

# A characterization of a rat model of trigeminal neuropathic pain by chronic constriction Injury of infraorbital nerve and pharmacological improvement by gabapentin



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## Background

Trigeminal neuralgia (TGN) is a neuropathic pain syndrome that is caused by the compression of the trigeminal nerve. TGN is the most common facial neuralgia and causes sudden pain attacks usually in the lower part of the face, thereby substantially reducing the quality of life of patients. In this study, we replicated a rat model of trigeminal neuropathic pain by chronic constriction injury (CCI) induction by surgical ligation of the infraorbital nerve (IoN). Behavioral response after surgery was measured using the von Frey test, observation of facial grooming behavior, and gait analysis. Furthermore, undisturbed rat behavior was observed in home cages using the Home Cage Analysis (HCA) system (Actual Analytics, UK).

## METHODS

### CCI-IoN model generation

- Male Sprague-Dawley rats were anesthetized and the facial skin between the eye and whiskers was incised. The muscle peripheral fascia was separated to expose the infraorbital foramen and then the distal segment of the IoN was ligated.

- For the sham group, the same surgical procedure was applied without the nerve ligation.

### Von Frey test and facial grooming observation

- Rats were acclimatized in a dark, quiet room, and placed in a custom cage. Von Frey filaments of a range of grades (2, 1, 0.4, 0.16, 0.02 g) were used to stimulate the vibrissa pad. Pain response to the mechanical stimulus was graded based on the intensity of the response.
- Facial grooming behavior was observed 5 and 26 days after surgery by recording the time spent face grooming for 10 minutes in a separate cage after acclimation.

### Gait analysis

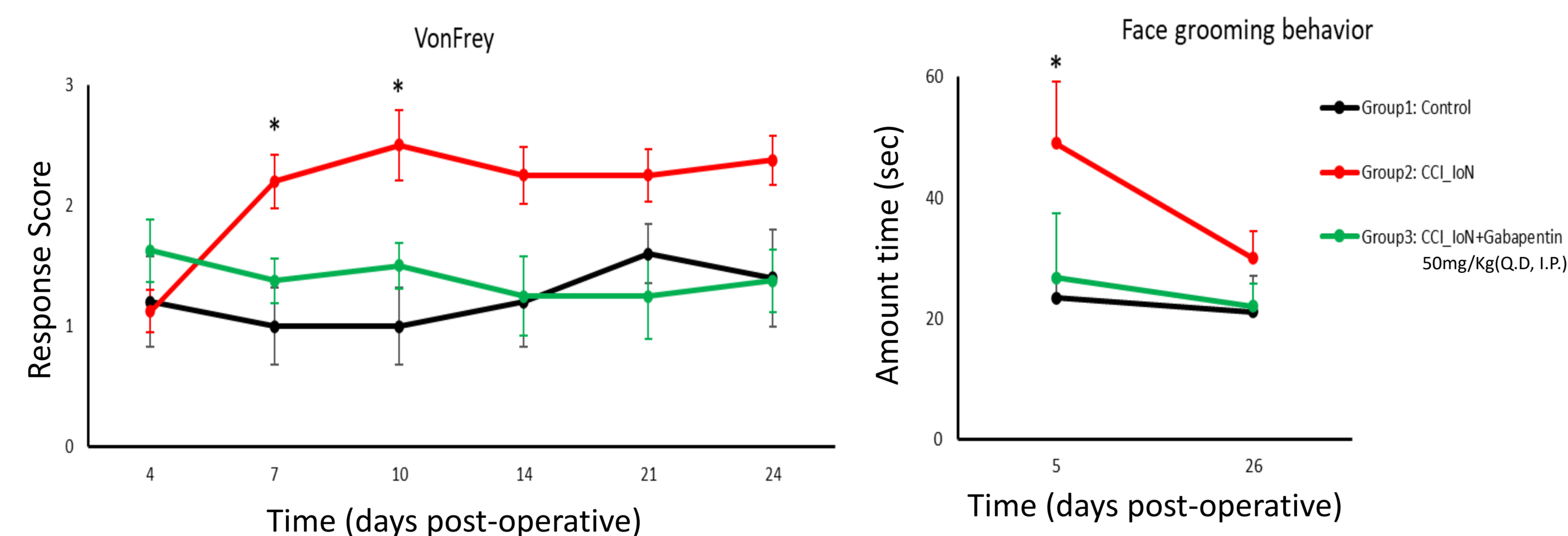
- Before the gait test, the right paws were colored red, and left paws blue.
- Rats walked on a translucent, 1 m platform, and this was recorded using a video camera from underneath the platform. Gait patterns were analyzed using a custom-made program.

### Home cage analysis (HCA)

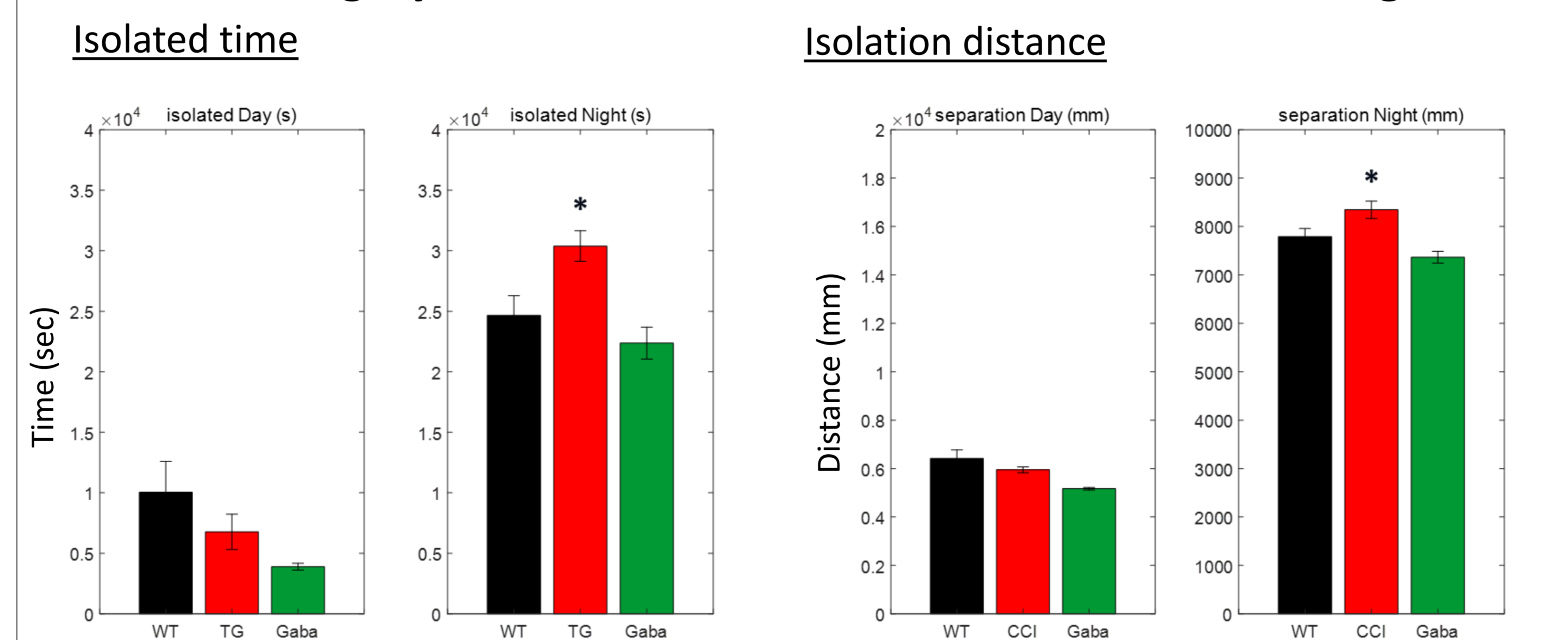
- RFID chips were inserted subcutaneously in the abdomen of rats before the study.
- Rats were housed in their home cages that were slotted inside the HCA apparatus, which consists of a baseplate RFID reader under the cage that records positional information, and an infrared HD video camera for continuous recording.
- Baseline recording was taken before the surgery. HCA recordings for control (no surgery) and CCI-IoN groups were taken 1 week after surgery.
- Locomotor activity and social interactions in the home cage were recorded and analyzed.

## RESULTS

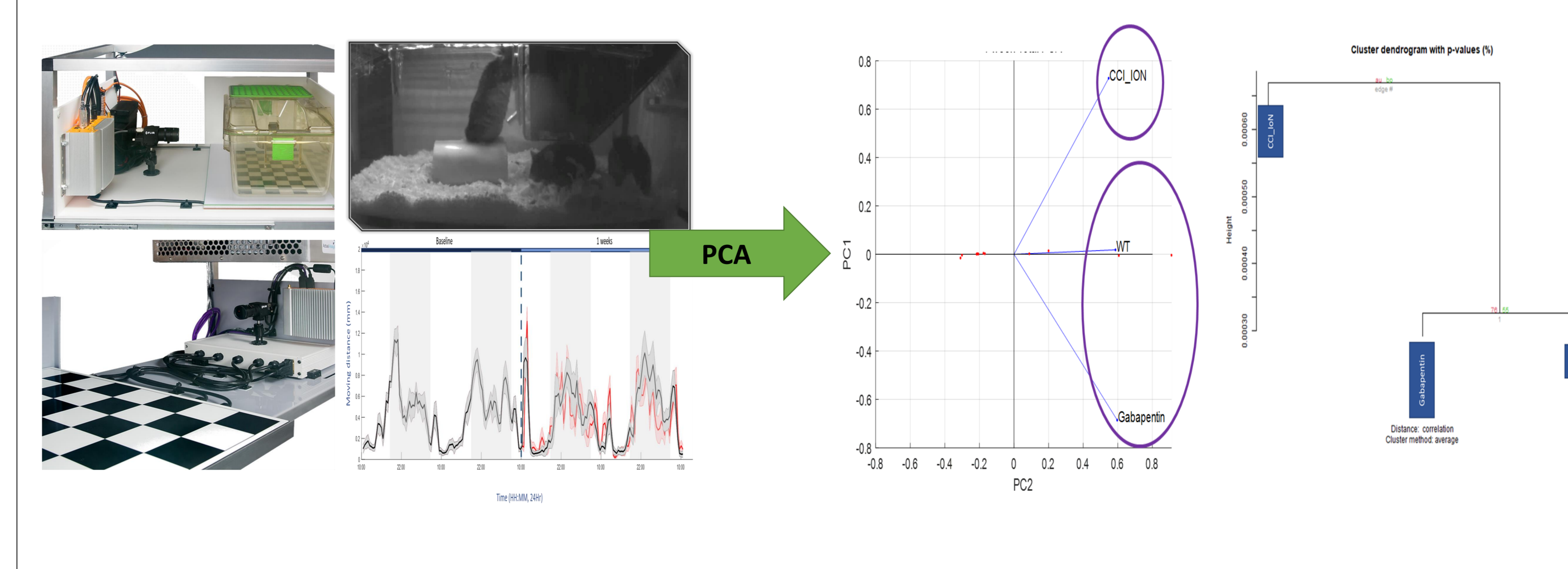
### 1. CCI IoN surgery increased pain response and facial grooming behavior in rats



### 2. CCI-IoN surgery affected rat social behavior in their home cage

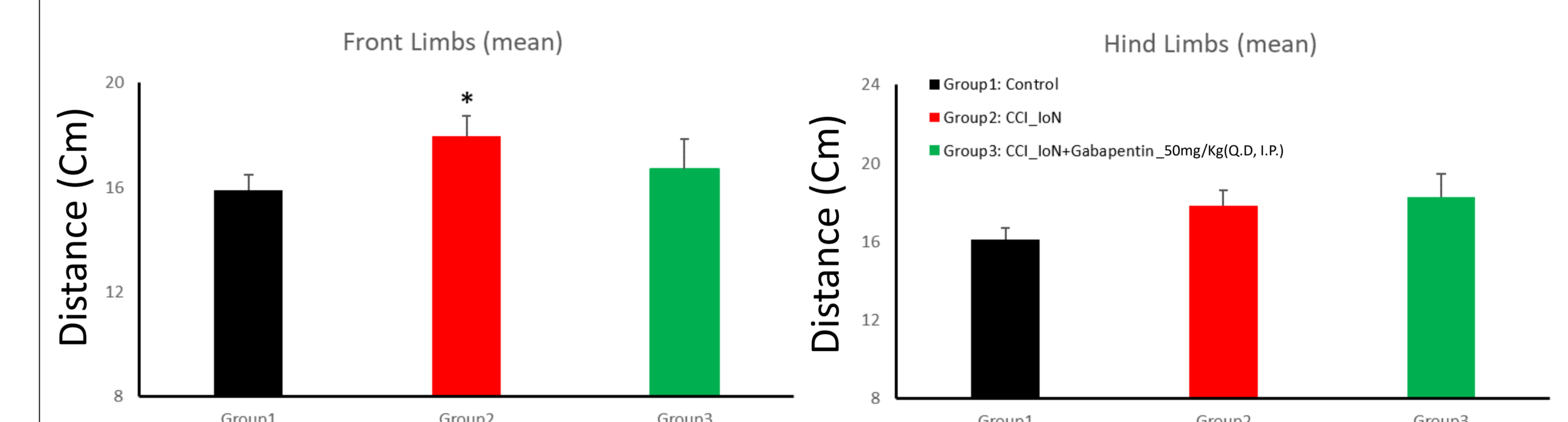


### Principal component analysis and cluster dendrogram using all measured parameters

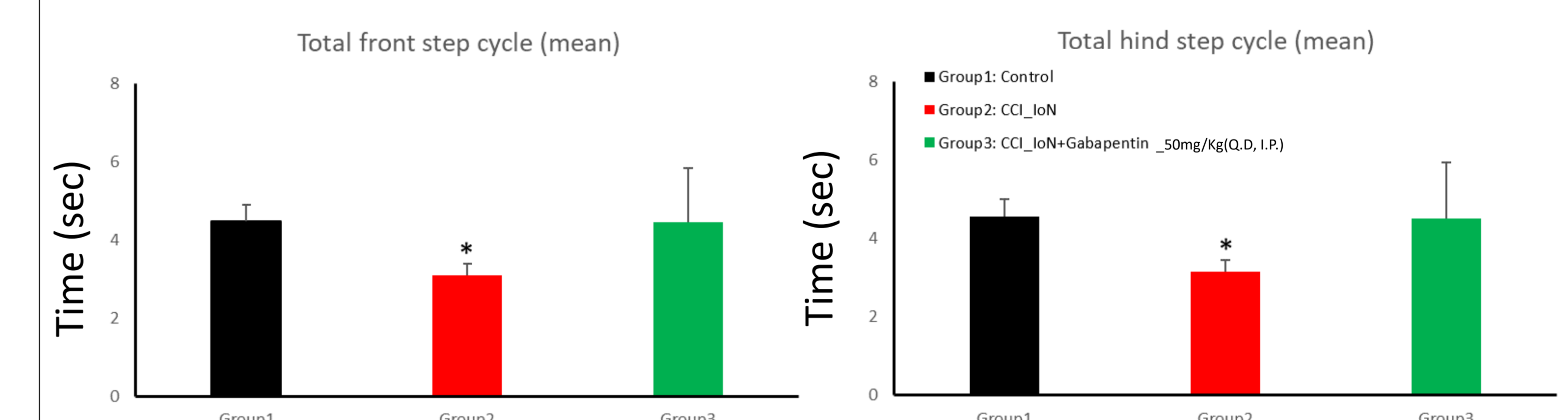


### 3. CCI-IoN surgery altered the gait pattern of rats

#### Gait distance



#### Step cycle duration



\*p<0.05; vs Control, 1-way ANOVA and LSD post-hoc test

## CONCLUSIONS

- Rats that underwent CCI-IoN surgery showed elevated pain response to mechanical stimuli that persisted up to 3 weeks post surgery.
- Operated rats also spent more time in face grooming behavior 5 days after surgery. This was attenuated 4 weeks after surgery.
- Operated rats spent significantly more time isolated from each other at night compared with baseline and control groups.
- Overall analysis of HCA parameters using PCA and cluster dendrogram grouped gabapentin and control groups together.
- In the gait analysis, operated rats had wider gaits and shorter step cycles compared with control rats.

CCI-IoN induced not only facial pain responses but also affected the social interactions and gait changes in rats, which was attenuated by gabapentin treatment. This rat model is may be useful for drug development in trigeminal neuralgia indication.