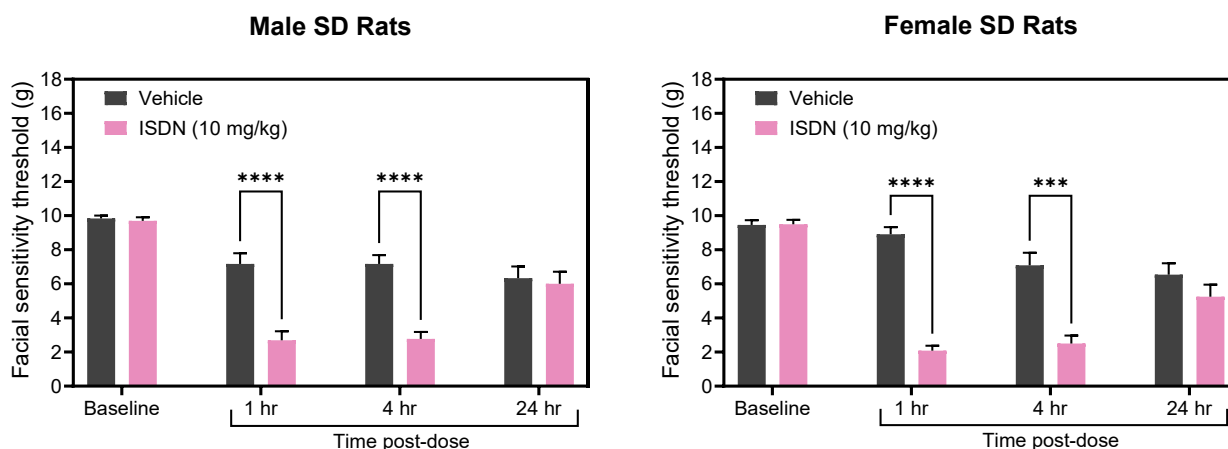


## Isosorbide Dinitrate (ISDN) Model of Headache

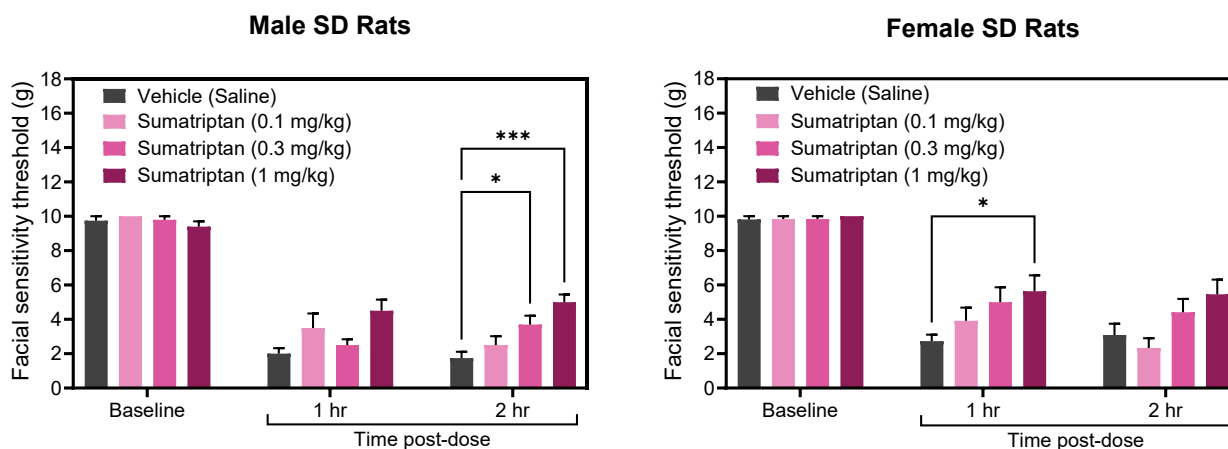
A rat model of headache has been described in which the NO donor isosorbide dinitrate (ISDN) is administered intraperitoneal (IP), and facial allodynia is measured by applying von Frey filaments to the periorbital region on the forehead. This model is commonly used to evaluate the efficacy of compounds for headaches and migraine.

### Behavioral Pain Phenotype: ISDN Administration Induces Facial Allodynia



**Figure 1:** Development of facial allodynia in male (left) and female (right) SD rats following a single administration of ISDN (10 mg/kg, IP) or vehicle (Saline). Facial allodynia is represented as decreased facial sensitivity threshold to von Frey filament stimulation in the periorbital area. Two-way ANOVA RM followed by a post-hoc Bonferroni's test. \*\*\*\*  $p < 0.0001$ , \*\*\*  $p < 0.001$ .

### Pharmacology: Sumatriptan Suppressed the Development of Facial Allodynia

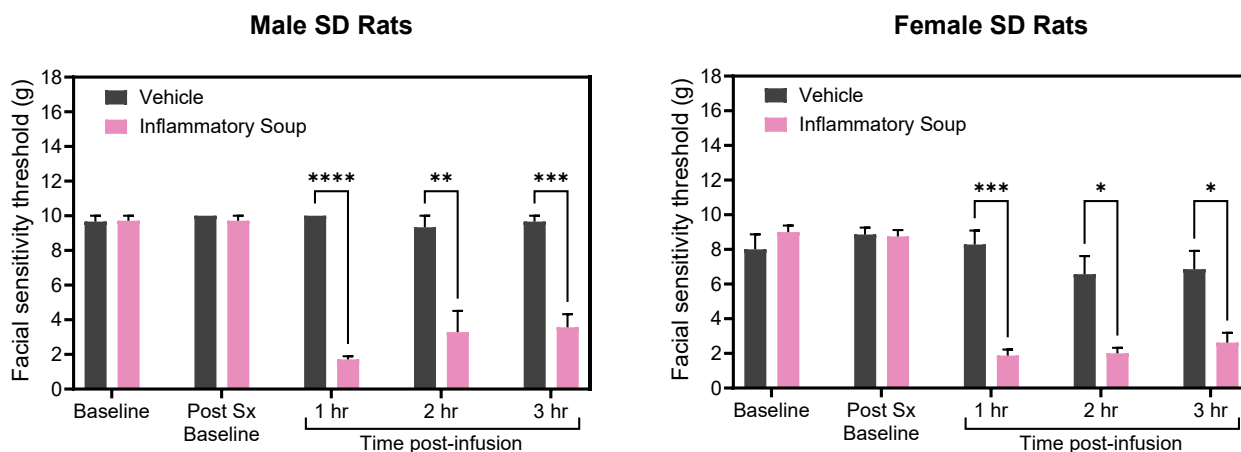


**Figure 2:** Effect of sumatriptan (0.1, 0.3, and 1 mg/kg, IP) on facial allodynia induced by a single ISDN (10 mg/kg, IP) administration in male (left) and female (right) SD rats at 1 and 2 hr post-dose of sumatriptan. Two-way ANOVA RM followed by a post-hoc Dunnett's test, \*\*\*  $p < 0.001$ , \*  $p < 0.05$ .

## Inflammatory Soup Model of Migraine

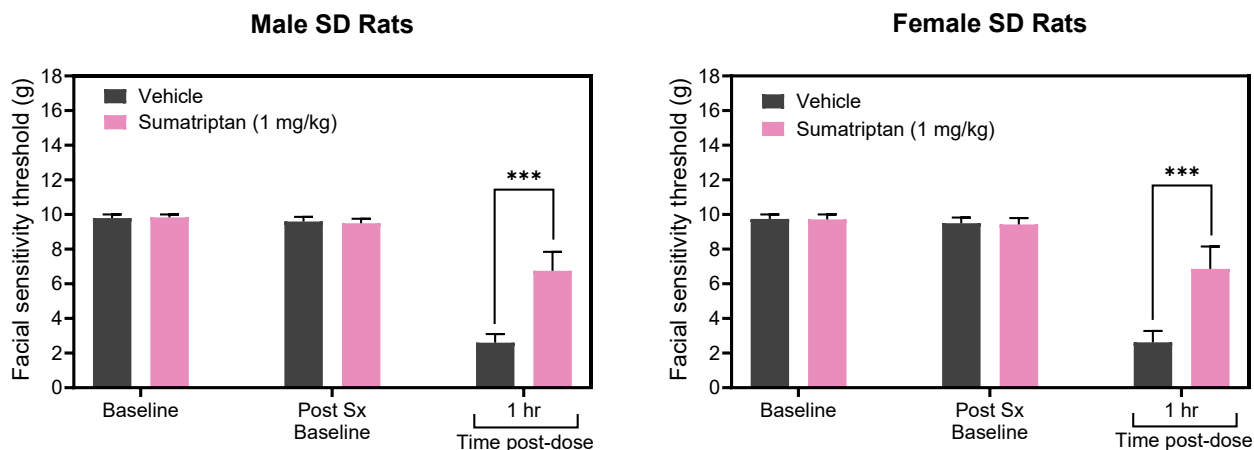
A rat model of migraine pain has been described in which inflammatory soup (IS) consisting of inflammatory mediators is infused onto the dura, and facial allodynia is measured by applying von Frey filaments to the periorbital region. This model can be used to evaluate the efficacy of compounds targeting the trigeminal nociceptive pathway associated with migraine headache.

### Behavioral Pain Phenotype: Time course



**Figure 3:** Development of facial allodynia in male (left) and female (right) SD rats following a single infusion of inflammatory soup (2 mM bradykinin, histamine, serotonin; 0.2 mM PGE<sub>2</sub>; pH=5.0, 10  $\mu$ L) or vehicle (aCSF). Facial allodynia is represented as decreased facial sensitivity threshold to von Frey filament stimulation in the periorbital area. Two-way ANOVA RM followed by a post-hoc Bonferroni's test. \*\*\*\*  $p < 0.0001$ , \*\*\*  $p < 0.001$ , \*\*  $p < 0.01$ , \*  $p < 0.05$ .

### Pharmacology: Sumatriptan Suppressed the Development of Facial Allodynia



**Figure 4:** Effect of sumatriptan (1 mg/kg, IP) on facial allodynia induced by a single infusion of inflammatory soup (10  $\mu$ L) in male (left) and female (right) SD rats at 1 hr post-dose of sumatriptan. Two-way ANOVA RM followed by a post-hoc Bonferroni's test, \*\*\*  $p < 0.001$ .