



Supplementary Figure S4- Effects of misplaced (out sites) injections of the drugs in mechanical and thermal sensitivity evaluated by the von Frey (panels A, C, E, G, I) and hot plate (panels B, D, F, H, J) tests, respectively. The drugs were microinjected 7 days after minipumps implantation, and their effects were assessed before and after the injection. The interactions between groups and time or treatments and time are presented at the bottom of the x-axis. Lidocaine increased withdrawal thresholds but did not fully reverse mechanical hypersensitivity (panel A). No significant effects were found for lidocaine in the hot plate test ($F_{1,4} = 0.7, p = 0.443$, panel B), or DAMGO (von Frey: $F_{1,6} = 0.6, p = 0.461$, panel C; hot plate: $F_{1,6} = 0.4, p = 0.529$, panel D) or H-89 (von Frey: $F_{1,5} = 0.0, p = 0.984$, panel I; hot plate: $F_{1,5} = 0.4, p = 0.535$, panel J). Ultra-low dose naloxone attenuated mechanical (panel E) and thermal (panel F) hypersensitivity. Pretreatment with naloxone restored DAMGO analgesic effects compared to DAMGO alone (panel G, H). Data are presented as mean \pm SD (Lidocaine : saline-infused animals $n = 3$, morphine- infused animals $n = 3$; DAMGO: saline-infused animals $n = 4$, morphine-infused animals $n = 4$; Naloxone: saline- infused animals $n = 3$, morphine- infused animals $n = 4$; Naloxone + DAMGO: $n = 4$; H-89: saline $n = 3$, H-89 $n = 4$). * $p < 0.05$, ** $p < 0.01$.