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# Spinal cord oxytocin circuits modulate pain responses by engaging circuits of affective touch.

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## Abstract

Top-down modulation of spinal sensory processing is constantly at play in our everyday life but it varies depending on our internal state (fear, stress, positive emotions) and neuromodulators play a key role in this descending modulation. Positive tactile interactions (caress, hug, massage, hand-holding...) induce the release of a key neuromodulator, oxytocin, by neurons of the hypothalamus in the central nervous system, including the spinal cord. We investigated whether underexplored spinal oxytocin circuits might influence how the spinal cord processes touch and pain peripheral input before the information is sent to the brain. We found that oxytocin-positive fibers project mainly to the superficial dorsal horn of the spinal cord, which overlaps with expression of the oxytocin receptor in spinal neurons that process pain input and social touch. We correlated this finding with similar expression patterns in the human spinal cord. Using anatomy, pharmacology and opto-genetics, behavior and electrophysiology, we discovered that this superficial spinal oxytocin circuit can drastically reduce sensory-evoked and ongoing neuropathic pain in mice. In conclusion, descending oxytocin projections tune the sensitivity of superficial spinal oxytocin circuits to modulate the first step of touch and pain processing. Our findings will provide a framework for the use of oxytocin for pain treatment and should inform us on how combined oxytocin administration and touch therapy can provide pain relief.

**Keywords:** affective touch, oxytocin, pain, spinal cord, descending modulation, neuromodulators

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