# Pain Recognition in Laboratory Animals

***biotecnologia habana 2017***

Watch this mouse: normal, or do you see signs of pain?

## Lessons for today

- **No simple test for pain**: must put together several types of evidence (history, behavior, physical exam, comparison with people, assessment of home environment)
- **Animal pain is difficult to treat**: best to prevent, and later, to euthanize/kill (humane endpoints)
- **Pain is rarely alone**: its companions are inflammation, injury, disease, dehydration, fever.
- **Pain can affect animal welfare AND the quality of research data**

## Starting point: Assumptions

- All vertebrate animals can feel true pain
- If it is painful to people, it is probably painful to animals
- Some experiments intentionally cause animals pain
- Some experiments unintentionally cause pain
- Sometimes, laboratory life can cause pain
- We humans have a duty to keep laboratory animal pain to a minimum
- Animals in pain are not physiologically normal

Why should we want to know if laboratory animals are in pain?

- For our Animals' Welfare
- For our Research Data
- (Animal models to study human pain & pain medicines)

## Effects on Animals & on Data

**Pain Medications**

- Suppress Immune Function
- Behavioral effects
- Effects on Cancer Biology
- Activates Stress system
- Change food intake
- Sleep disruption
- Wound & Bone Healing
- Respiratory effects
- Altered metabolism

**Untreated Pain & Inflammation**

- Suppress Immune Function
- Behavioral effects
- Effects on Cancer Biology
- Activates Stress system
- Change food intake
- Sleep disruption
- Limb disuse: bone healing
- Respiratory effects
- Altered metabolism

## Animal Pain is Difficult to Treat - 1

- Analgesic medicines like morfino & buprenorfino are hard to get
- Medicines have side effects that may make animals sick
- Most pain medicines only work for a few hours, even through the night

## Animal Pain is Difficult to Treat - 2

- Not enough good information about best doses, drugs and frequency for most animals
- Getting medicines into animals is challenging (injections; drugs in drinking water)
- Scientists have concerns that medicines will affect their research data.

- Put it all together: know the history; know the normal for your animal (species & individual); watch the behavior
- Focus on the "pain behaviors" that match this animal's research history

## Why diagnose this animal's possible pain?

- Research data to measure effects of treatments
- To decide if this animal needs pain medicines (animals do not get treatments they need if people do not recognize they are in pain)
- Pilot work to plan the full experiment
- To decide if animal should be euthanized

## We need to know normal And we need to know history

Historia:

- The project is a study of bone cancer pain
- Surgery to implant tumor cells in the tibia: many opportunities for pain
  - **Post-surgical pain?** ( up to ~5 days after surgery)
  - **Infected bone pain?** (variable time of onset & duration)
  - Bone Cancer Pain? (weeks after tumor cell implantation)
  - Or normal / No Pain?

## Putting it together: know the history, know the normal for your animal (species & individual), watch the behavior

Laboratory Animal Pain is Difficult to Diagnose.

- No human language
- We only see them a few minutes / day
- Human presence changes animal behavior
- Many identical animals per cage

**So, if you do something painful (e.g., surgery), do assume they are in pain**

Risk of Pain for Laboratory Animals

- Painful Procedures --- surgery
- Painful diseases --- cancer, inflammation
- Animal fights
- Rough handling
- Old age (arthritis, etc)

## Evidence of Pain

- Behavior
- Physiology

Physiology: limited value & Non-Specific

- "Stress hormones" (catecholamines, corticosterone)
- Heart rate & respiratory rate
- Body temperature
- Blood pressure

These CAN be signs of pain, but have many other causes too, and can be difficult to measure --

- Suggestive of PAIN, but Non-diagnostic

Pain Assessment: Behavior

- Watch what they do
- Watch what they do not do
- Assess what they have done
- Look at spontaneous postures & movements
- Elicit reaction to manipulations (make them move, touch their incision, offer treats
- Response to analgesic treatment
- BEST if you can QUANTIFY / SCORE

Observing animals for pain behaviors: WHEN

- Think about when they are most likely to feel pain
  - For example: at night, after surgical anesthetic has worn off
- And look during their active period (most likely to show pain)
  - For example: at night

WHEN

- Anticipate that surgical pain is most intense just after the anesthetic recovery, and usually diminishes over a few days.
- Otherwise --- know your model ! --- inflammatory, neuropathic, cancer pain may take days or weeks or months to develop
- Pain can be sharp, acute, intermittent, dull, only when manipulated . . . Uncommon for pain to be intense non-stop for hours or more

Steps for Pain Diagnosis

1. Know the animals' history
2. Observe without touching
3. Examine the enclosure for signs of recent behaviors
4. Examine the animal
5. Ask the animal does it hurt? Where?
6. Administer analgesics, then reassess later
7. [ not for clinical use ] Have the animals tell you how much the pain bothers them

Steps for Pain Diagnosis

1. Know the animals' history: Guides you to WHEN animal is most likely to be painful, and WHERE on the body you should focus
2. Observe without touching
3. Examine the enclosure for signs of recent behaviors
4. Examine the animal
5. Ask the animal does it hurt? Where?
6. Administer analgesics, then reassess later
7. [ not for clinical use ] Have the animals tell you how much the pain bothers them

Steps for Pain Diagnosis

1. Know the animals' history
2. Observe without touching:

Posture

Coat / fur

Facial expressions

Pain behaviors

Normal movement and behavior

1. Examine the enclosure for signs of recent behaviors
2. Examine the animal
3. Ask the animal does it hurt? Where?
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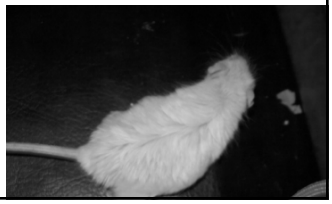
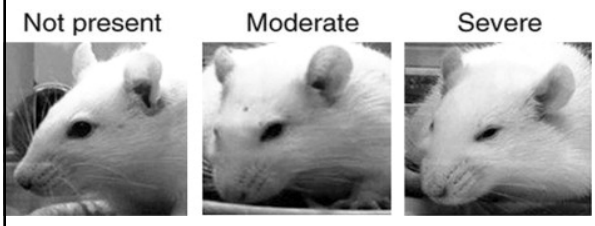
Posture, Coat

Example: assess and quantify grooming:

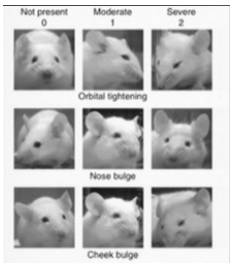
Score hair coat:
1 = Normal
2 = Not grooming

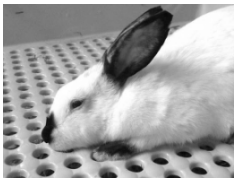


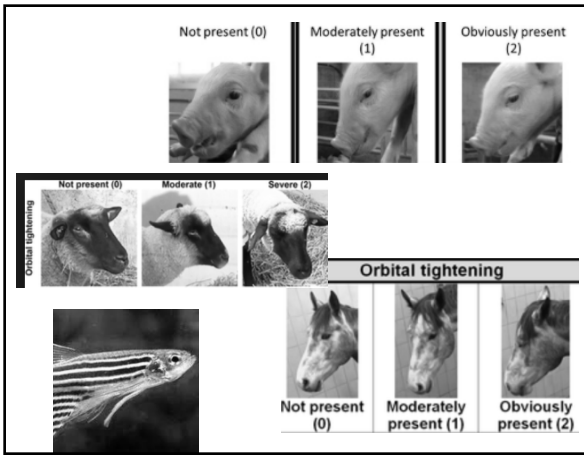
Facial expression




For clinical assessment, no special equipment or complicated score-sheet required.
Score: 1 = normal 2 = abnormal






## "Grimace Scales are not highly sensitive nor highly specific

If you DO see a "pain face" or grimace:

- Pain is likely
- Other illness with pain is possible

If you do NOT see a "pain face" or grimace:

- Pain is still possible
- Low frequency of grimacing
- Human observer may scare the animal

## Assessing pain behaviors in "real time"

- Observer must:
- Know normal behavior of species
- Know normal behavior of individual
- Observe behavior:
  - Abnormal Behaviors the animal is doing
  - Normal Behaviors the animal is *not doing*

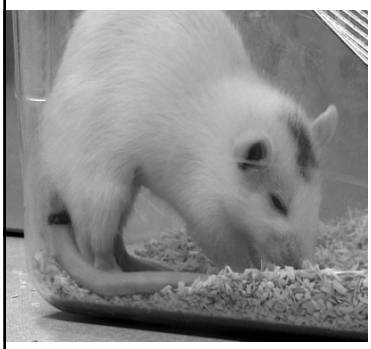
## Normal Behaviors animals may not do when painful

- Eat / Drink
- Ambulate
- Interact / Play
- Groom
- Relax
- Sleep
- Build nest

## Abnormal Behaviors animals may do when painful:

- Be immobile or stiff
- Be grumpy or non-interactive
- Abnormal postures and facial expressions
- Writhing, pawing, self mutilation, witching
- Vocalize ( can human hear it? )


Rat Video: shows abnormal emergent "pain behaviors" --- Twitches and spasms;
arching his back (4:00) as a cat does when awaking.



You need to know normal species behavior: back-arching is normal behavior in cat, uncommon in rat (unless the rat has abdominal pain)

Notice the squinty eyes, too

Ay! Ascua! Ouch!

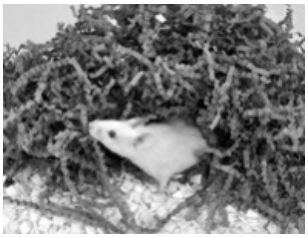
- Video of two rabbits: one moves about while the other sits --- the key to understanding this case: Both are normal rabbits but one is video-recorded by person in room (so rabbit doesn't move). The other by a video on tripod.
- Knowing HOW and WHEN to "observe" is crucial.

## Steps for Pain Diagnosis

1. Know the animals' history
2. Observe without touching
3. **Examine the enclosure for signs of recent behaviors**
4. Examine the animal
5. Ask the animal does it hurt? Where?
6. Administer analgesics, then reassess later
7. [ not for clinical use ] Have the animals tell you how much the pain bothers them

## Assess what animals have done since you last observed

- Did they eat (several mice in a cage: can you tell if all of them ate?)
- Did they drink?
- Did they defecate?
- Did they build a nest?
- Did they move (has bedding been moved?)



- Sick mice in pain will not build a good nest.
- Animals may run less, play less, groom less, socialize less

## Steps for Pain Diagnosis

1. Know the animals' history
2. Observe without touching
3. Examine the enclosure for signs of recent behaviors
4. **Examine the animal**

**Weight the animal; feel Body Condition**

1. Ask the animal does it hurt? Where?
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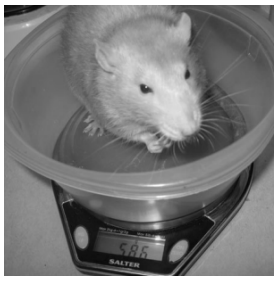
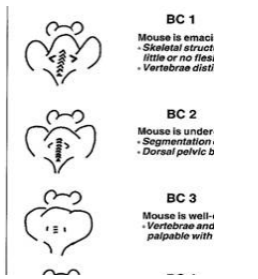





## Steps for Pain Diagnosis

1. Know the animals' history
2. Observe without touching
3. Examine the enclosure for signs of recent behaviors
4. Examine the animal
5. **Ask the animal does it hurt? Where?**

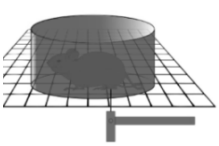
**Elicit pain by palpation**

**Make the animal move**

**Encourage the animal to move with favored objects / treats**

1. Administer analgesics, then reassess later
2. [ not for clinical use ] Have the animals tell you how much the pain bothers them

Poke, prod, palpate for pain sensitivity: ask the animal "Are you sensitive?" "Where does it Hurt?"



- TIN Test: Time to Incorporate Nest Material

Offer the rat a treat and see If s/he will stretch and stand to get it

- Video of two pigs: both eat well, move well, and take treats --- the key to diagnosis in this case: know the individuals. When the dominant pig lets the other go first, that CAN be a sign of pain.

Steps for Pain Diagnosis

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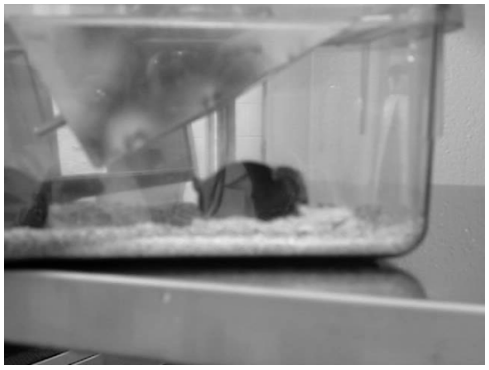
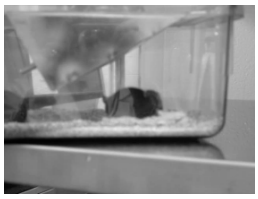
6. Administer analgesics, then reassess later

This only works if you can accurately recognize pain and have an analgesic you know willl work

1. [ not for clinical use ] Have the animals tell you how much the pain bothers them

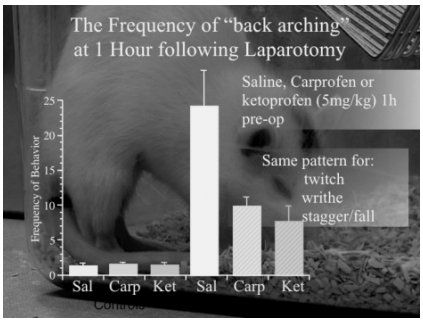




The analgesic helps the animals, AND helps you feel confident that the abnormal behavior you see IS the result of pain

In video of mice, one did not get analgesics.
He is not moving, because of PAIN, not because pain medication is allowing him to sleep

The others are busy, building nest and exploring cage, because the pain medication improves their pain levels enough for them to live their lives.




Staff CAN learn to quantify these behaviors in less than a 5 minute assessment per animal.

## Steps for Pain Diagnosis

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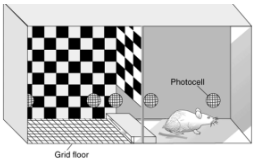
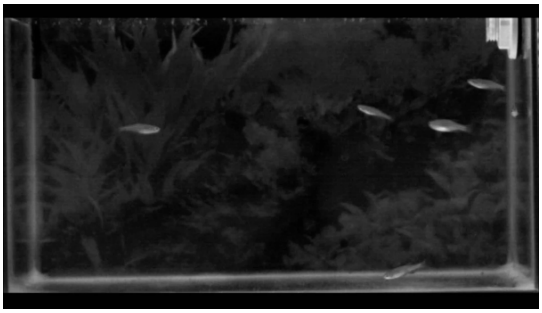
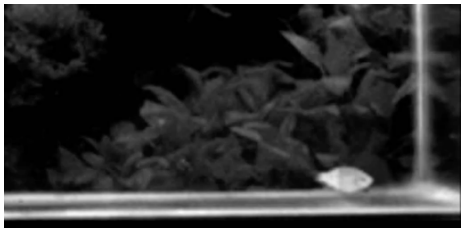
Self-Administration of pain medicines

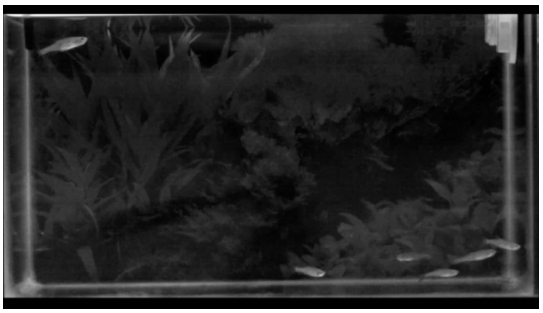
Learned Place Aversion / Preference





History
Examine spontaneous behavior
Observe face? How has animal used the environment?
Response to analgesics



Social behavior and Pain

## Lessons of today

- **Pain can affect animal welfare AND the quality of research data**
- **No simple test for pain**: must put together several types of evidence (history, behavior, exam, comparison with people)
- **Animal pain is difficult to treat**: best to prevent, and later, to euthanize/kill (humane endpoints)
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