

# PAIN MODELS



PORSOLT HAS AN EXTENSIVE PORTFOLIO OF SERVICES SUPPORTING DRUG DISCOVERY AND DEVELOPMENT. THE DOMAINS OF ACUTE AND CHRONIC PAIN AND INFLAMMATION ARE ACTIVE AREAS OF RESEARCH AT PORSOLT MATCHING THE NEEDS OF THE INDUSTRY.

PORSOLT REMAINS COMMITTED TO MAINTAINING A RECOGNIZED EXPERTISE IN THESE IMPORTANT THERAPEUTIC AREAS BY CONTINUING TO EXPAND ITS BROAD PAIN CAPABILITIES.



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## PAIN MODELS

### Acute Pain

#### • Acute nociception in rodents:

#### PINCHMETER | HOT PLATE | TAIL FLICK | COLD PLATE

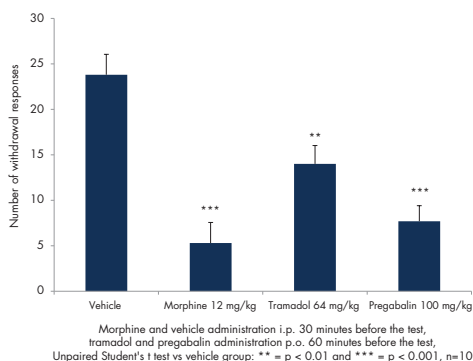
**Several acute pain assays** measuring responses to tactile and thermal stimulation are available in rodents.

Classically, the pinchmeter (*alternative method to the Randall and Selitto test*) is used to assess tactile hyperalgesia, while the hot plate, cold plate and tail flick tests evaluate thermal hyperalgesia.

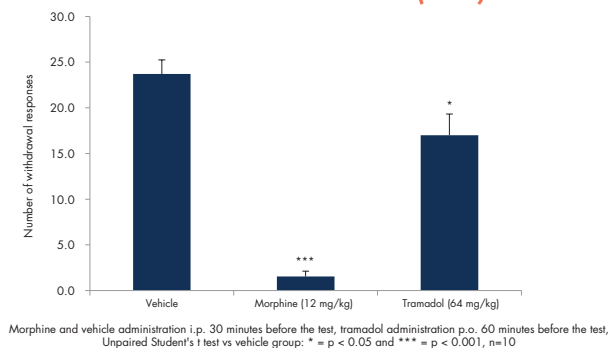
SPECIES	REFERENCE	ROUTE	EFFECT
<b>■ PINCHMETER</b>			
Mouse/Rat	Morphine	i.p.	✓
Mouse/Rat	Tramadol	p.o.	✓
<b>■ HOT PLATE</b>			
Mouse/Rat	Morphine	p.o., i.p., s.c., i.v.*	✓
Mouse/Rat	Paracetamol	i.p., p.o.	✓
Mouse	Tramadol	p.o.	✓
Mouse	Codeine	p.o.	✓
<b>■ TAIL FLICK</b>			
Mouse/Rat	Morphine	p.o., i.p., s.c., i.v.*	✓
Mouse/Rat	Tramadol	p.o.	✓
Mouse	Codeine	p.o.	✓
Rat	Fentanyl	s.c.	✓
<b>■ COLD PLATE</b>			
Mouse/Rat	Morphine	i.p.	✓
Mouse/Rat	Tramadol	p.o.	✓
Rat	Pregabalin	p.o.	✓

\* In the mouse only

#### COLD PLATE TEST IN THE RAT (-3°C)



#### COLD PLATE TEST IN THE MOUSE (-2°C)



### Neuropathic Pain

#### • Bennett (CCI) model of neuropathic pain in the rat:

Neuropathic pain develops over the 7 days following chronic loose ligation of the sciatic nerve.

#### • Chung (SNL) model of neuropathic pain in the rat:

Neuropathic pain develops over the 14 days following chronic tight ligation of the dorsal root nerve (L5-L6).

MEASURE	REFERENCE	ROUTE	EFFECT*
<b>■ BENNETT   CHUNG IN THE RAT</b>			
Plantar, Cold Plate, Electronic von Frey, Pinchmeter	Morphine	i.p.	✓
Plantar, Cold Plate, Electronic von Frey, Pinchmeter	Pregabalin	p.o.	✓
Plantar, Cold Plate, Electronic von Frey, Pinchmeter	Tramadol	i.p.	✓
Plantar, Cold Plate, Pinchmeter	Duloxetine	p.o.	✓

\* Positive effects are observed on selected measures

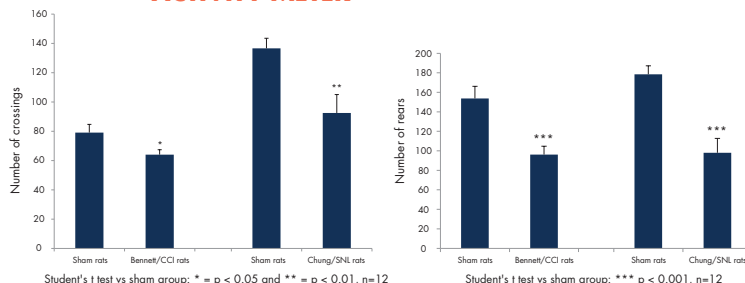
#### ➤ Several pain measures can be used:

- Thermal stimulation (*heat hyperalgesia or cold allodynia*): measured using the Hargreaves method or the cold plate test (4°C), respectively.

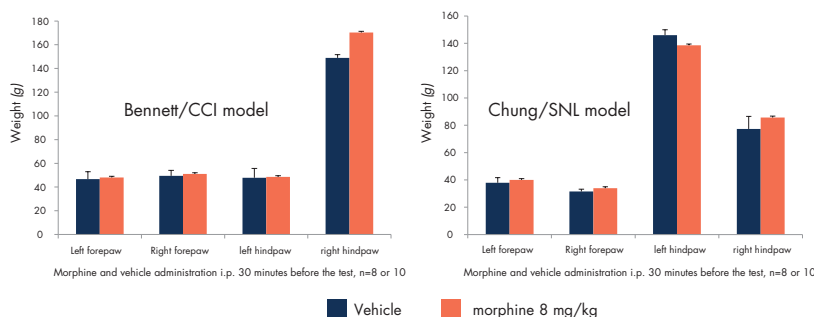
- Tactile stimulation (*tactile allodynia or tactile hyperalgesia*): measured using an electronic von Frey apparatus or a pinchmeter.

#### ➤ Optional non-evoked pain measures:

##### ACTIVITY METER



#### DYNAMIC WEIGHT BEARING (DWB<sup>(1)</sup>)

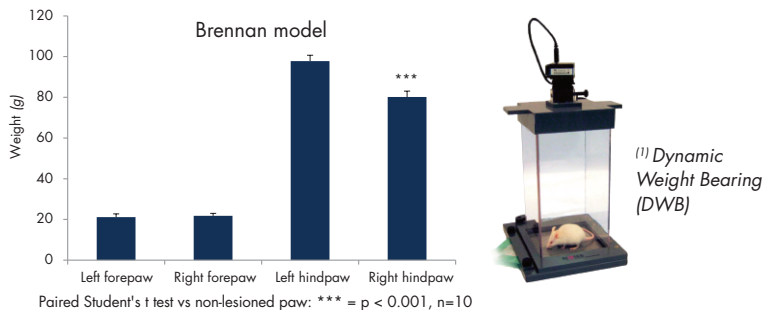


## Post-Operative Pain

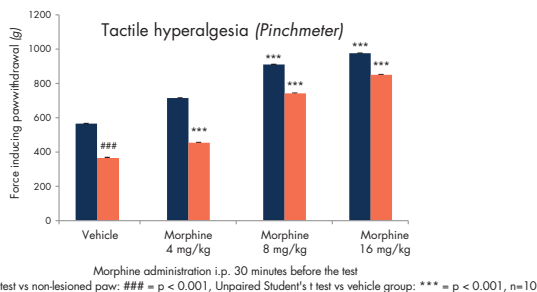
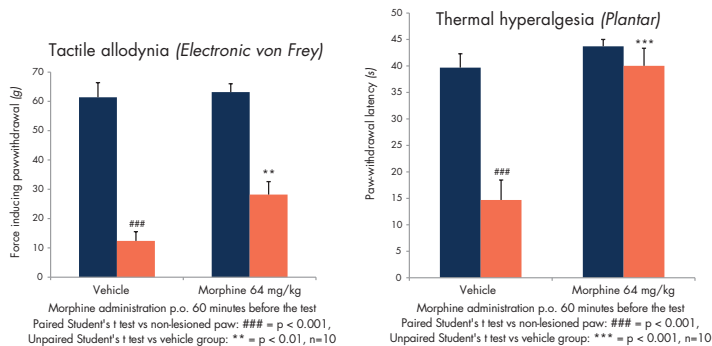
### • Brennan model of post-operative pain in the rat:

- A longitudinal incision of skin, fascia and muscle of the plantar aspect of the rat hindpaw is performed under anesthesia.
- Tactile allodynia, tactile hyperalgesia and thermal hyperalgesia can be measured as early as 3 hours after surgery and up to 3-4 afterwards.
- Dynamic Weight Bearing (DWB<sup>(1)</sup>) evaluation can also be used.

MEASURE	REFERENCE	ROUTE	EFFECT
<b>■ BRENNAN IN THE RAT</b>			
Electronic von Frey, Plantar, Pinchmeter	Morphine	p.o., i.p., s.c.	✓
Electronic von Frey	Ibuprofen	p.o.	✓
Electronic von Frey, Plantar	Anandamide	i.p.	✓
Electronic von Frey, Plantar, Pinchmeter	Bupivacaine	SNB (Sciatic Nerve Block)	✓



### BRENNAN MODEL OF POST-OPERATIVE PAIN IN THE RAT: EFFECTS OF MORPHINE 24 HOURS AFTER SURGERY



## Inflammatory Pain

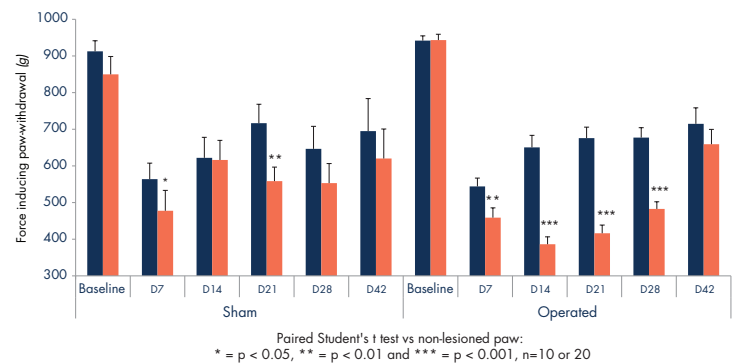
### • Inflammatory pain in rodents:

- **FORMALIN** (early and late phase) (rat and mouse)
- **CAPSAICIN** (rat and mouse)
- **CARRAGEENAN MODEL** (rat and mouse)  
Rats are injected with carrageenan into the lower surface of the right hindpaw and evaluated at least 2 hours later.
- **COMPLETE FREUND'S ADJUVANT MODEL** (rat and mouse)  
Rats are injected with CFA into the lower surface of the right hindpaw and evaluated 24 hours later.
- **CHRONIC INFLAMMATORY PAIN** (CFA-induced monoarthritis) (rat)  
Rats are injected with a suspension of Mycobacterium butyricum (Freund's adjuvant) into the tibio-tarsal joint. Testing phase can be performed 7 and/or 14 days after induction
- **OSTEOARTHRITIS: MIA MODEL** (rat)  
Monosodium iodoacetate (MIA) is injected through the infra patellar ligament into the joint space of one knee. Testing phase is performed 14 days after induction
- **SURGICAL OSTEOARTHRITIS** (guinea-pig) (anterior cruciate ligament ACL transection combined to meniscal lesion)

### ➤ Several pain measures can be proposed:

- Tactile stimulation (tactile allodynia or tactile hyperalgesia): measured using an electronic von Frey apparatus or a pinchmeter (applied to the paw and to the knee).
- Thermal stimulation (heat hyperalgesia): measured using the plantar test.

### PINCHMETER TEST (KNEE) IN THE SURGICAL OSTEOARTHRITIS MODEL IN GUINEA-PIG



■ Non-lesioned paw  
■ Lesioned paw



## PAIN MODELS

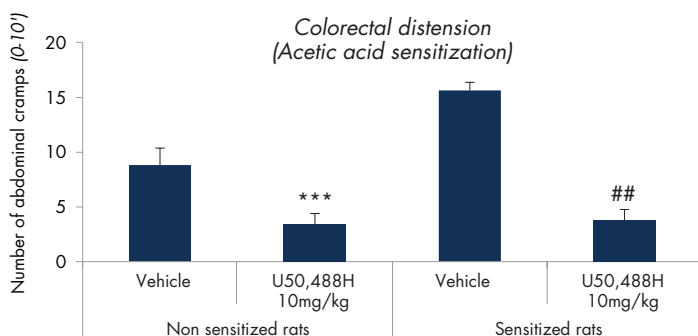
### Visceral Pain

#### • Acetic acid or Parabenzoquinone-induced writhing in the mouse:

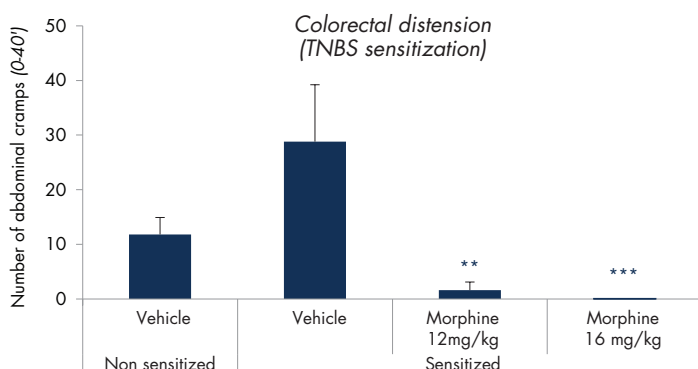
- Animals are injected with acetic acid or parabenzoquinone (*i.p.*).
- The number of writhes is counted for 10 minutes, beginning 5 minutes after the injection of reagent substance.

REFERENCE	ROUTE	EFFECT
<b>■ ACETIC ACID-INDUCED WRITHING IN THE MOUSE</b>		
Morphine	p.o., i.p., i.v.	✓
Tramadol	p.o.	✓
Duloxetine	i.p.	✓

#### • Colorectal distension in the rat (acetic acid or TNBS model)



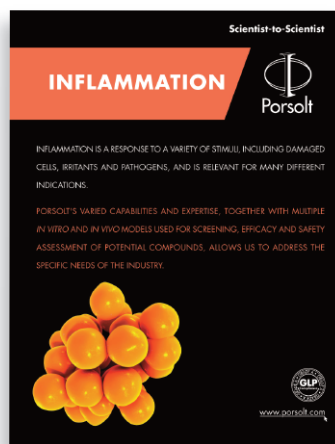
U-50,488H administration p.o. 60 minutes before the test  
Mann-Whitney U test vs non sensitized rats: ## =  $p < 0.01$ ,  
vs vehicle group: \*\* =  $p < 0.01$  and \*\*\* =  $p < 0.001$ ,  $n=10$



Morphine administration i.p. 30 minutes before the test  
Mann-Whitney U test vs non sensitized rats vs vehicle group:  
\*\* =  $p < 0.01$  and \*\*\* =  $p < 0.001$ ,  $n=10$

### Inflammation

- YEAST HYPERTHERMIA
- LPS SEPTIC SHOCK
- AIR POUCH
- EAR EDEMA
- ACUTE CARRAGEENAN



Read also  
our leaflet  
'INFLAMMATION'  
for further details!

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- Biomarker Analysis Services & Image Analysis Solutions



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