

Study on the Evaluation System of Post-Stroke Pain Model in Rats

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COI開示

- ☑ 発表内容に関連し、過去3年間、
開示すべきCOI関係にある
企業などはありません

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Objective

Central post-stroke pain (CPSP) is one of the most troublesome sequelae of stroke. It is characterized by persistent pain, resulting in marked deterioration in daily living activities and quality of life (QOL). In recent years, the rat model of CPSP using collagenase-IV induced cerebral hemorrhage has been increasingly reported.

In this study, we attempted to establish an assessment system of analgesics in CPSP model. Male SD rats were induced cerebral hemorrhage by means of microinjection of collagenase-IV into the lateral thalamic area. The pain thresholds was evaluated with von Frey filament.

Materials and Methods

Experiment 1: Confirmation of the hemorrhagic lesion induced by intra-thalamic collagenase

【Animal】

Male rat, Crl:CD(SD), 8 weeks of age (at the model preparation)

【Group configuration】

Group	Dose level (IU/head)	Dose volume (μL/head)	Dosing route	N
Model	0.125	0.5	i.c.	3

i.c.: intracerebral administration

【Experiment schedule】



Materials and Methods

【Animal】

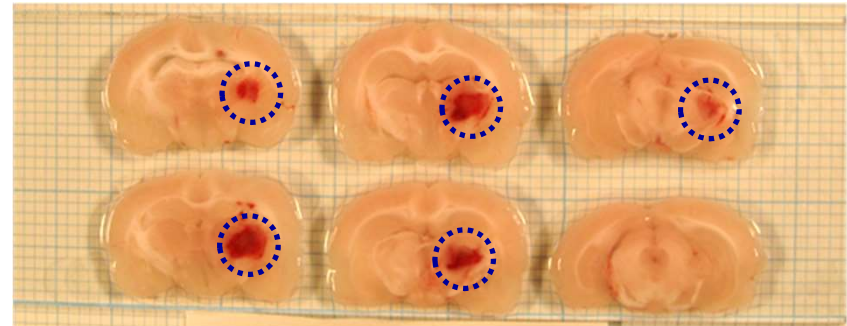
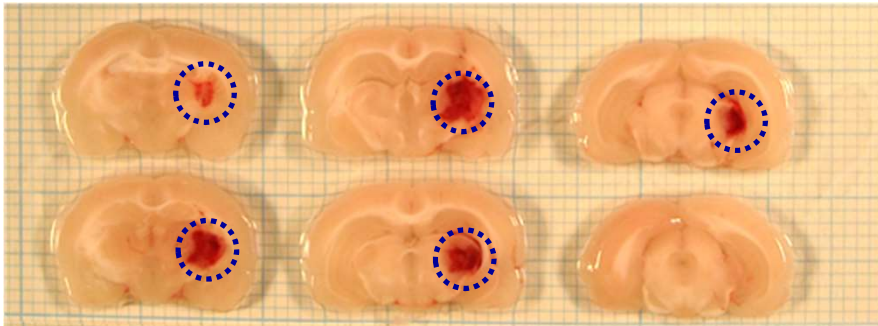
Male rat, Crl:CD(SD), 8 weeks of age (at the model preparation)

【Preparation of CPSP model】

- (1) The animals were maintained under anesthesia with 2% isoflurane during surgery.
- (2) The animals were injected with type IV collagenase (FUJIFILM Wako Pure Chemical Corporation, 0.125 IU/0.5 μ L saline) into the lateral thalamic area (anterior/posterior, -3.5 mm from bregma; lateral, 3.6 mm from the midline; ventral, 6.0 mm from the dura) using a stereotaxic frame.
- (3) Sham-operation animals were injected with 0.5 μ L saline only.

Results

Experiment 1: Confirmation of the hemorrhagic lesion induced by intra-thalamic collagenase



Photos showing representative examples of the spatial extent of the hemorrhagic lesion induced by intra-thalamic collagenase microinjection.

Materials and Methods

Experiment 2: Confirmation of the central post-stroke pain (CPSP)

【Animal】

Male rat, Crl:CD(SD), 8 weeks of age (at the model preparation)

【Group configuration】

Group	Dose level (IU/head)	Dose volume (μ L/head)	Dosing route	N
Sham operation	0	0.5	i.c.	7
CPSP model	0.125	0.5	i.c.	5

i.c.: intracerebral administration

【Evaluation of the pain】

von Frey filament test

Materials and Methods

Experiment 2: Confirmation of the central post-stroke pain (CPSP)

【Evaluation of the pain】

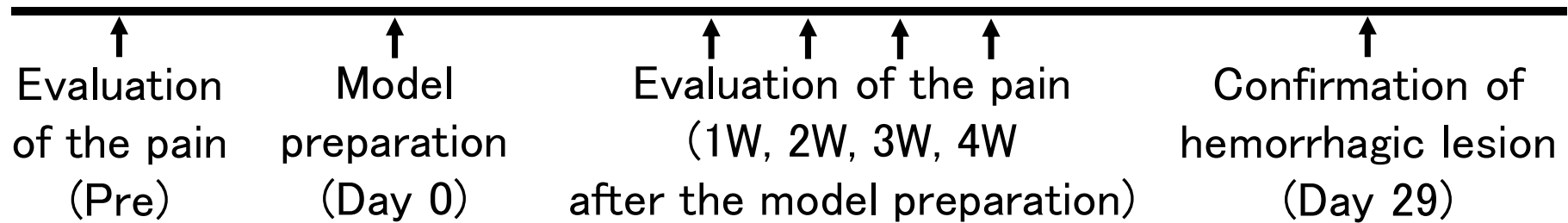
Measurement of pain threshold with von frey filament

Each of the filaments (0.4, 0.6, 1, 2, 4, 6, 8, 15, 26 g) was used according to Chaplan's method.

Materials and Methods

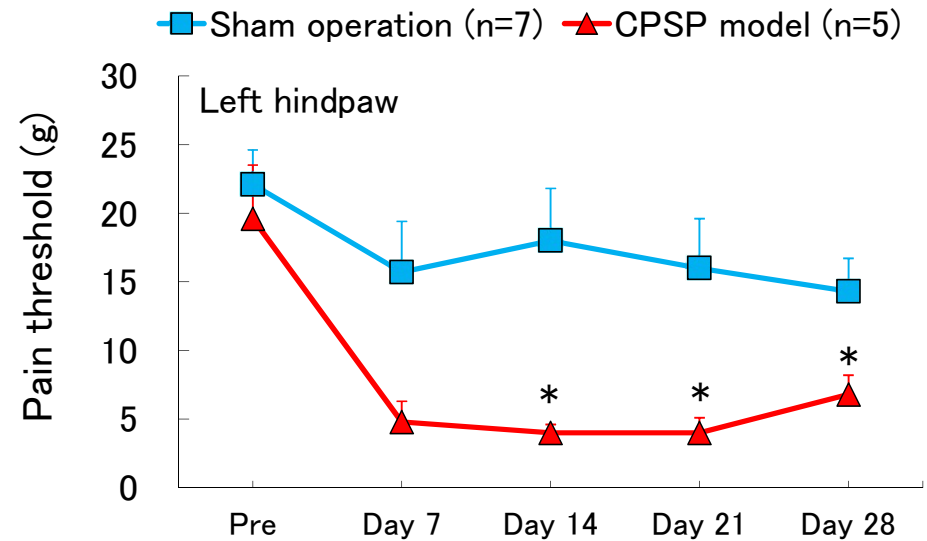
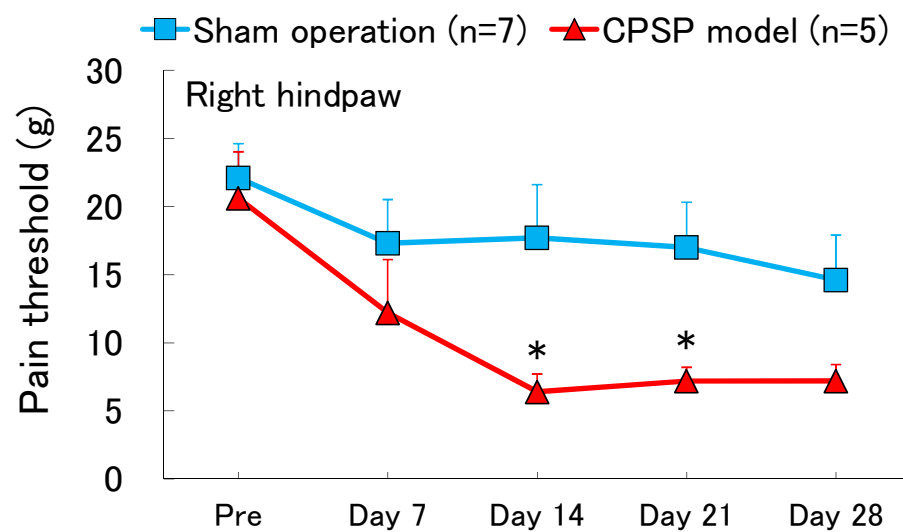
Experiment 2: Confirmation of the central post-stroke pain (CPSP)

【Experiment schedule】



Results

Experiment 2: Confirmation of the central post-stroke pain (CPSP)



Mean \pm S.E.

*: $p < 0.05$, Significant difference from the sham operation group (Student's t -test).

Compared with the sham operation group, the CPSP model group showed lower pain thresholds from Day 7 onwards, and a significant difference from Day 14 to Day 21 in both the left and the right hindpaws.

Materials and Methods

Experiment 3–1: Pharmacological study using CPSP model

【Animal】

Male rat, Crl:CD(SD), 8 weeks of age (at the model preparation)

【Group configuration】

Group	Dosing solutions	Dose level (mg/kg)	Dose volume (mL/kg)	Dosing route	N
Sham operation	saline	0	2	p.o.	5
Vehicle	saline	0	2	p.o.	7
Pregabalin	pregabalin	30	2	p.o.	6

i.c.: intracerebral administration

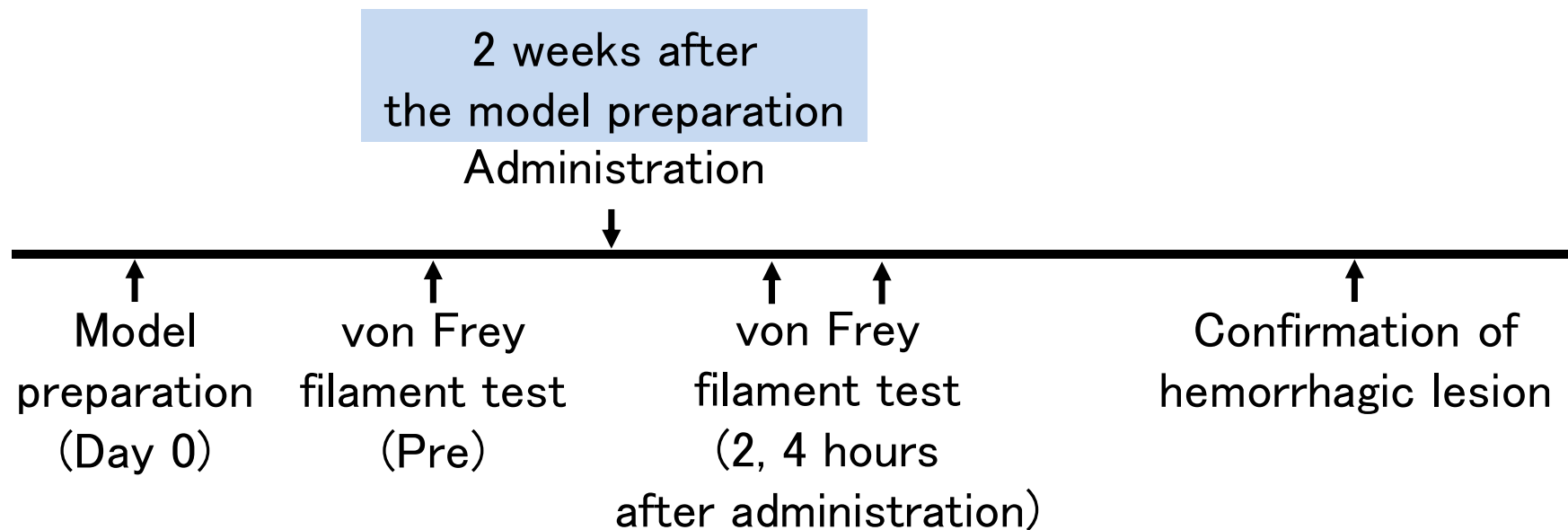
【Evaluation of the pain】

von Frey filament test

Materials and Methods

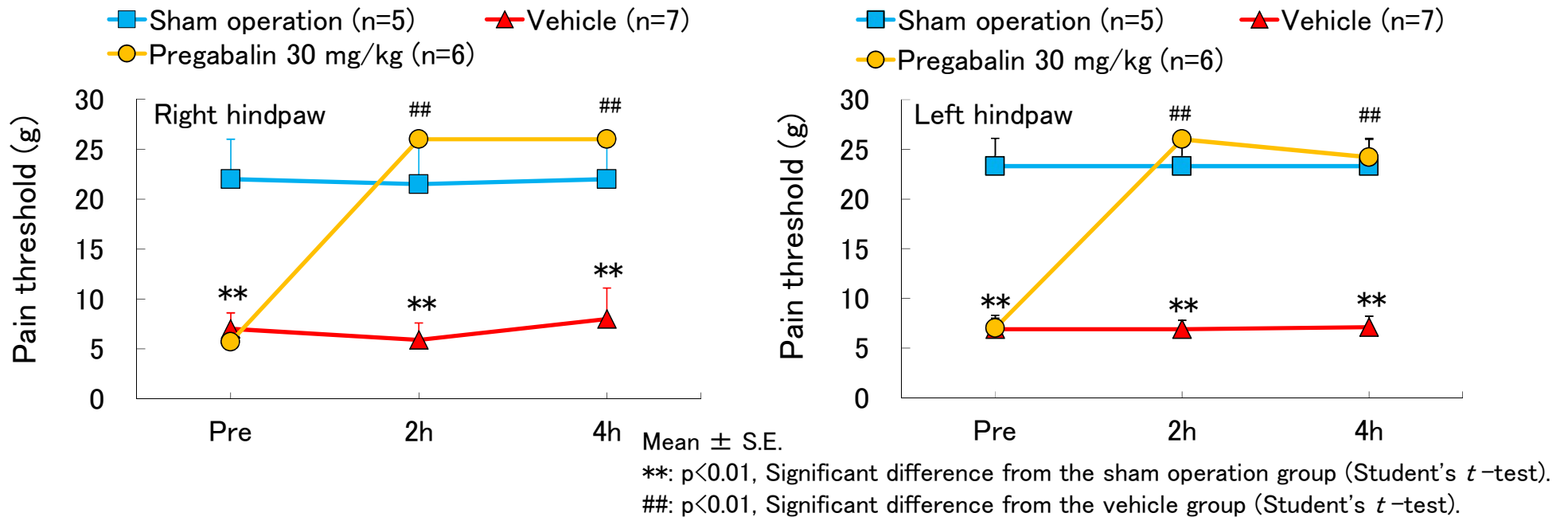
Experiment 3-1: Pharmacological study using CPSP model

【Experiment schedule】



Results

Experiment 3-1: Pharmacological study using CPSP model (CPSP)



Compared with the sham operation group, the vehicle group showed a lower pain threshold, and a significant difference was observed.

Compared with the vehicle group, the pregabalin group showed a higher pain threshold 2 hours and 4 hours after administration, and a significant difference was observed in both left and right hindpaws.

Materials and Methods

Experiment 3–2: Pharmacological study using CPSP model

【Animal】

Male rat, Crl:CD(SD), 8 weeks of age (at the model preparation)

【Group configuration】

Group	Dosing solutions	Dose level (mg/kg)	Dose volume (mL/kg)	Dosing route	N
Sham operation	saline	0	2	p.o.	7
Vehicle	saline	0	2	p.o.	8
Pregabalin	pregabalin	10	2	p.o.	8

i.c.: intracerebral administration

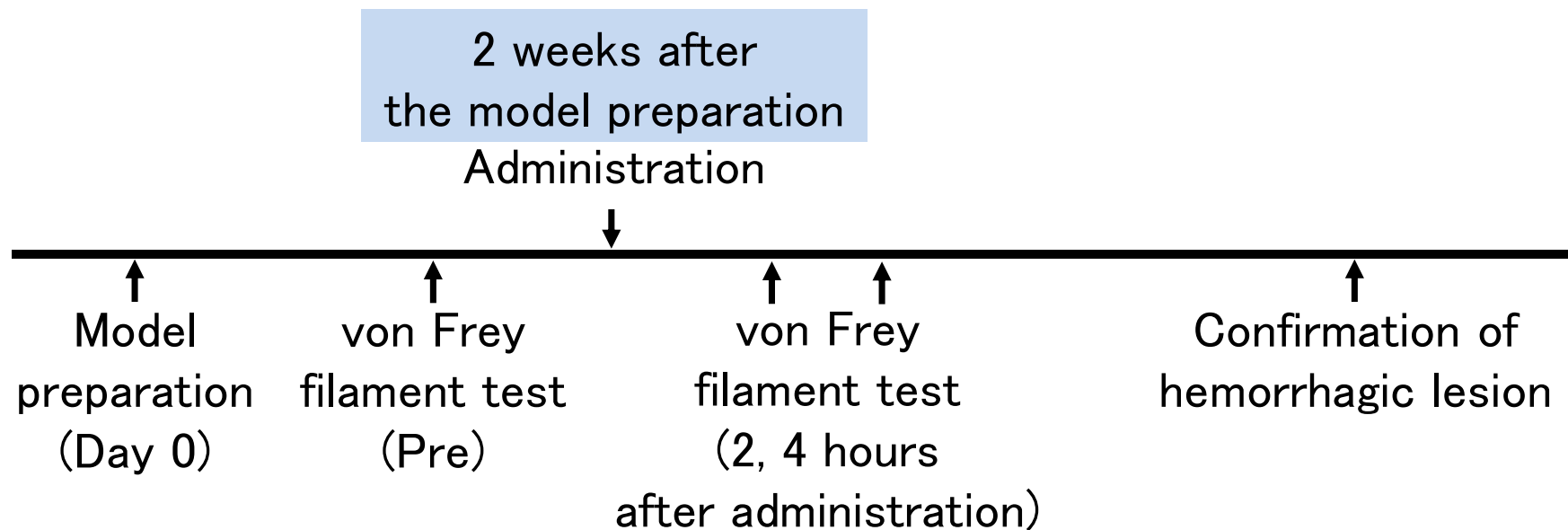
【Evaluation of the pain】

von Frey filament test

Materials and Methods

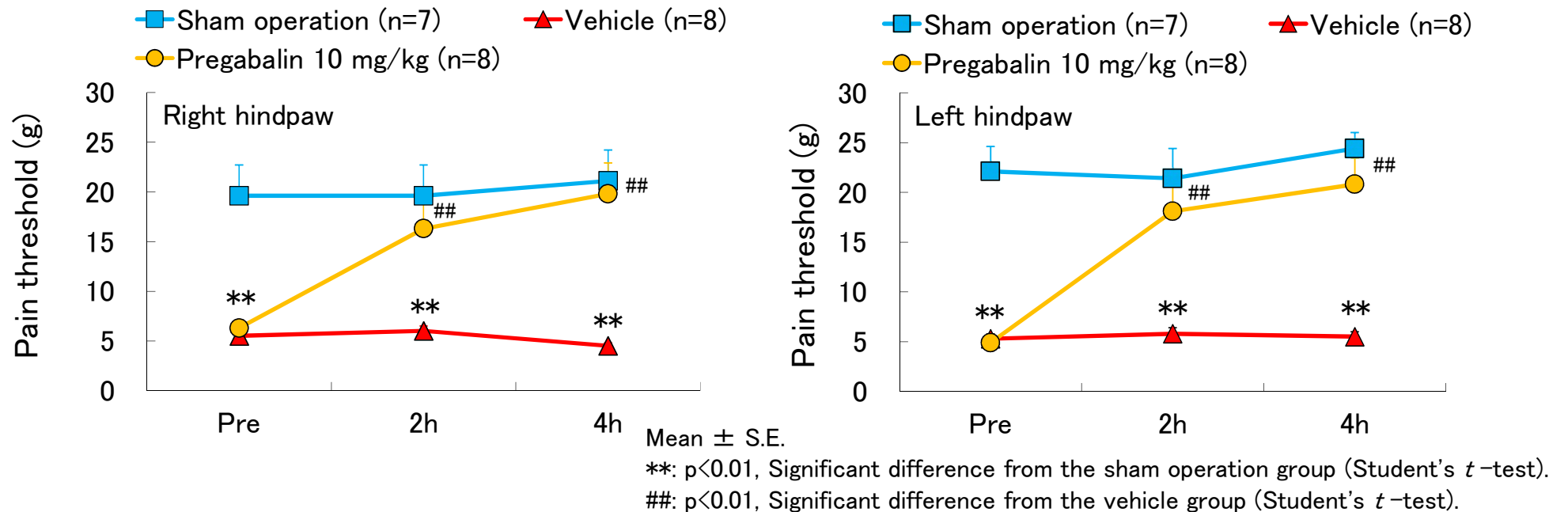
Experiment 3-2: Pharmacological study using CPSP model

【Experiment schedule】



Results

Experiment 3-2: Pharmacological study using CPSP model (CPSP)



Compared with the sham operation group, the vehicle group showed a lower pain threshold, and a significant difference was observed.

Compared with the vehicle group, the pregabalin group showed a significantly higher pain threshold administration in both the left and the right hindpaws at 2 and 4 hours after administration.

Discussion

- Male SD rats were used to prepare CPSP model rats by inducing cerebral hemorrhage via a microinjection of collagenase-IV into the lateral thalamic area.
- Hemorrhagic lesions were observed in the lateral thalamic region of the CPSP model rats prepared by this method.
- Pain was observed in the CPSP model rats compared with that in the sham operation rats. In addition, the analgesic efficacy of the pregabalin was confirmed in the CPSP model rats.
- The results indicate that the CPSP model was established in rats.
- Moreover, the CPSP model rats would be useful to evaluate potential efficacy of newly introduced analgesics.