ApoA-I binding protein (AIBP) decreases mechanical hypersensitivity after plantar incision in a rat model of post-operative pain

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Background

- Acute post-operative pain is common in surgical patients, with many reporting inadequate pain relief[1]. This can lead to cardiopulmonary complications, delayed mobilization, longer hospitalization, sleep disturbances, and psychological stress[2].
- Pro-inflammatory cascades triggered by toll-like receptor 4 (TLR4) activation contribute to chronic pain. TLR4 localizes to lipid rafts and dimerizes, initiating inflammatory signaling[3].
- Apolipoprotein A-I binding protein (AIBP), a secreted protein that has been shown to bind ApoA-I and high-density lipoprotein, can reduce lipid rafts by removing excess cholesterol from the plasma membrane[4]. Modified AIBP that binds to TLR4 has been shown to reduce hypersensitivity in preclinical models of inflammatory and neuropathic pain[5].

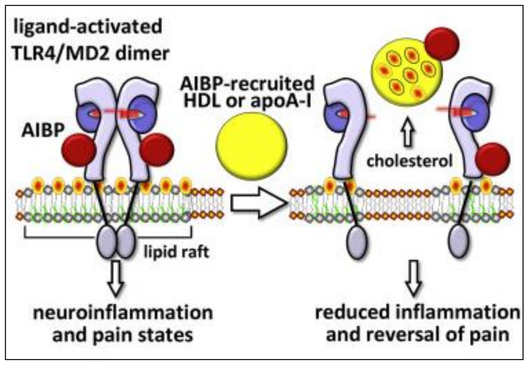

Figure 1. AIBP binds to TLR4, selectively regulating cholesterol removal and reducing pain[5].

Objective

To investigate the effects of AIBP on a rat model of post-operative incision pain and wound healing.

Methods

- Adult male and female Wistar rats from Harlan were used. The rats in the AIBP treatment group were injected intravenously with 0.3 mg AIBP.
- All rats received a 15 mm incision through the skin and fascia of the plantar hind paw. The plantaris muscle was stressed, then the wound was closed with two sutures.
- Von Frey filaments (0.4, 0.6, 1, 2, 4, 8, 10, and 15 g) were used to determine mechanical paw withdrawal threshold via the up-down method. Rats were tested before surgery and at 2 hr, 4 hr, 24 hr, 48 hr, 72 hr, 7 days, and 10 days after surgery.
- Images were taken at 3, 6, 9, and 10 days after surgery to determine wound size and healing.

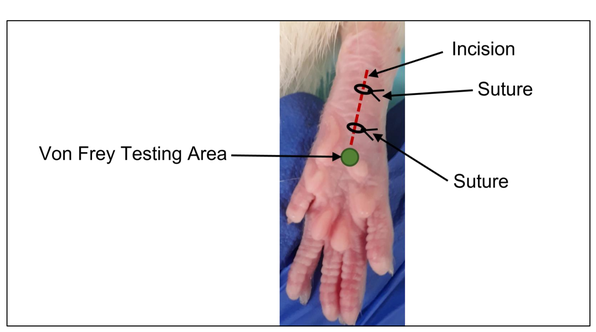

Figure 2. The plantar incision surgery site and post-operative pain testing area.

Results

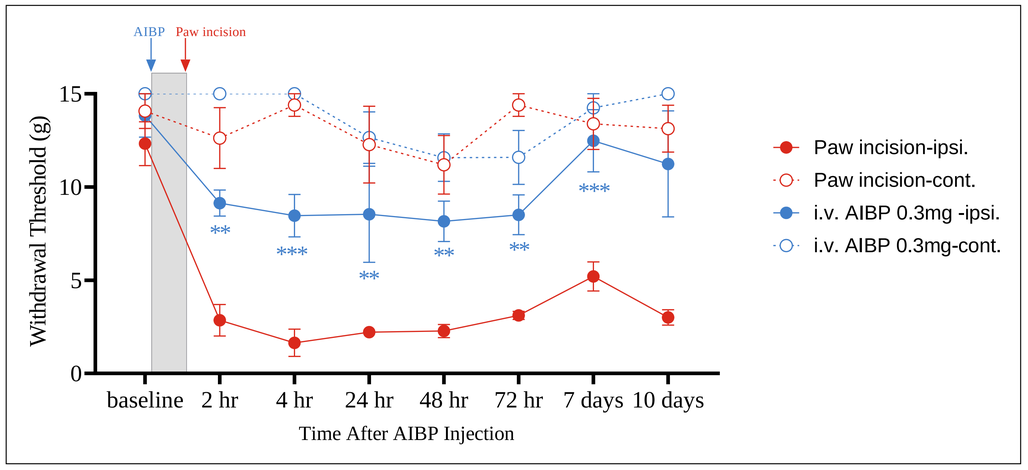

Figure 3. The withdrawal threshold of the male rats, with measurements for the ipsilateral and contralateral paws. i.v. AIBP pre-treatment significantly attenuates paw incision-induced mechanical hypersensitivity in the ipsilateral hind paw compared to untreated controls.

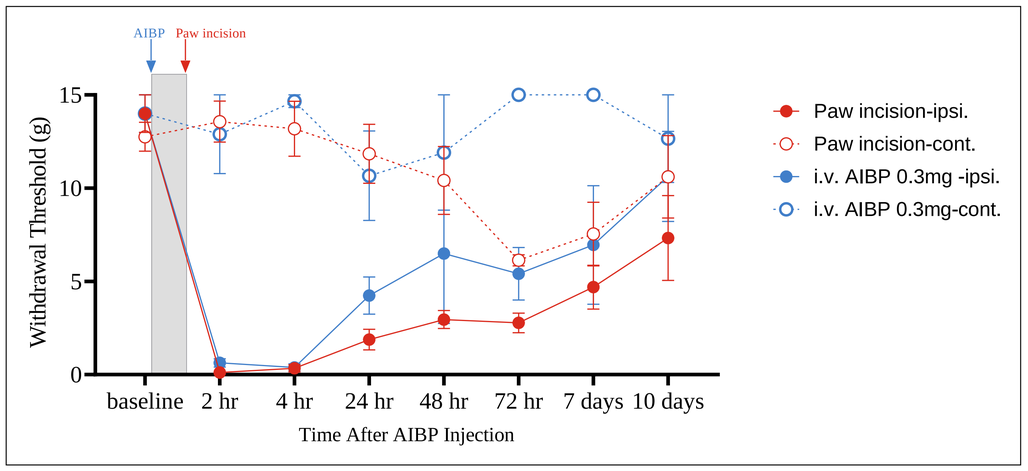

Figure 4. The withdrawal threshold of the female rats, with measurements for the ipsilateral and contralateral paws. There was no significant difference in mechanical hypersensitivity of the ipsilateral hind paw between treated and control groups.

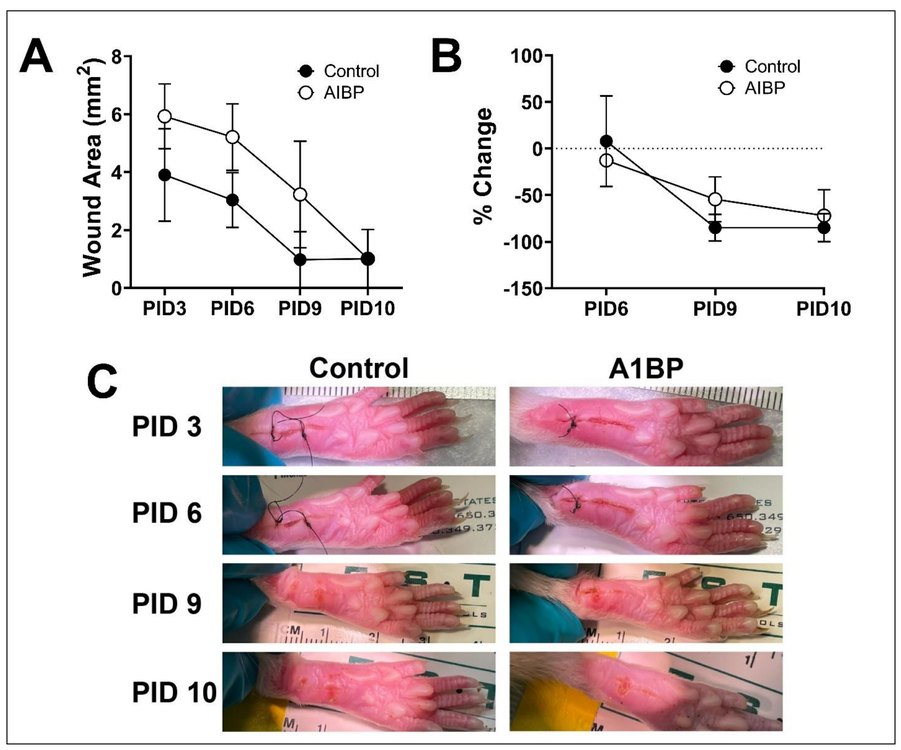

Figure 5. Wound healing in the female rats. A) The wound size did not differ between control and AIBP-treated rats. B) The rate of healing between the two groups did not differ. C) The incision sites of one control and one AIBP-treated rat on different post-incision days (PID).

Conclusion

- AIBP decreased mechanical hypersensitivity in males but not females.
- AIBP had no significant impact on wound healing in females.
- Targeting TLR4 lipid rafts with AIBP could be an effective method to reduce post-operative incision pain without compromising wound healing.
- Ongoing studies are investigating wound healing in males and the mechanisms that caused the mechanical hypersensitivity difference between males and females.
- Additional subjects are still needed in order to have sufficient statistical power.

References

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