

# Femoral Fracture in a Mouse Model Induces Evoked and Naturalistic Pain Behaviours

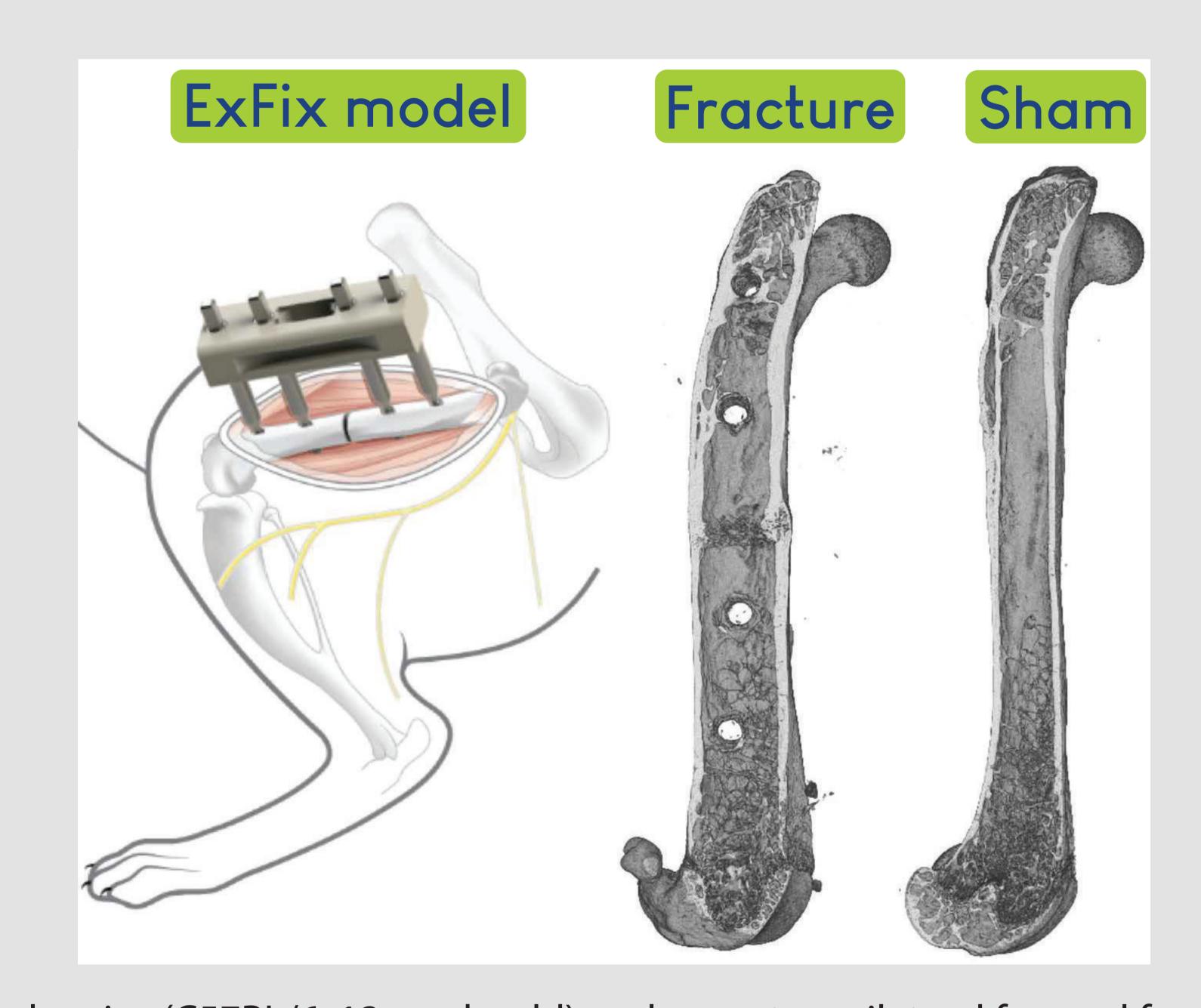


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#### Introduction

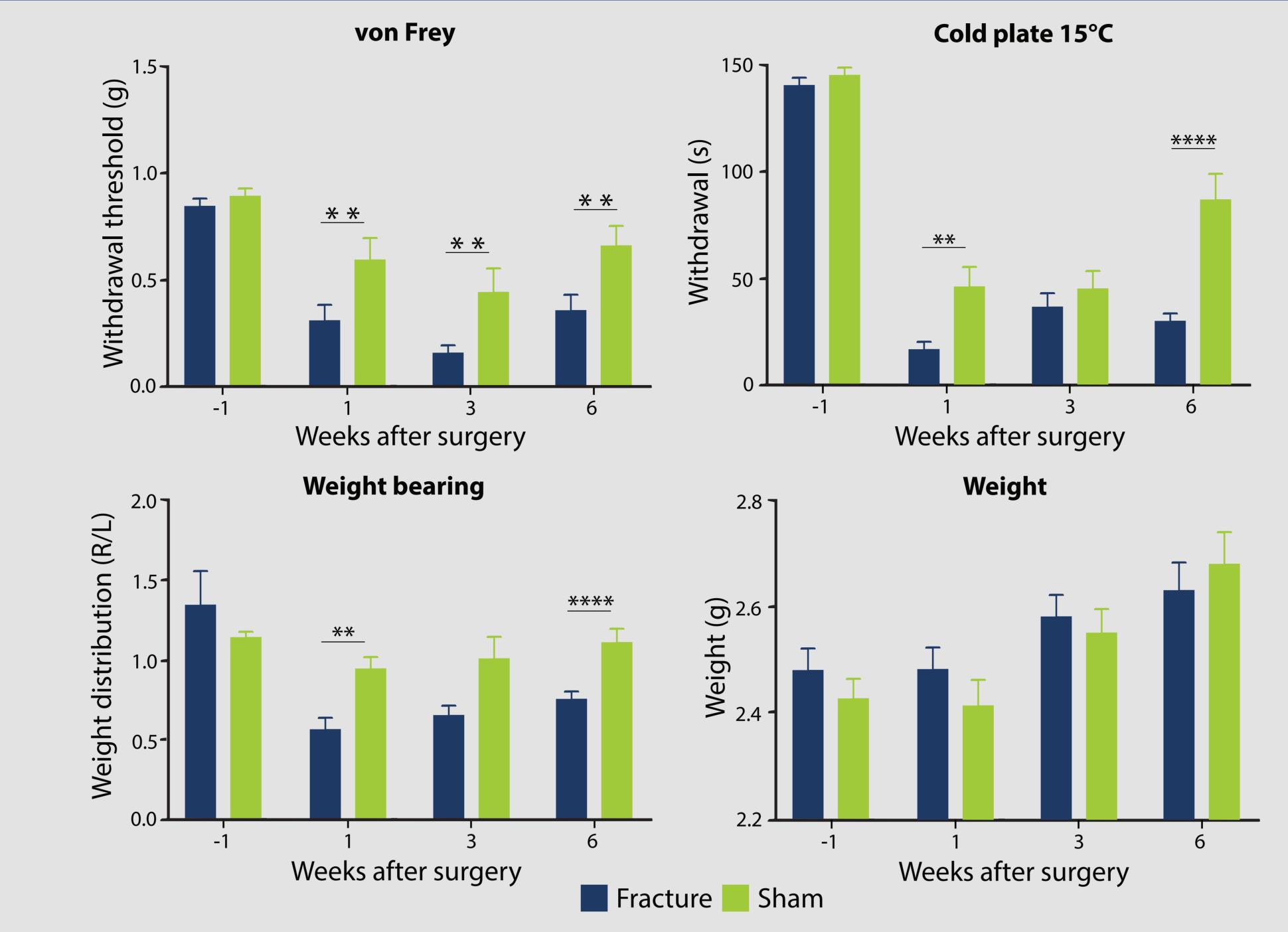
- Bone fractures are increasingly common due to the ageing population and can be immensely painful. The mechanisms leading to this pain are poorly understood. The development of standardised rodent models of fracture has led to their increased use to assess the biology of fracture healing.
- No work has exhaustively examined the time course, phenotype and mechanism of naturalistic and evoked pain behaviours during bone repair in rodent models of fracture.
- The aim of our study was to characterise naturalistic and evoked pain behaviours after fracture surgery during the different phases of bone repair in a frequently used femoral fracture model in mice.

#### Methods



- Adult male mice (C57BL/6, 12 weeks old) underwent a unilateral femoral fracture maintained by an external fixator (Fracture) or a sham surgery (Sham).
- Evoked pain behaviours were measured in the daylight phase from baseline to six weeks after fracture surgery.
- Naturalistic behaviours were measured with LABORAS over the night phase from baseline to six weeks after surgery.
- All animal procedures underwent institutional ethical review and were performed under the Animal (Scientific Procedures) Act 1986.

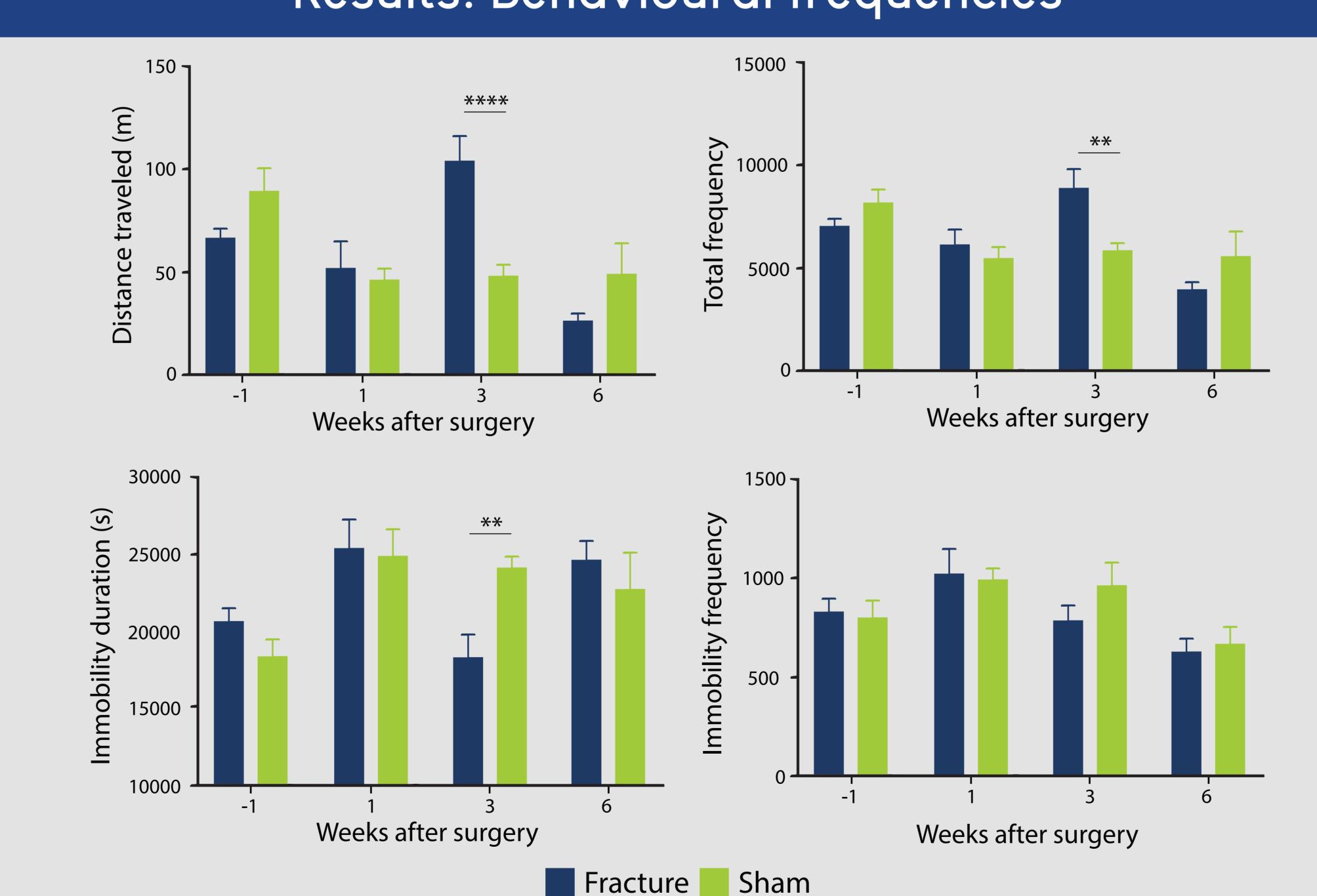
### Results: Fracture-induced evoked pain



**Figure 2** Evoked pain behaviors in mice. Results are expressed as means  $\pm$  SEM, n = 7 - 10/group. Multiple t-tests Holm-Sidak method:

- \*\* p < 0.01 Fracture compared to Sham; \*\*\* p < 0.001; \*\*\*\* p < 0.0001.
- Mechanical and thermal hyperalgesia, in addition to decreased weight-bearing are established after fracture and are sustained for six weeks

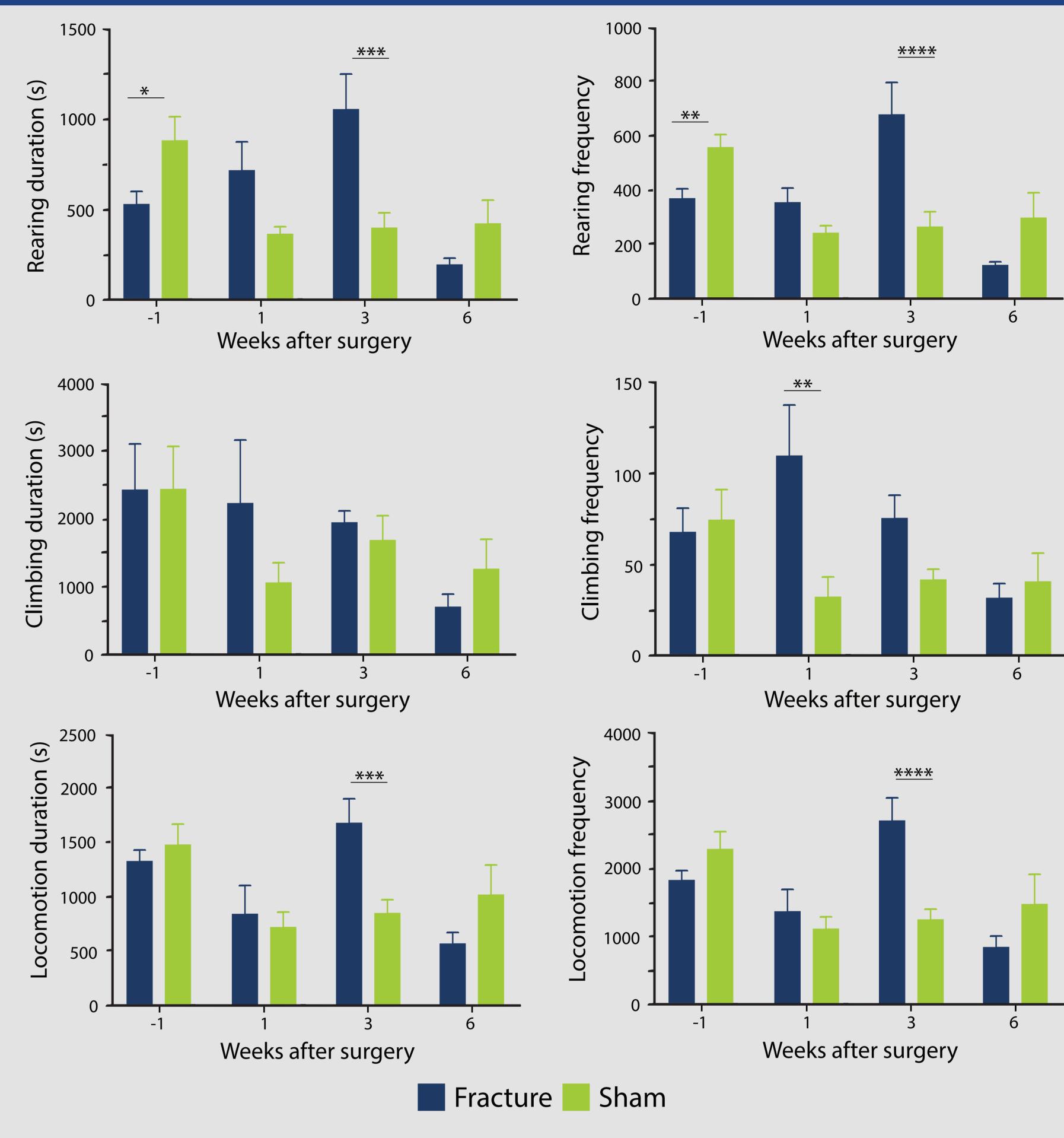
## Results: Behavioural frequencies



**Figure 3** Changes in naturalistic behavior frequencies and distance traveled in mice. Results are expressed as means  $\pm$  SEM, n = 7 - 10/group. Multiple t-tests Holm-Sidak method: \*\* p < 0.01 Fracture compared to Sham; \*\*\* p < 0.001; \*\*\*\* p < 0.0001.

- Mice that undergo fracture have increased frequency of behaviours but a less time overall spent on movement.
- Fractured mice move as much as sham mice in the week after surgery, but their movement is then increased

### Results: Naturalistic pain behaviours



**Figure 4** Changes in naturalistic behaviors in mice. Results are expressed as means  $\pm$  SEM, n = 7 - 10/group. Multiple t-tests Holm-Sidak method:  $T^{**}$  p < 0.01 Fracture compared to Sham; \*\*\* p < 0.001; \*\*\*\* p < 0.0001.

- Fracture surgery induces changes in naturalistic behaviours
- Locomotion is increased in fractured mice

#### Conclusions

- -Our results demonstrate that fracture surgeries in mice models are painful, with an observable pain phenotype remaining stable for up to six weeks after surgery.
- Von Frey, cold plate and static weight bearing captured the differences between Fractured and Sham mice.
- -Using Laboras we show a naturalistic pain phenotype in the Fracture group.
- -Our data suggest it is important to consider appropriate analgesia in rodent fracture models as signs of pain are not easily observed without specialised pain measurements.

## Acknowledgements

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