

Although opioids effectively treat moderate to severe pain, they carry high risks of addiction and dangerous side effects, including respiratory depression, constipation, sedation, nausea, and dizziness. Even when prescribed for acute pain, up to 10% of patients become persistent users, and unused tablets frequently fuel community misuse. Consequently, there is an urgent need for novel therapeutics that provide robust analgesia without these liabilities. Abalone Bio has developed an antibody agonist targeting the μ -opioid receptor (MOR). In a mouse model of inflammatory pain, peripherally administered antibody significantly reduced pain without inducing the tolerance or physical dependence observed with morphine. Furthermore, the antibody did not alter locomotor activity or cause respiratory depression, indicating peripheral restriction. The continued development of MOR agonist antibodies with extended half-lives has the potential for infrequent outpatient administration, minimizing both abuse potential and adverse side effects.

There is an urgent need for safe and non-addictive treatment of pain

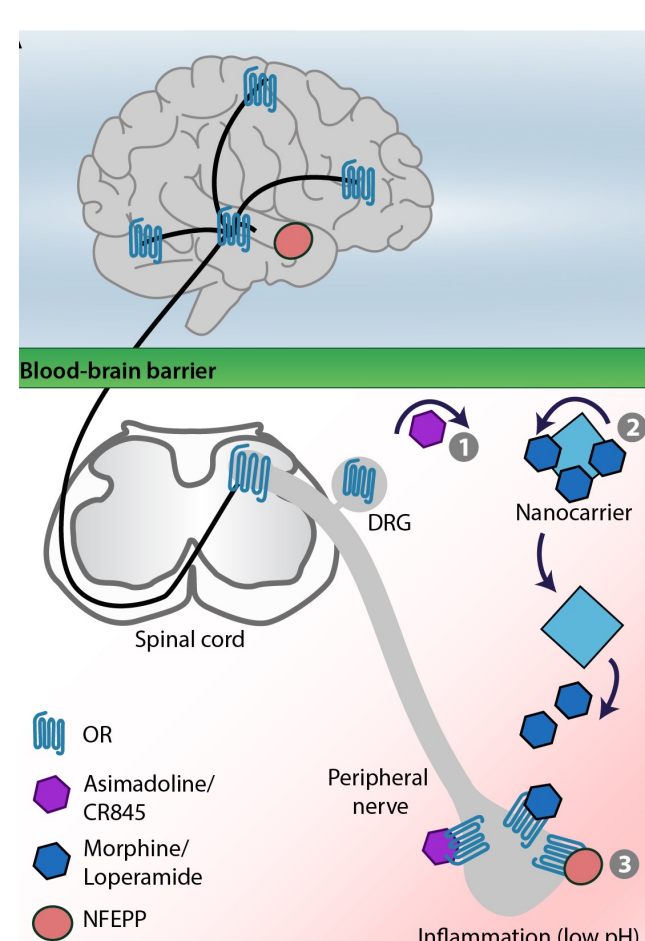
Opioids: proven effective, but plagued by many well-known side-effects

- Addiction
- Tolerance
- Respiratory depression
- Nausea and constipation

Previous drugs point the way: CNS exclusion/peripheral restriction

- Peripherally-biased oxycodone analog: efficacy with fewer side effects
- Abandoned due to lack of data on misuse and liver toxicity.

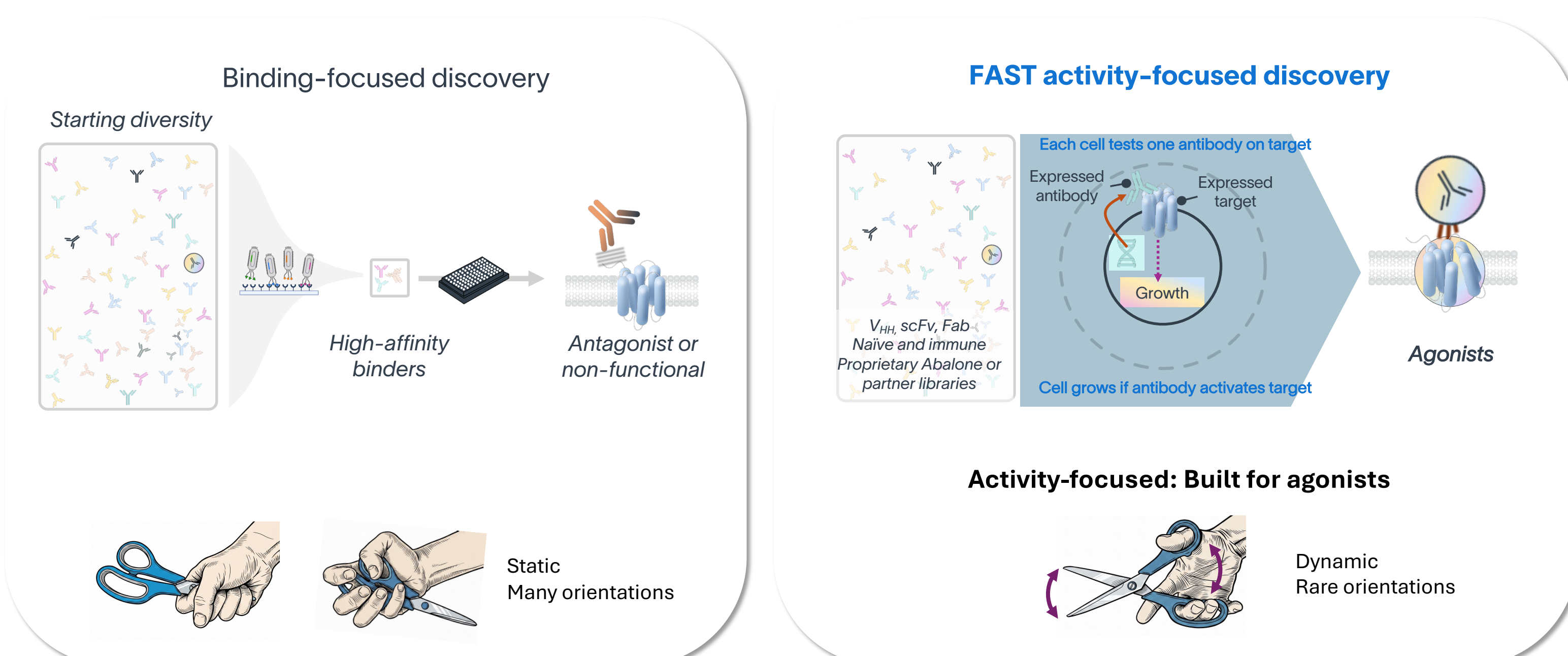
MOR agonists with less CNS penetration show efficacy



Machelska, H and Celik, MO. Advances in achieving opioid analgesia without side effects. Front Pharmacol. 2018 Nov 29;9:1388. doi: 10.3389/fphar.2018.01388.

MOR agonist antibody discovered using Functional Antibody Selection Technology (FAST) at Abalone Bio

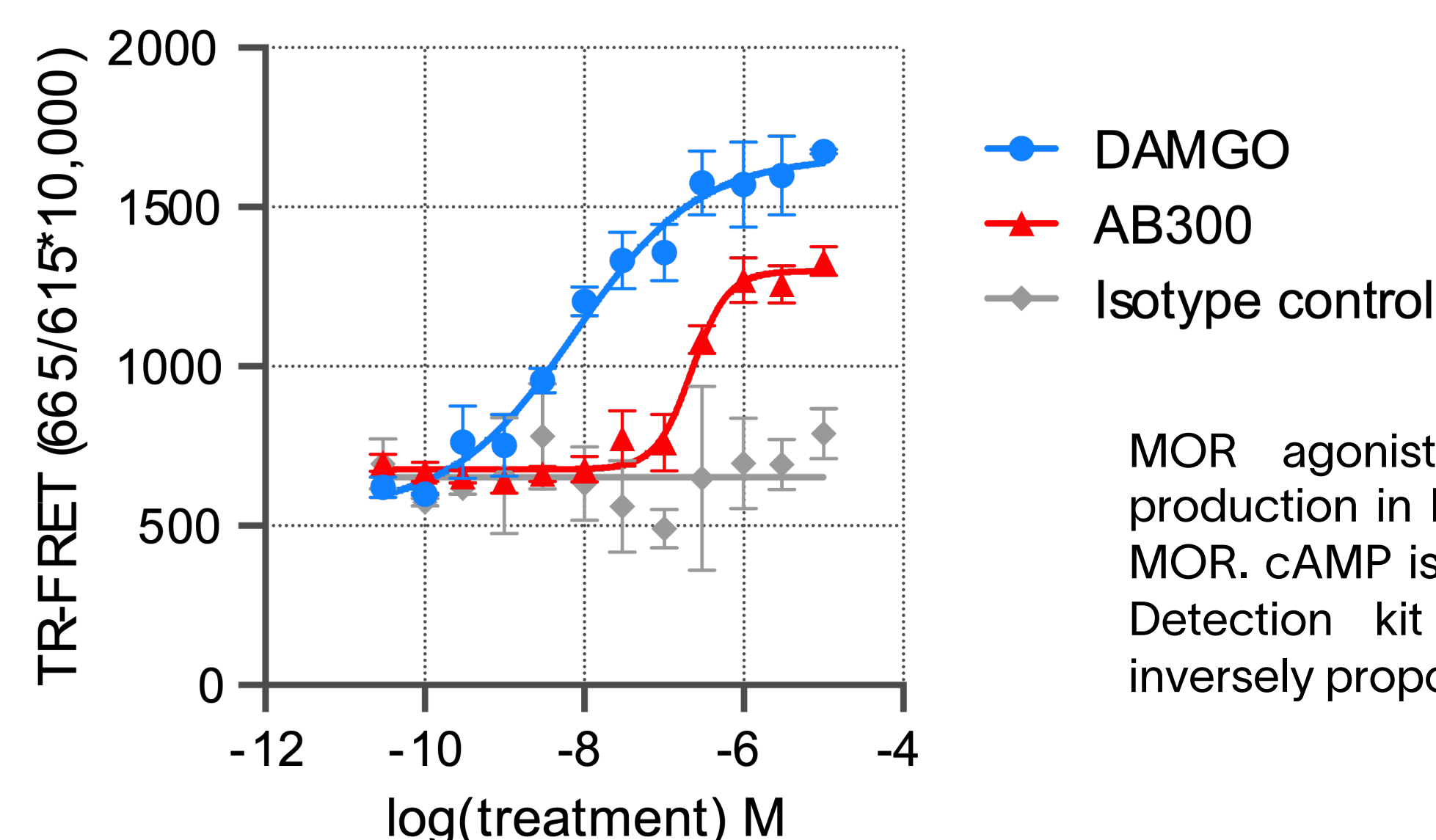
Focuses on activity to discover agonists



Antibodies have advantages over competing small molecule drugs

- Naturally restricted by the blood-brain barrier from the CNS, where key side effects originate
- Low cross-reactivity with other opioid receptor subtypes due to specificity
- Long-lasting; infrequent dosing
- Partial agonism can reduce desensitization and prolong efficacy

All minimize harmful side effects that plague conventional opioids



MOR agonist inhibits NKH477 induced cAMP production in HEK293 cells over expressing human MOR. cAMP is measured using the HTRF cAMP Gi Detection kit (Revvity). cAMP concentration is inversely proportional to TR-FRET signal.

Conclusions

AB300 is a promising candidate for treatment of pain

- AB300 is a peripherally restricted μ -opioid receptor agonist
- AB300 attenuates pain without inducing tolerance or physical dependence enabling repeated dosing
- AB300 has no effect on locomotion, ambulatory activity, or respiration confirming peripheral restriction

Next Steps

Optimize potency and developability properties of AB300 to improve efficacy, duration of action, and stability

Acknowledgements

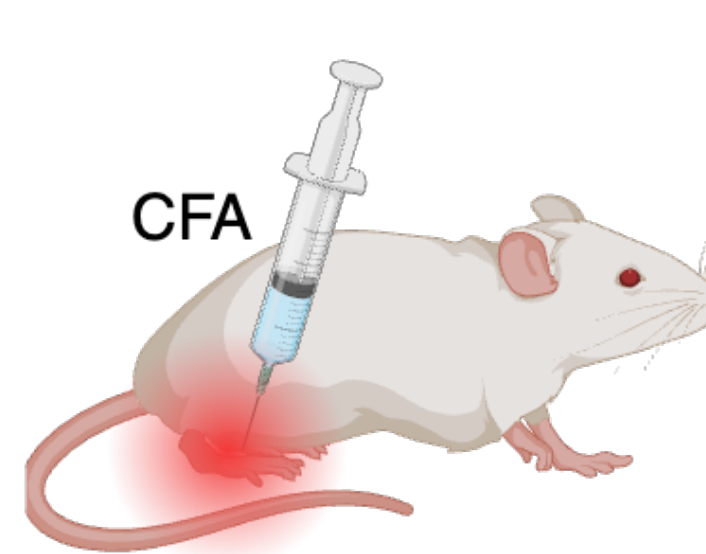
Supported by NIH SBIR R43DA060776. IS is supported by NIDA Institutional training grant (T32DA024628)



Contact us:
info@abalonebio.com

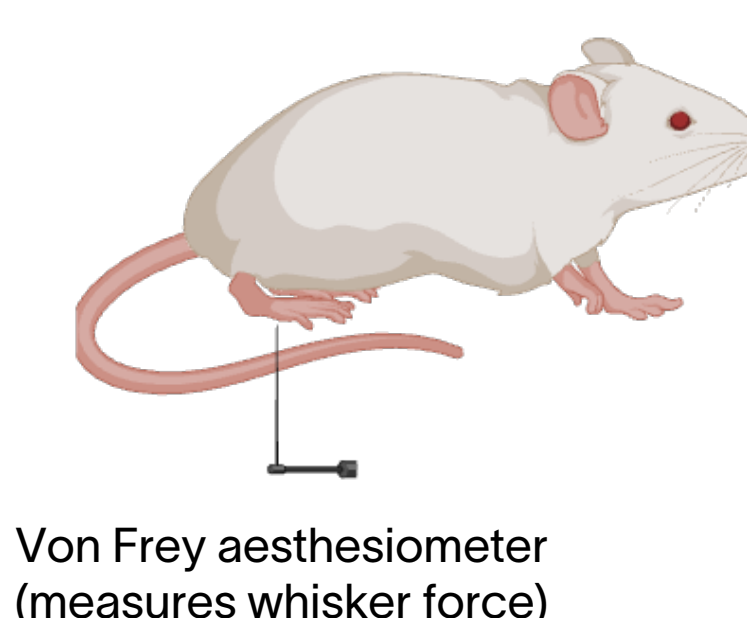
MOR antibody agonist is effective in a mouse inflammatory pain model

Inflammatory pain induction

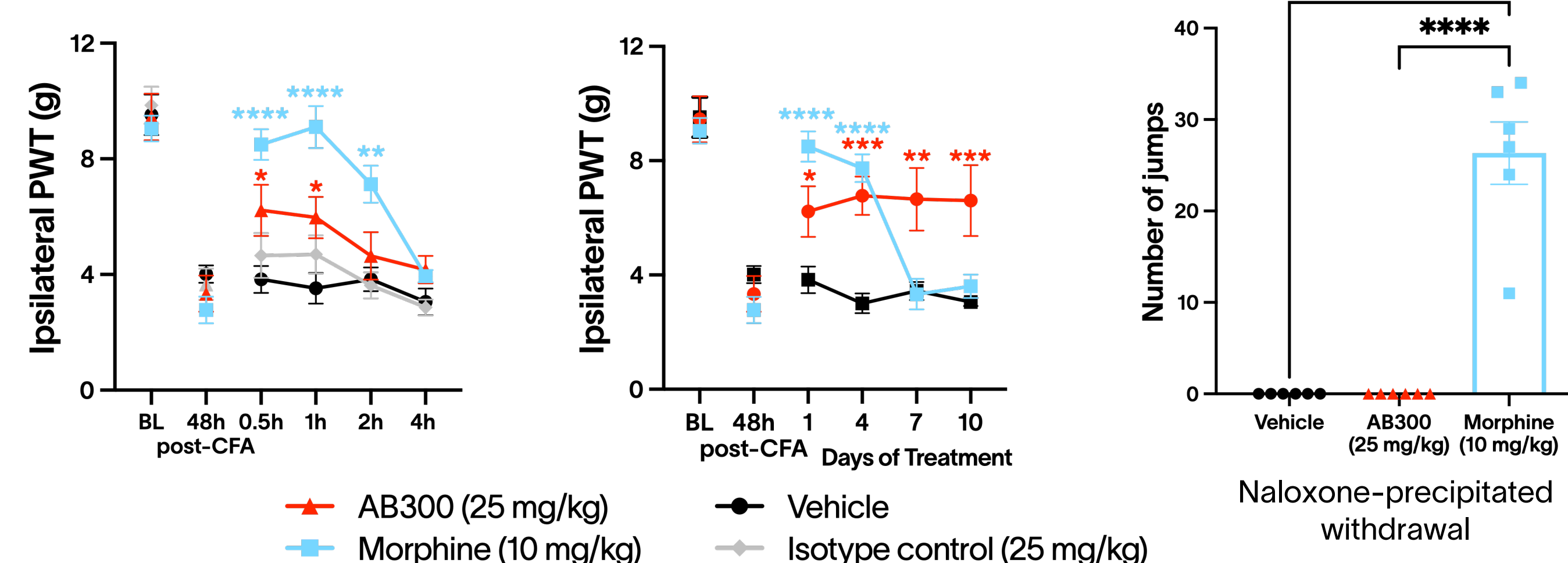


Systemic agonist treatment

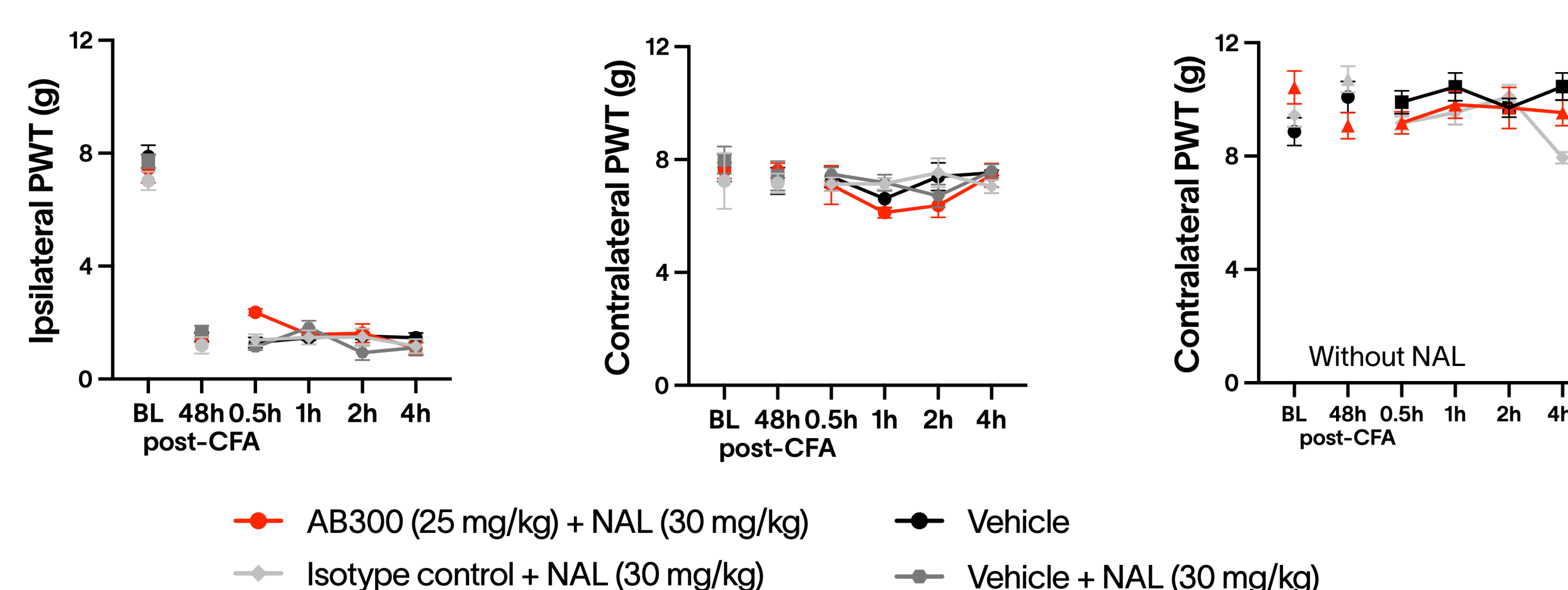
Paw withdrawal tolerance (PWT) measurement after treatment



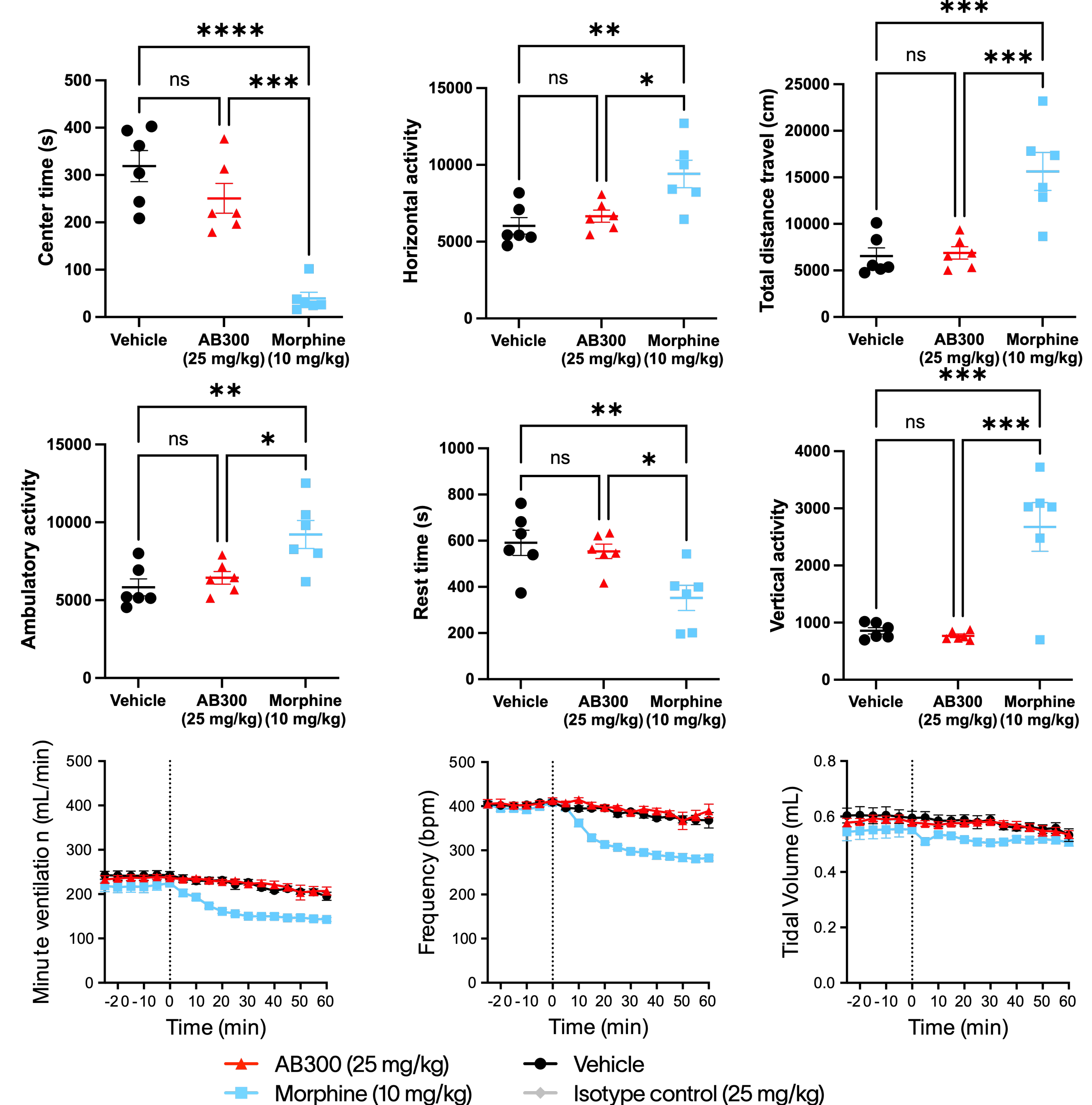
AB300 attenuates pain without producing tolerance or physical dependence



The peripherally-restricted MOR antagonist naloxone methiodide (NAL) blocked the anti-nociceptive effects of AB300



AB300 has no effect on locomotion, ambulatory activity, or respiration



Treatments were delivered i.p. to naïve mice.

Locomotor testing: Open field locomotor activity was measured for 30 minutes following i.p. injections
Respiratory Testing: Whole body plethysmography was used to measure respiratory parameters including the minute ventilation, respiratory frequency and tidal volume. Mice were habituated for 30 mins to the chamber in room air prior to the experiment. Pre-injection baseline in the chamber was measured for 50 mins. Respiratory function was measured 60 min post-injection