Scientists develop a new non-opioid pain killer with fewer side effects
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BnOCPA is a potent analgesic without causing sedation or motor impairment. a BnOCPA did not induce sedation or affect motor function when injected intraperitoneally (IP; 10 µg kg\(^{-1}\)) or intravenously (IV; 10 or 25 µg kg\(^{-1}\)). In contrast, morphine caused sedation and motor impairment (15 mg kg\(^{-1}\) subcutaneously, SC). Saline (Veh, SC) did not affect rotarod performance. Data points (mean ± SEM; n = 6 for each compound) are normalized to pre-dose performance and are offset for clarity. b, c BnOCPA alleviates mechanical allodynia in neuropathic pain when administered b via an intrathecal (IT) or c IV route. Pre-surgery (pre-surg) animals had similar sensitivity to tactile stimulation as assessed by von Frey hair stimulation. Spinal nerve ligation caused hypersensitivity to touch (mechanical allodynia) at 1 week after surgery as evidenced by the reduction in the tactile pressure necessary to elicit paw withdrawal (paw withdrawal threshold; PWT). PWT reaches a similar nadir across all groups prior to the vehicle or BnOCPA infusion (pre-dose). Administration of BnOCPA significantly increased PWT in the limb ipsilateral to the site of injury in a dose-dependent manner (one-way ANOVA (pre-dose, 1, 2 and 4 hrs) for IT BnOCPA F(3,88) = 21.9, P = 1.10 \times 10^{-10}; for IV BnOCPA F(3,92) =18.1, P = 2.70 \times 10^{-16}). Fisher LSD post hoc comparisons showed significant differences at: IT 1 nmol at 1 and 2 hrs, P = 0.001 and 4.16 \times 10^{-9}, respectively, and 3 nmol at 1, 2 and 4 hrs, P = 9.52 \times 10^{-11}, 1.42 \times 10^{-11} and 1.41 \times 10^{-8}, respectively; IV 3 µg kg\(^{-1}\) at 1, 2 and 4 hrs, P = 0.044, 0.008 and 0.019, respectively, and 10 µg kg\(^{-1}\) at 1, 2 and 4 hrs, P = 1.37 \times 10^{-8}, 6.81 \times 10^{-14} and 3.23 \times 10^{-4}, respectively. b, c n = 6 per treatment, except for 1 nmol BnOCPA, n = 5. d The analgesic effects of BnOCPA (6 µg kg\(^{-1}\) IV) were prevented by the A1R antagonist DPCPX (1 mg kg\(^{-1}\) IP), but not the A3R-selective antagonist MRS1523 (2 mg kg\(^{-1}\) IP). Post hoc LSD comparisons across all four groups and four-time points (pre-dose, 1, 2 and 4 hrs; F(15,116) = 26.8, P = 0) revealed that BnOCPA at 6 µg kg\(^{-1}\) (IV) elicited significant analgesia compared to vehicle-treated animals at 1, 2, and 4 h post-dosing (P = 4.69 \times 10^{-79}, 3.50 \times 10^{-16}, 4.69 \times 10^{-78}, respectively), which persisted in the presence of the selective A3R antagonist MRS1523 over the same time period (P = 4.42 \times 10^{-73}, 3.38 \times 10^{-74}, 1.81 \times 10^{-70}, respectively). In contrast, the PWT in DPCPX-treated animals did not differ from those in the vehicle group (P = 0.872, 0.748, 0.453 at 1, 2, and 4 h, respectively). n = 11 for BnOCPA and vehicle groups; n = 6 for the DPCPX group and n = 5 for the MRS1523 group. Averaged data are presented as mean ± SEM. ns, not significant; *, P