Pain, Fear, and Frustration
There is extensive commonality in the mechanisms underlying frustration and fear.

We saw before that the anterior cingulate cortex participates in both.

There are also behavioral similarities, as shown next.

Gray’s (1987) FEAR = FRUSTRATION hypothesis: Gray argued that the only way to distinguish between these two emotions is by knowing the source.

Is it possible that without knowing what caused it, my feelings of frustration and fear would be indistinguishable?

In most studies, fear conditioning is triggered by peripheral pain:

\[ \text{Pain} \rightarrow \text{Fear} \]

In most studies, secondary frustration is triggered by primary frustration:

\[ \text{Primary frustration} \rightarrow \text{Secondary frustration} \]

Let’s look at some relevant results.
Partial reinforcement and partial punishment extinction effects (PREE, PPEE)

<table>
<thead>
<tr>
<th>Group</th>
<th>Acquisition</th>
<th>Extinction</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>Run→50% food</td>
<td>Run→no food or shock</td>
</tr>
<tr>
<td>P</td>
<td>Run→100% food, 50% shock</td>
<td>Run→no food or shock</td>
</tr>
<tr>
<td>C</td>
<td>Run→100% food</td>
<td>Run→no food or shock</td>
</tr>
</tbody>
</table>

Runway procedure (instrumental)

- **Acquisition** (only last trial block shown in figure): rats learned to find food and/or shock in goal box.
- Group N: food available on a random 50% of trials.
- Group P: 100% food, but also shock on a random 50% of trials.
- Group C: 100% food, no shock.
- **Extinction** (shown in figure): no food or shock in any trial.
- **PREE**: Group C (continuous) extinguished faster than Group N (partial).
- **PPEE**: Group C (continuous) extinguished faster than Group P (partial punishment).

- We new that **reward uncertainty** increased behavioral persistence in extinction.
- But **punishment uncertainty** actually has the same effect on behavioral persistence.
- Surprising nonreward and surprising punishment have equivalent effects.

Partial reinforcement and partial punishment extinction effects

### Runway procedure (instrumental)

- **Acquisition** (only last trial block shown in figure): rats learned to find food and/or shock in goal box (same as preceding experiment).
- **Group N**: food available on a random 50% of trials.
- **Group P**: 100% food, but also shock on a random 50% of trials.
- **Group C**: 100% food, no shock.
- **Punishment** (shown in figure): no food, continuous shock in every trial.
  - **Group C** (continuous) tolerated shock less than **Group N** (partial), even though none of these groups had prior experience with shock.
  - **Group C** (continuous) tolerated shock less than **Group P** (partial punishment).

- These results demonstrate the equivalence between surprising nonreward (Group N) and surprising punishment (Group P).
- Both conditions lead to greater tolerance of punishment, even in the absence of food.

---

**Group** | **Acquisition** | **Punishment**
--- | --- | ---
N | Run→50% food | Run→100% shock
P | Run→100% food, 50% shock | Run→100% shock
C | Run→100% food | Run→100% shock

---

Frustration-induced hypoalgesia

Jimenez Garcia et al., 2016, PLoS One


**cSNC (consummatory)**
- Immediately after a reward downshift in the cSNC, rats are tested for pain sensitivity in 3 situations.
  - **Hot plate**: rat is placed on a warm piece of metal and the latency to lick one paw indicates pain sensitivity.
  - **Von Frey**: a paw is stimulated with filaments of increasing diameter until a paw flexion is detected.
  - **Hargreaves**: heat induced by a laser beam is projected to a paw until there is a paw flexion.
- These three tests show that rats that have just experienced reward loss are less sensitive to physical pain.
Summation of physical and psychological pain

- An injection of formalin is applied to a rat’s hind foot.
- Formalin induces inflammatory physical pain.
- When formalin is applied before incentive downshift, it increases cSNC.

**cSNC** (consummatory)
- Peripheral pain interferes with recovery from reward downshift (32-to-4% sucrose downshift)
- Peripheral pain induces a cSNC effect when the discrepancy does not support the effect (16-to-4% sucrose downshift).

Ortega et al., 2011, Learn Motiv, 42, 203-209.
Opioid receptors and ligands

Opioid receptors

- Traditionally involved in pain.

- More recently found to attenuate fear.

- It also attenuates frustration and loss.
Opioid receptors

- Difused distribution.
- Overlap.
- Each concentrated in different areas.
- Some areas have cells expressing all of them (e.g., amygdala).
Manipulations that enhance freezing (e.g., context change, see Group DS) are mimicked by naloxone treatment (see Group SN).

Manipulations that enhance negative contrast (e.g., incentive disparity) are most sensitive to naloxone (greater suppression in 32-6 than 16-6).

Young & Fanselow, 1992, J Exp Psychol: Anim Behav Proc

Daniel et al., 2009. Neurobiol Learn Mem
Morphine, a nonselective opioid receptor agonist, attenuates cSNC

Fear extinction

- Rats receive training in the fear conditioning situation.
- Then, they are shifted to fear extinction.
- Freezing decreases in fear extinction
- Saline: white symbols.
- Naloxone: black symbols.
- Naloxone retards the extinction of fear.

cSNC

- Rats receive access to 32% or 6% sucrose.
- A 32-to-6% sucrose downshift produces little evidence of the cSNC effect (circles).
- However, naloxone enhances the cSNC effect and interferes with recovery (triangles).
Opioid receptors and memory

Introini-Collison et al., 1989, Brain Res

Post-training drug administration used to study memory consolidation.
Post-training naloxone impaired fear memory.
Propanolol (noradrenaline antagonist) reversed the effects of naloxone.
Opioid receptors facilitate fear memory.

Daniel et al., 2009, Neurobiol Learn Mem

Post-training naloxone did not affect cSNC.
Similar results were found with other opioids.
Do opioid receptors play a role in frustration memory?