

A comparison of pain thresholds in surgically and chemically induced osteoarthritis rat models using the Von Frey's filaments and a pressure algometer



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Introduction

Many animal models of induced osteoarthritis (OA) have been developed to study inflammation-associated pain and to evaluate therapeutic agents. Similarly, there are a number of approaches to assess pain threshold in said models.

Here we:

- Compared a surgical and chemical rat model of femorotibial joint OA;
- Employed Von Frey's filaments and a pressure algometer to quantify the animals' level of discomfort.

The femorotibial joints of these models were also evaluated histopathologically.

Experimental Procedures

- Osteoarthritis was induced in the right hind femorotibial joint of female Sprague-Dawley rats either by anterior cruciate ligament transection^(A) or by intra-articular injection of sodium-iodoacetate (200 µl of 15 mg/mL)^(B).
- 7 days following joint conditioning, half the rats subject to the surgical procedure were treated daily with both Carprofen (5 mg/kg, SC) and Pregabalin (30 mg/kg, PO) for 40 days.
- All the other rats received saline (1mL/kg, SC) daily as a placebo for the same duration (see table).
- Hind paw withdrawal using the Von Frey filaments (North Coast Medical)^(C) and an algometer (Force Ten™ FDX, Wagner Instruments)^(D) was assessed on Days -1, 7, 14, 21, 28 and 35.



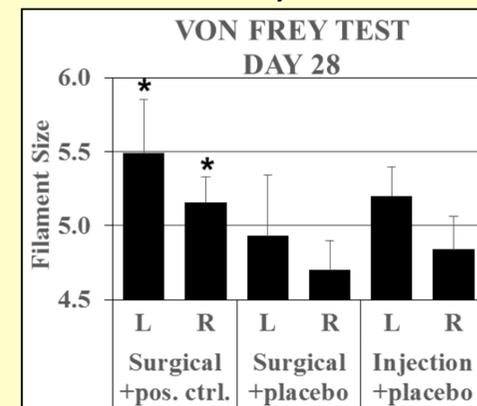
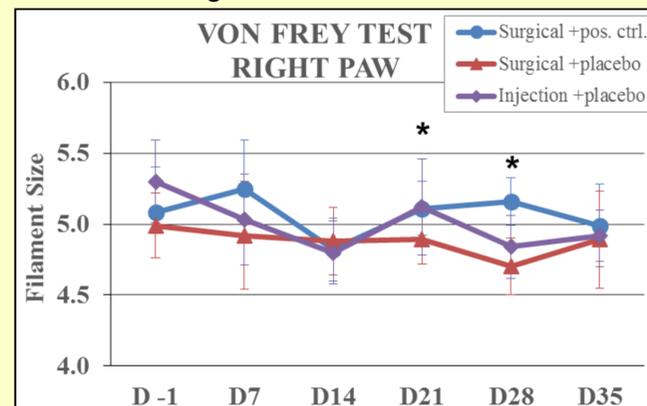
Joint Conditioning	Treatment	Number of Animals
Surgical	Pregabalin + Carprofen	10
	Placebo	10
Injection	Placebo	10



Results

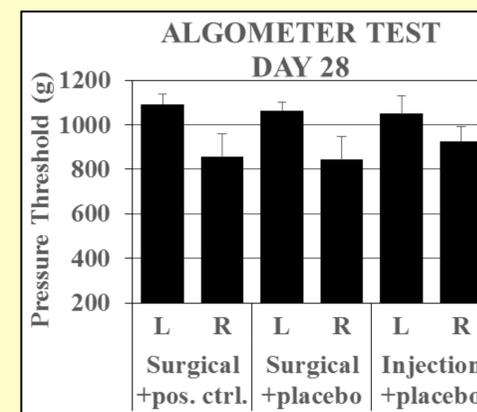
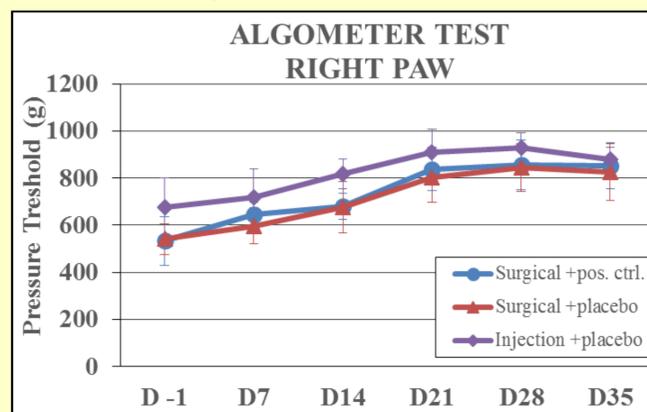
Von Frey Filaments

- There was no significant difference between the two OA models.
- A significant difference was noted between placebo and positive control treated rats on Day 7 and Day 28 for the left paw ($p=0.014$ and 0.004) and on Day 21 and Day 28 for the right paw ($p=0.038$ and <0.001).
- There was no significant difference between the conditioned and intact joint.



Algometer (or Pressure Application Measurement)

- Pain thresholds increased over time in both models, reaching a plateau by Day 28.
- This test showed a clear difference between both joints for each animal.
- There was no significant difference between the two OA models.
- There was no significant difference between the positive control and placebo treated rats.



Histopathology

Histopathology showed diffuse chronic inflammation and granular basophilic material in the cavity of the conditioned joint in both models, but with a higher incidence and severity in the sodium-iodoacetate injected groups when compared with the surgical groups.

Number of Animals	Surgical	Injection	
	Pregabalin +Carprofen	Placebo	Placebo
Chronic inflammation (diffuse)	10	10	10
<i>minimal</i>	4	3	0
<i>mild</i>	6	7	5
<i>moderate</i>	0	0	5
Granular basophilic material	0	2	5
<i>minimal</i>	0	2	4
<i>mild</i>	0	0	1

Conclusions

- Similar pain thresholds and histopathology were noted in rat models of femorotibial joint OA induced by anterior cruciate ligament transection or by injection of sodium-iodoacetate over 40 days.
- Algometer measurements showed good quantification of pain threshold for the conditioned joint but did not show effect of the treatment.
- Von Frey's filaments showed similar results in both conditioned and intact joints, although a significant difference was noted between positive control and placebo groups on Days 21 and 28.
- Von Frey's filaments therefore appear to provide a positive means to quantify discomfort level and evaluate the effect of potential therapeutic agents in the induced OA rat models.

The study plan was reviewed and approved by the Animal Care Committee (ACC) of ITR to ensure that the study met the criteria established by the animal care regulators. ITR is accredited by the Canadian Council on Animal Care (CCAC) and the Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC).