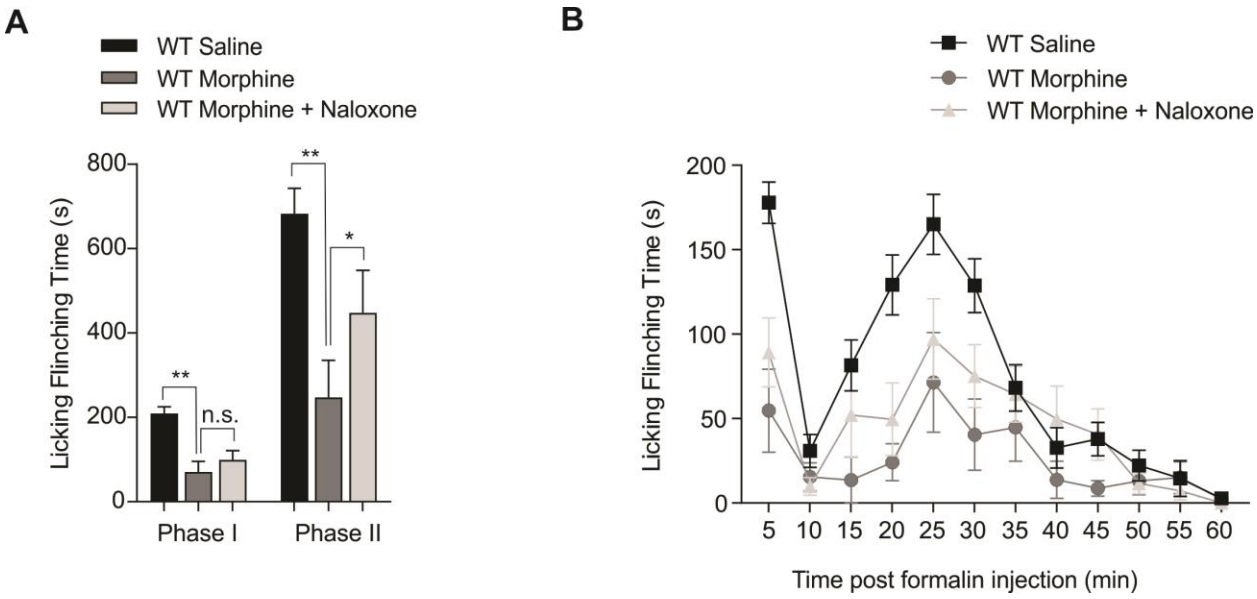
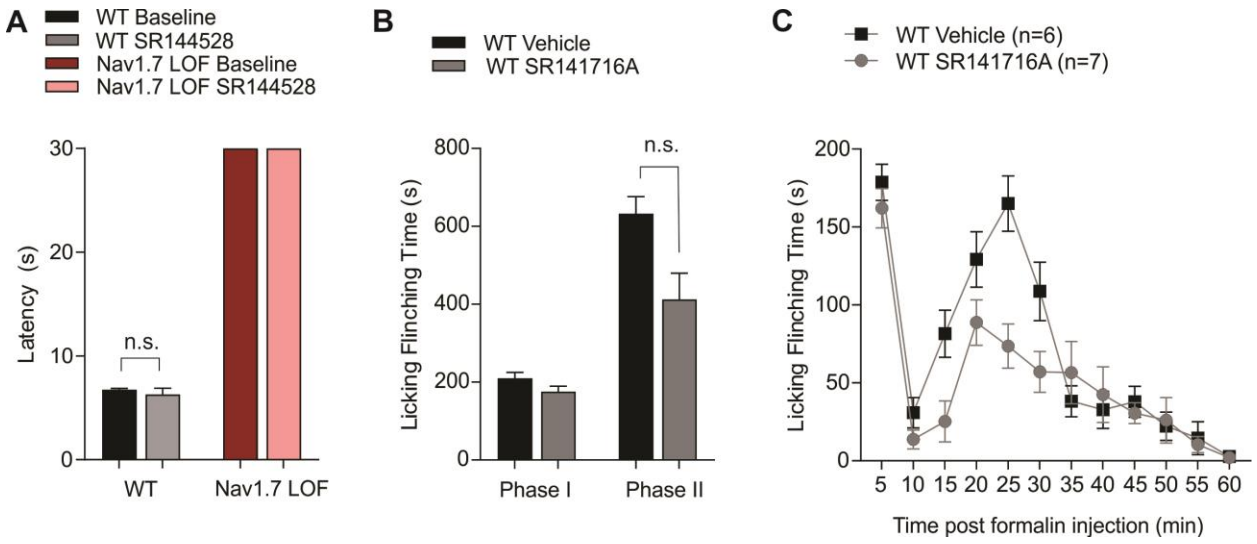


Supplementary Fig 1. Effects of morphine on acute pain sensitivity in WT rats

(A-B) Formalin test. Morphine treatment (10 mg/kg, i.p.) in WT rats significantly decreases licking and flinching durations in both Phase I (Saline, 208.7 ± 16.1 s, n=6; Morphine, 70.1 ± 20.7 s, n=7) and Phase II (Saline, 682.3 ± 60.7 s, n=6; Morphine, 247.0 ± 88.1 s, n=7) of the formalin test. Naloxone (2 mg/kg) reverses analgesia caused by morphine in Phase II (Morphine, 247.0 ± 88.1 s, n=7; Morphine + Naloxone, 447.6 ± 100.7 s, n=7; * p <0.05) of the formalin test. * p <0.05, ** p < 0.01, Mann-Whitney U test.



Supplementary Fig 2. Effects of CB2 blocker SR144528 on acute pain sensitivity in Nav1.7 loss-of-function rats and effects of CB1 blocker SR141716A on acute pain sensitivity in WT rats

(A) Hot plate test, 52 °C. Paw withdrawal latency in wild-type rats is not affected by SR144528 (10 mg/kg, i.p.) (WT Baseline, 6.7 ± 0.1 s; WT SR144528, 6.3 ± 1.6 s; n=8). SR144528 does not induce paw withdrawal response in Nav1.7 LOF rats. **(B-C)** Formalin test. SR141716A treatment in WT rats does not affect licking and flinching durations in either Phase I (Vehicle, 209.5 ± 15.5 s, n=6; SR141716A, 175.7 ± 13.9 s, n=7) or Phase II (Vehicle, 632.3 ± 44.2 s, n=6; SR141716A, 412.6 ± 67.1 s, n=7) of the formalin test.