



The stressed rat: out of sight but not out of mind

Lucie Low, PhD

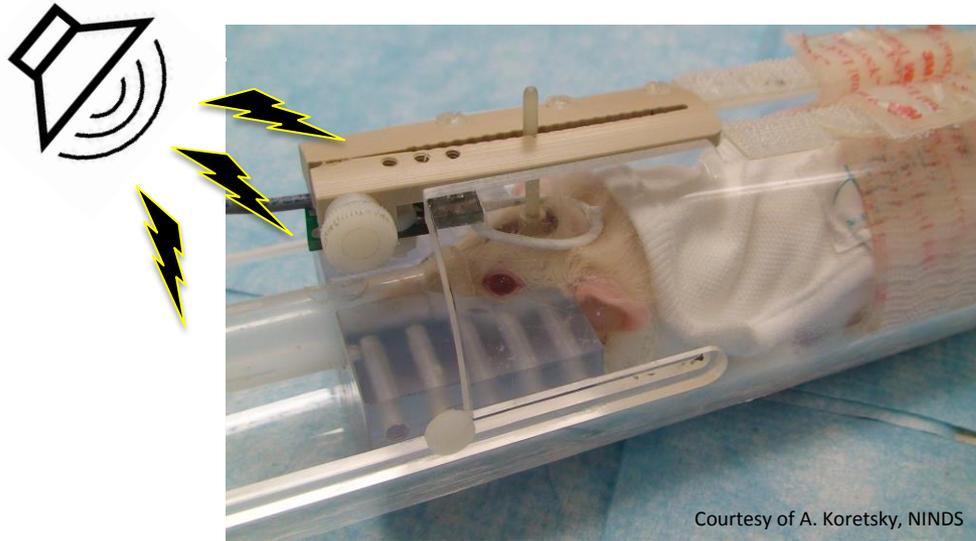
2015 NIH Pain Consortium Symposium



National Center for
Complementary and
Integrative Health

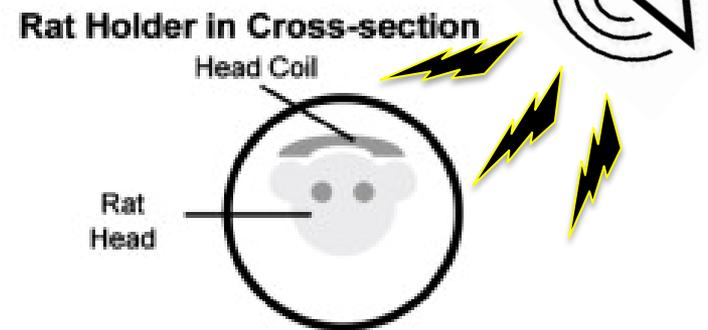
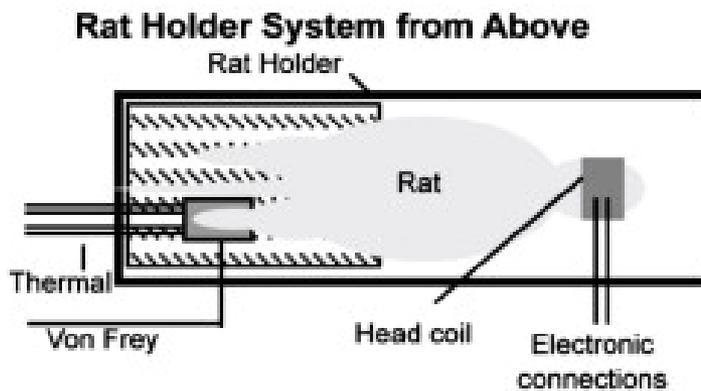


Training for MR imaging of awake rodents



Courtesy of A. Koretsky, NINDS

← **RESTRAINT +
NOISE**



From Becerra et al (2010)

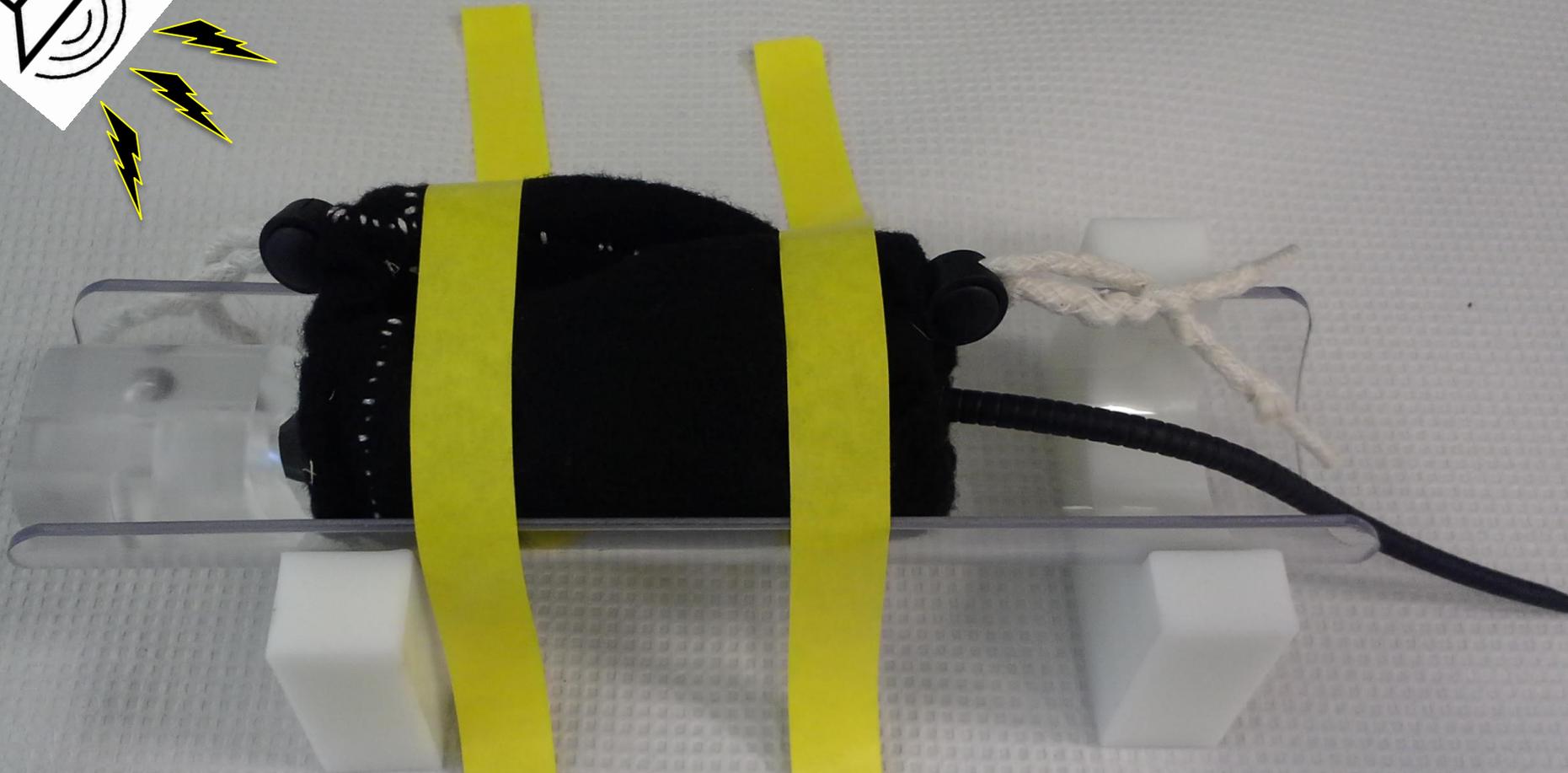
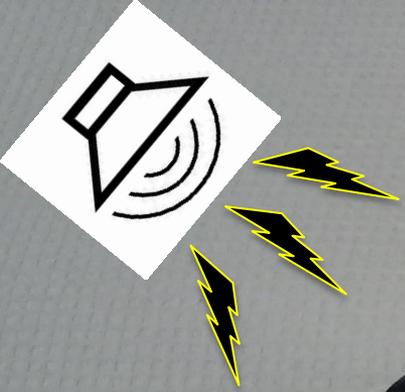
RESTRAINT + NOISE = ?

Stress-induced analgesia

- Follows acute, intense stressor (footshock, swim, restraint, noise...)
- Associated with fear responses
- Mediated by descending modulatory systems
- Opioids, monoamines, cannabinoids, GABA, glutamate....all involved

Stress-induced hyperalgesia

- Follows chronic, repeated stressor (footshock, swim, restraint, noise...)
- Associated with anxiety responses
- Mediated by descending modulatory systems
- Opioids, monoamines, cannabinoids, GABA, glutamate....all involved



RESTRAINED



NON-RESTRAINED





NON-EXPOSED



Experimental timeline

Day 1

Baseline mechanical sensitivity + baseline thermal sensitivity + CORT



Days 2 + 3

Restraint/treatment (30 mins) + mechanical sensitivity + thermal sensitivity + CORT



Day 5

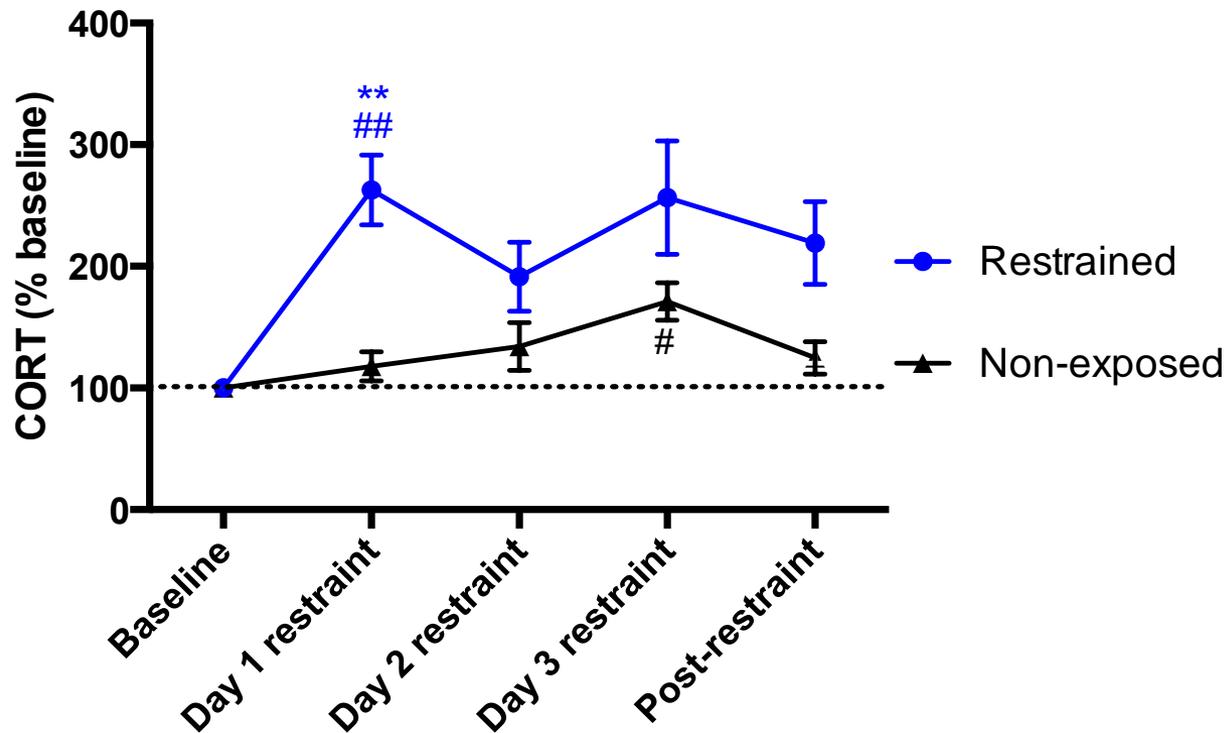
Post-treatment mechanical sensitivity + thermal sensitivity + CORT



Day 4

Restraint/treatment (30 mins) + heat stimulus to paw (4 x 48°C for 36s, 36s ISI) + mechanical sensitivity + thermal sensitivity + CORT

Restrained animals show stress responses...



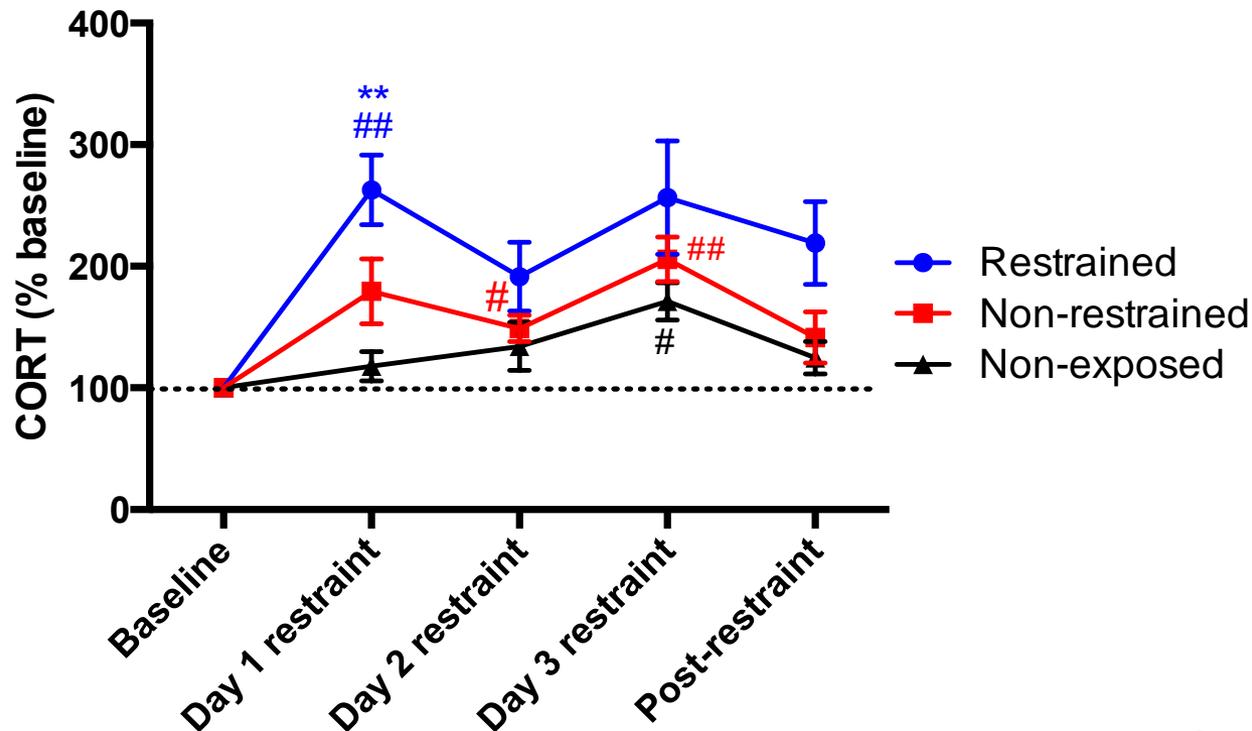
** = versus other groups

= versus baseline

All mean±SEM

n=9-12

But so do **non-restrained** controls



$F_{(2,64)}=13.1, p<0.0001$

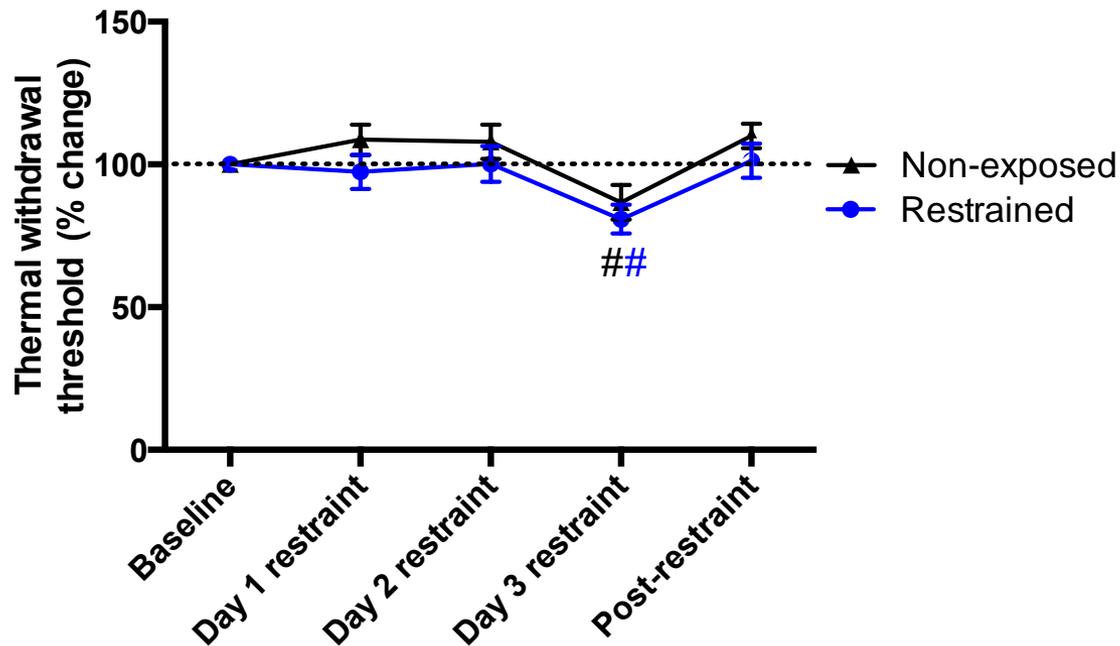
** = versus other groups

= versus baseline

All mean \pm SEM

n=9-12

Restrained rats show no difference to controls

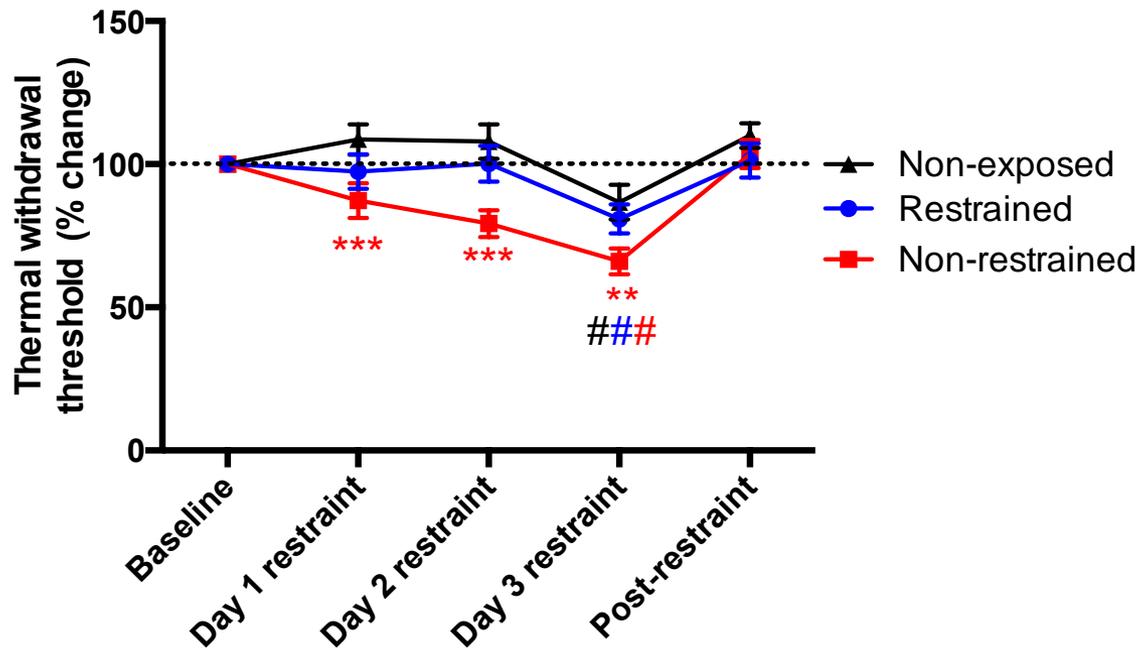


= versus baseline

All mean ± SEM

n=9-12

But **non-restrained** rats become hypersensitive



$F_{(2,336)}=36.6, p<0.0001$

** = versus other groups

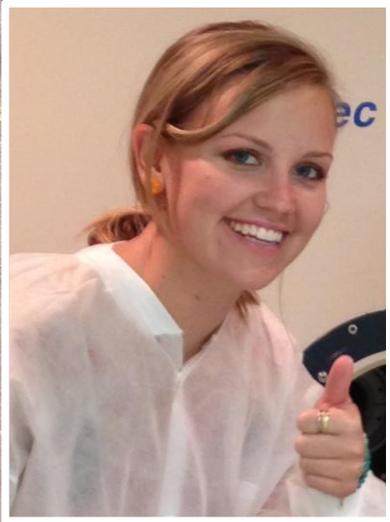
= versus baseline

All mean \pm SEM

n=9-12

Summary

- Increases in stress hormones and pain behaviors seen in **non-restrained control** animals
 - These were rats tested in the same room where other rats had previously been restrained
 - Suggests a form of olfactory stress-induced hyperalgesia
- **MRI restraint training** causes increases in stress hormones but no changes in thermal pain behaviors .



QUESTIONS?

Graffiti courtesy of Banksy