

Does environment affect a chronic pain?

Ken Takahashi[†], Satoshi Okumura, Jun Sato and Kazue Mizumura

Department of Neural Regulation
Research Institute of Environmental Medicine
Nagoya University, Nagoya 464-8601, JAPAN

[†]: Tel.: +81-52-789-3863 Fax: +81-52-789-3889 Email: spacevet@v001.vaio.ne.jp

In the international space station (ISS), atmospheric pressure is maintained at 1 bar. However, if you have to go out and conduct Extravehicular Activities (EVA), you have to put on space suits, in which the pressure is 0.3 bar.

Meanwhile, it is reported that patients suffer from chronic pain *rheumatoid arthritis*, for example often complain that their pains get worse either when a low pressure front is reaching or when the temperature falls. However, there is no scientific evidence for that phenomenon.

Therefore, we intended to investigate whether environment like atmospheric pressure and the temperature really affect a chronic pain, using animals (rat).

Preliminary experiment: making a model of a chronic pain

- Subject: Adult male **Sprague-Dawley** rats
- Animal model: **Adjuvant-induced monoarthritis**
- Rats were divided into two groups: adjuvant-injected group (**ADJ**, n=10) and saline-injected group (**CTR**, n=10).
 - **ADJ** group was injected 0.05 ml complete adjuvant (containing 300 µg killed *Mycobacterium butyricum*) into the tibio-tarsal joint.
 - **CTR** group was injected 0.05 ml saline in the left tibio-tarsal joint.
- We applied the **von Frey hair** (bending force: 53.9 mN) to the plantar surface of the left hindpaw 10 times at 2-3 sec intervals, and counted the number of paw withdrawal response.
- This number was regarded as an index of pain intensity.
- We performed the von Frey hair test twice a week from the pre-injection period to 5 weeks post injection.



Fig. 1. Method to apply mechanical stimulation. Von Frey hairs were used to apply mechanical stimulation to the plantar surface of the hindpaw. Left: von Frey hairs. Each hair was calibrated to give constant force (from left to right, 34.0, 53.9 and 126.7 mN). In this experiment, we used 53.9 mN force, which does not cause pain sensation when applied to the experimenter. Right: a figure of von Frey hair test. The von Frey hair was applied to the plantar surface of the rat's left (treated) hindpaw.

Modification of the pain sensitivity

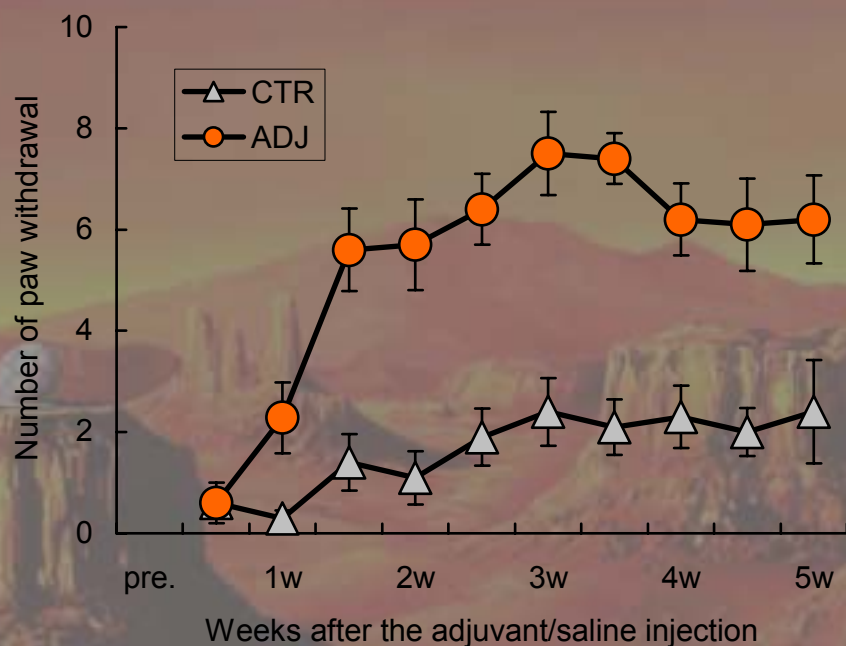


Fig. 2. Modification of the number of paw withdrawal in response to mechanical stimulation (von Frey hairs) in rats with adjuvant-induced monoarthritis. Data are expressed as mean \pm SEM (bar). Von Frey hairs were applied to the plantar surface of the left hindpaw. Rats were injected with 0.05 ml complete adjuvant (containing 300 µg killed *Mycobacterium butyricum*) in the left tibio-tarsal joint (ADJ). Control animals (CTR) were injected 0.05 ml saline in the left tibio-tarsal joint. Measurements of the paw withdrawal responses were performed from the pre-injection period to 5 weeks post injection. In the ADJ group, the paw withdrawal responses increased shortly after the adjuvant injection and reached the peak in the 3rd week.

Exposure to meteorological changes

- Animals: the same animals used in the preliminary experiment.
- We used a **climate-controlled room** to simulate meteorological changes:
 - Low pressure (LP): 20 mmHg below the normal atmospheric pressure
 - Low temperature (LT): 15°C (baseline room temperature: 22°C)
- Exposures were performed 2 weeks post injection.
- We performed the von Frey test 3 times:
 - **pre**: 60 min before exposure
 - **mid**: 30 min after reaching LP/LT conditions
 - **post**: 90 min after returning to the normal condition

Effect of Low Pressure

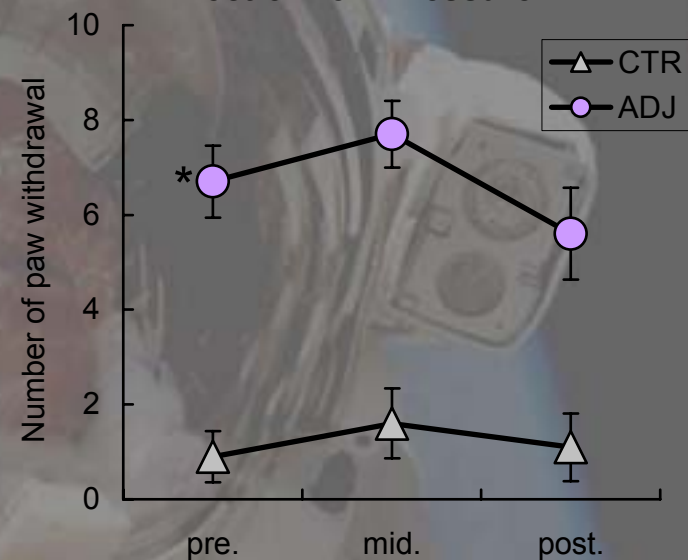


Fig. 3. Effect of LP exposure on mechanical hyperalgesia. Data indicate the number of paw withdrawal responses to mechanical stimulation (von Frey hairs) to the plantar surface of the hindpaw. Data are expressed as mean \pm SEM (bar). pre: 60 min before LP exposure; mid: 30 min after reaching the lowest pressure; post: 90 min after returning to the normal pressure. *: $P < 0.05$, significant data difference with pressure factor (Friedman test). LP affected the paw withdrawal response only in adjuvant-injected rats.

Effect of Low Temperature

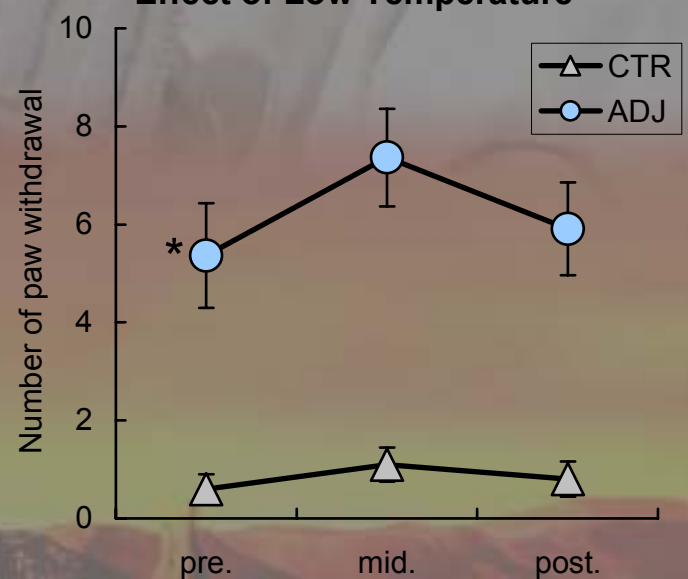


Fig. 4. Effect of LT exposure on mechanical hyperalgesia. Data indicate the number of paw withdrawal responses to mechanical stimulation (von Frey hairs) to the plantar surface of the hindpaw. Data are expressed as mean \pm SEM (bar). pre: 60 min before LT exposure; mid: 30 min after reaching 15°C; post: 90 min after returning to 22°C. *: $P < 0.05$, significant data difference with temperature factor (Friedman test). LT affected the paw withdrawal response only in adjuvant-injected rats.

Results

- LP and LT conditions aggravated mechanical hyperalgesia in the adjuvant-injected rats.
- These effects seemed to disappear when the conditions were returned to the baseline level.
- These results indicate that the meteorological change in a natural range aggravate mechanical hyperalgesia seen in chronically inflamed condition, such as rheumatoid arthritis.

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Background photos: courtesy of NASDA