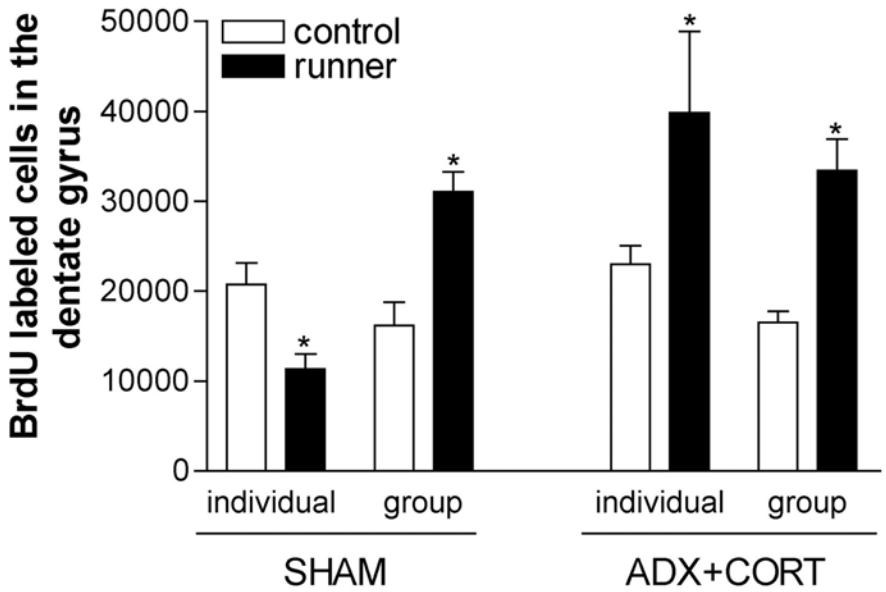


Baseline, stress, recovery -9-11AM

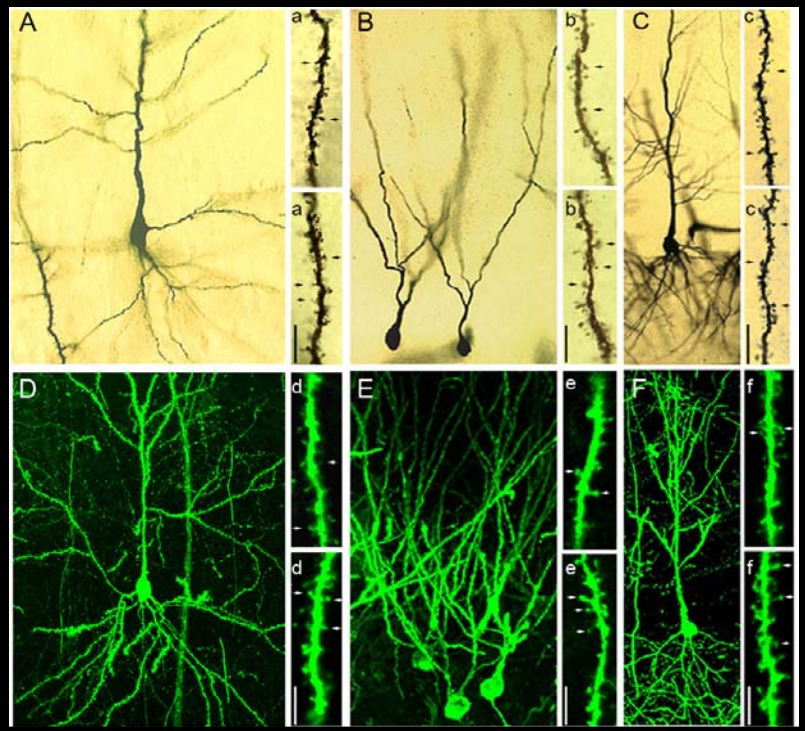


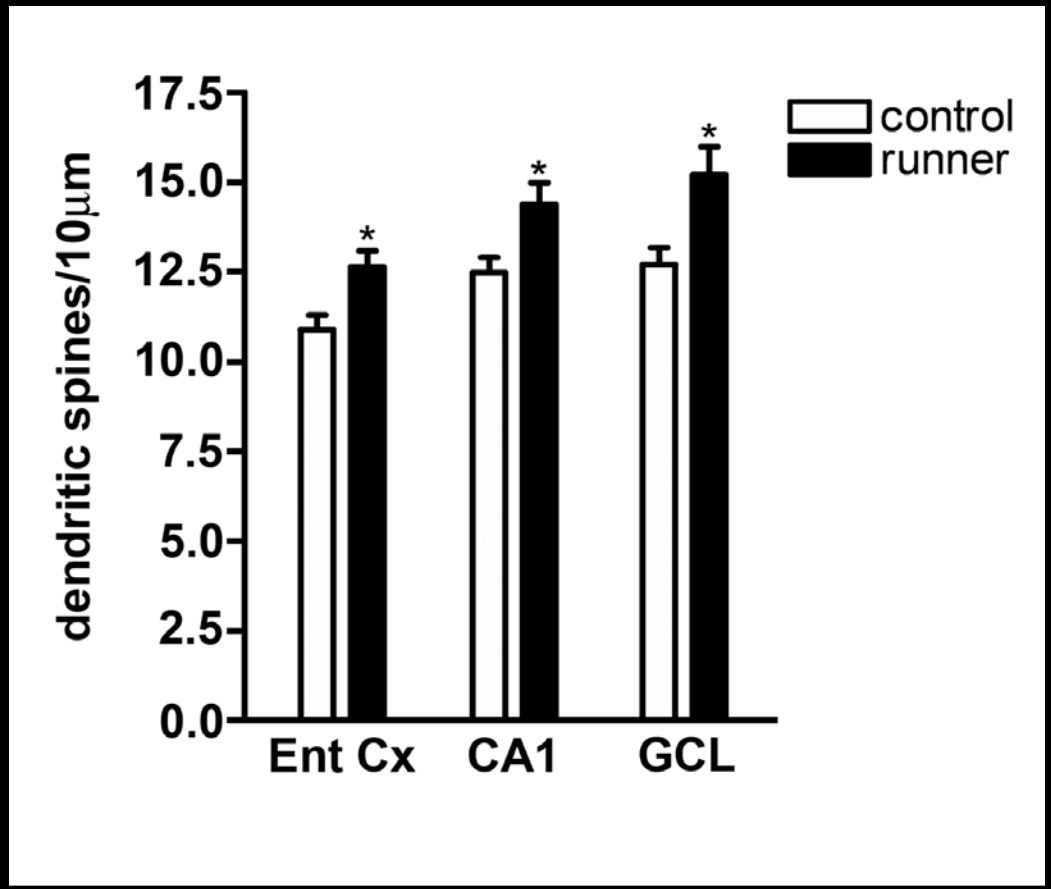
Are glucocorticoids responsible for running effects on neurogenesis?





Running enhances dendritic spine density on multiple neuron types



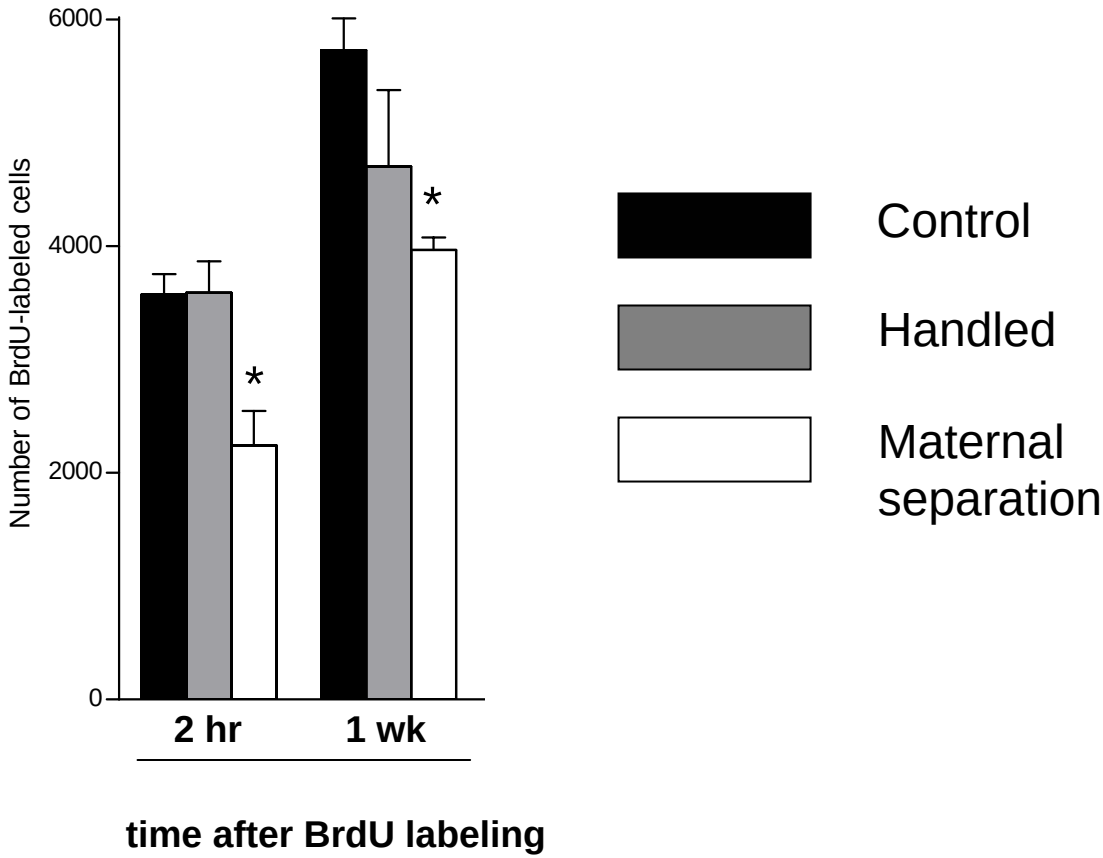


Running alters hippocampal function:

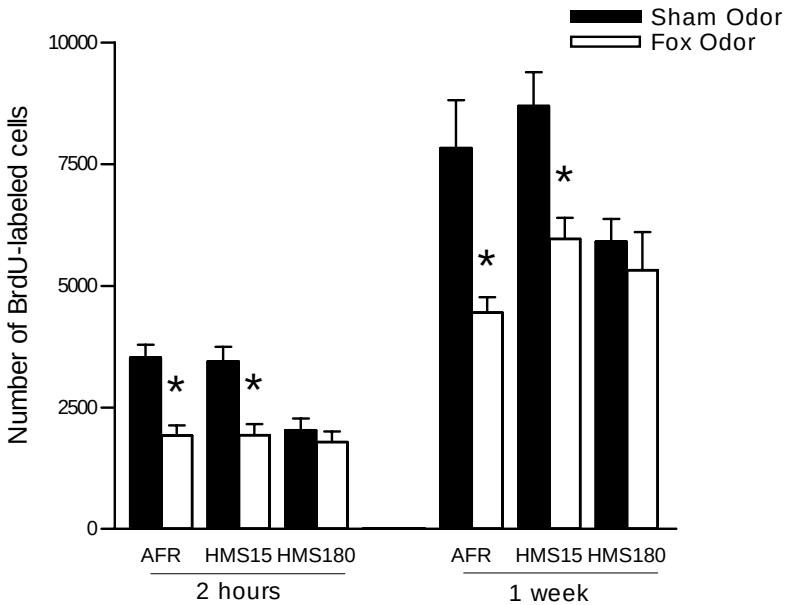
- **Learning** (van Praag et al 1999; Anderson et al 2000; Baruch et al 2004)

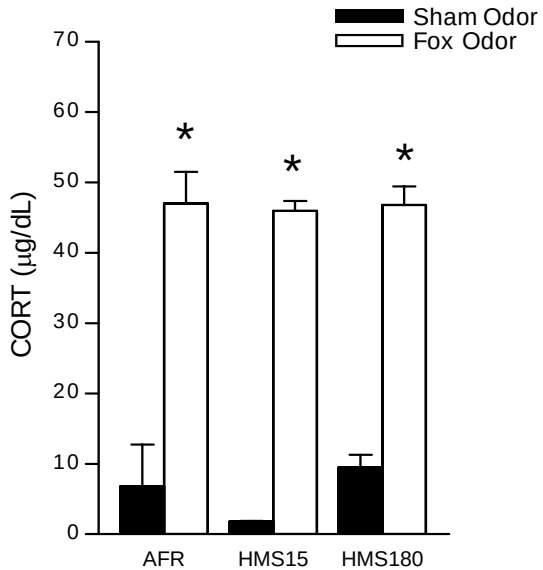
- **Anxiety** (Fulk et al., 2004; Chaouloff et al., 1994)

Does early life experience modulate adult neurogenesis?



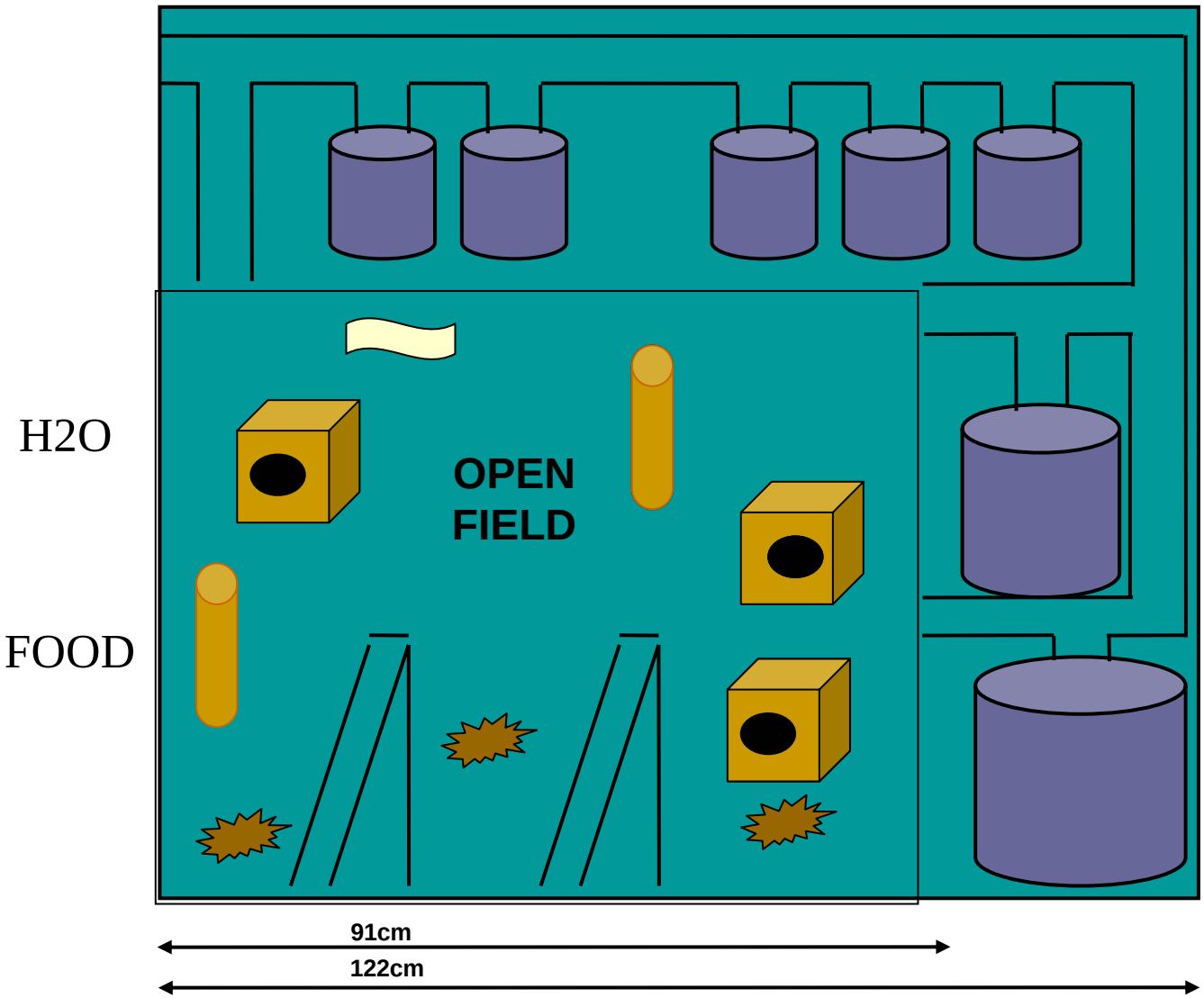
Do maternally deprived animals have normal stress responses in adulthood?



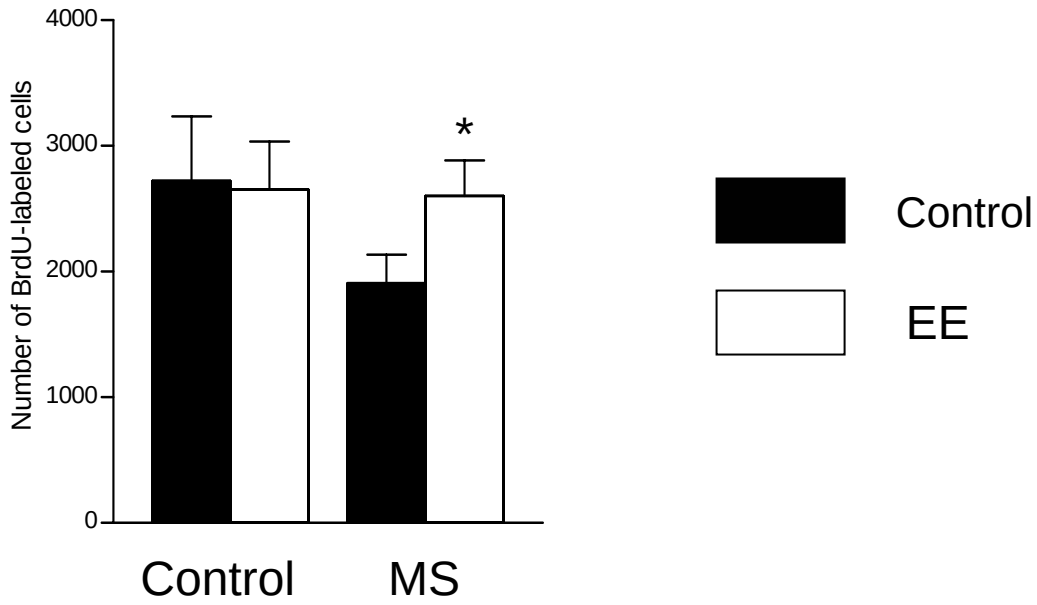


Are these effects permanent?

Enriched Environment



Can other types of experience alter adult neurogenesis in maternally deprived animals?



Enriched environment living reverses the effects of maternal separation on adult neurogenesis

Conclusions

- The adult brain is structurally plastic
- Social context can determine the endocrine and neural response to stress
- Developmental experience can alter the response of the brain to stress – some of these effects are reversible

Acknowledgments

Ben Leuner
Erica Glasper
Alexis Stranahan
Christian Mirescu
Yevgenia Kozorovitskiy
Meghan McBreen
Catherine Kopil
Lisa Battaglia
Patima Tanapat
Nicholas Hastings
David Khalil
Brad Heller