Mouse group	Enk-ir innervations		mOR-ir + GFP-positive innervations	
	Day 1 (n=4)	Day 9 (n=4)	Day 1 (n=4)	Day 9 (n=4)
Sham	5.9±2.9	9.0±7.4	9.4±3.1	11.2±5.8
hsvCON	7.3±2.9	8.6±2.0	*6.5±5.1*[#]	*6.4±5.1*[#]
hsvMOR	6.5±3.9	10.5±8.1	12 ±9.2	18±6.4[*]
hsvPPE	12.3±9.1[#]	24.8±11.4[**,##]	14.6±3.0	13.2±8.4
hsvMOR+PPE	8.2±5.3	20.5±6.4[**,##]	10.4±9.1	16.6±9.0[*]

Supplemental Digital Content 4. Virus-mediated changes in enkephalin immunoreactivity (Enk-ir) and co-labeled mu opioid receptor immunoreactivity (mOR-ir) and GFP-positive epidermal nerve fibers in plantar hind paw skin (mean ± SD).

Days indicate time after infection with control virus (hsvCON), herpes simplex virus vectors that encode the mu opioid receptor (hsvMOR), preproenkephalin (hsvPPE), or both (hsvMOR+PPE) on day 7 post-L5 spinal nerve ligation or infection with hsvCON on day 7 post-sham surgery (Sham). Statistically significant (P<0.05) decreases in expression are indicated in italics.

vs. sham; # significant at P<0.05; ## significant at P<0.01; ### significant at P<0.001

* vs. control virus-treated (hsvCON);* significant at P<0.05; ** significant at P<0.01; *** significant at P<0.001

	Sham (n=4)	hsvCON (n=4)	hsvMOR (n=4)	hsvPPE (n=4)	hsvMOR+PPE (n=4)
% of cells Enk-ir					
Day 1					
Large	9.9 ± 3.4	8.1 ± 2.1	10.8 ± 3.9$^{*,\#}$	2.4 ± 3.5*	11.07 ± 2.2
Medium	7.6 ± 2.2	7.9 ± 1.2	12.3 ± 3.1	14.9 ± 2.0$^{***, \#\#\#}$	12.5 ± 2.2$^{*, \#}$
Small	9.8 ± 2.5	9.0 ± 1.8	12.4 ± 2.2	14.7 ± $^{\#, **}$	11.0 ± 1.2
Total	8.4 ± 2.2	8.4 ± 1.4	12.5 ± 0.8	14.8 ± 1.4$^{\#, *}$	11.3 ± 1.0
Day 9					
Large	12.0 ± 2.0	9.5 ±4.8	17.6 ± 2.0$^{***, \#}$	22.2 ± 2.8***	21.9 ± 2.5$^{***, \#\#\#}$
Medium	14.0 ±2.2	12.4 ± 2.3	19.1 ± 2.0**	28.8 ± 4.2$^{***, \#\#\#}$	34.8 ± 3.4$^{***, \#\#\#}$
Small	14.2 ± 2.5	16.2 ± 3.3	21.2 ± 1.6$^{\#\#}$	28.4 ± 4.1$^{***, \#\#\#}$	34.5 ± 3.9$^{***, \#\#\#}$
Total	14.3 ± 0.9	14.8 ± 1.9	19.9 ± 0.4	28.6 ± 6.9$^{**, \#\#}$	31.4 ± 0.7$^{***, \#\#\#}$
% of cells mOR-ir + GFP					
Day 1					
Large	13.7 ± 3.2	9.4 ± 2.4	20.9 ± 2.1*	43.8 ± 6.8$^{***,\#\#\#}$	34.1 ± 6.4$^{***,\#\#\#}$
Medium	15.3 ± 3.4	18.4 ± 2.6	42.7 ± 3.2$^{***,\#\#\#}$	55.2 ± 5.2$^{***,\#\#\#}$	46.0 ± 6.2$^{***,\#\#\#}$
Small	31.3 ± 3.7	22.8 ± 2.2	55.7 ± 2.3$^{***,\#\#\#}$	24.3 ± 3.2	33.1 ± 9.8*
Total	24.1 ± 1.8	19.2 ± 2.5	51.7 ± 11.3$^{***,\#\#}$	35.4 ± 6.2	36.7 ±13.5*

Day 9					
Large	8.9 ± 2.1	7.4 ± 1.3	15.5 ± 2.3$^{***,\#\#\#}$	31.8 ± 2.9$^{***,\#\#\#}$	29.7 ± 5.8$^{***,\#\#\#}$
Medium	19.5 ± 2.8	18.6 ± 2.2	32.1 ± 1.9$^{***,\#\#\#}$	27.0 ± 2.1$^{***,\#\#\#}$	30.0 ± 4.7$^{***,\#\#\#}$
Small	25.3 ± 2.2	*19.4 ± 2.8*$^{\#\#}$	38.3 ± 2.4$^{***,\#\#\#}$	*13.8 ± 1.4*$^{**,\#\#\#}$	*14.5 ± 1.1*$^{*,\#\#\#}$
Total	21.0 ± 1.5	17.6 ± 3.2	32.9 ± 1.4$^{***,\#\#\#}$	21.3 ± 3.9	23.4 ± 3.1

Supplemental Digital Content 5. Virus-mediated changes in enkephalin immunoreactivity (Enk-ir) and co-labeled mu opioid receptor immunoreactivity (mOR-ir) and GFP-positive dorsal root ganglion cells (mean ± SD).

Days indicate time after infection with control virus (hsvCON), herpes simplex virus vectors that encode the mu opioid receptor (hsvMOR), preproenkephalin (hsvPPE), or both (hsvMOR+PPE) on day 7 post-L5 spinal nerve ligation or infection with hsvCON on day 7 post-sham surgery (Sham). Statistically significant (P<0.05) decreases in expression are indicated in italics.

vs. sham; # significant at P<0.05; ## significant at P<0.01; ### significant at P<0.001

* vs. control virus-treated (hsvCON);* significant at P<0.05; ** significant at P<0.01; *** significant at P<0.001.

	Sham (n=4)	hsvCON (n=4)	hsvMOR (n=4)	hsvPPE (n=4)	hsvMOR+PPE (n=4)
Density of Enk-ir (% of sham)					
Day 1					
Lamina I	100% ± 8.2	82.0 ± 3.4	106.2 ± 2.8	*63.6 ± 4.9* $^{\#\#\#}$	*59.9 ± 6.6* $^{\#\#}$
Lamina II	100% ± 10.0	96.5 ± 5.04	146.7 ± 6.6 $^{***, \#\#\#}$	*67.4 ± 8.4* $^{**, \#\#}$	*73.1 ± 8.0* $^{\#}$
Lamina III	100% ± 25.6	142.7 ± 12.5 $^{\#}$	267.6 ± 16.8 $^{***,\#\#\#}$	*86.4 ± 28.3* ***	*92.1 ± 18.5* ***
Day 9					
Lamina I	100% ± 7.6	94.3 ± 6.1	152.9 ± 7.6 $^{***, \#\#\#}$	213.1 ± 5.9 $^{***, \#\#\#}$	183.8 ± 11.2 $^{***, \#\#\#}$
Lamina II	100% ± 8.1	*76.8 ± 6.3* $^{\#\#\#}$	121.9 ± 7.8 ***	181.2 ± 5.5 $^{***, \#\#\#}$	162.5 ± 13.0 $^{***, \#\#\#}$
Lamina III	100% ± 7.5	*69.7 ± 7.2* $^{\#\#\#}$	111.5 ± 7.6 ***	165.8 ± 6.2 $^{***, \#\#\#}$	169.5 ± 12.6 $^{***, \#\#\#}$
Density of mOR-ir (% of sham)					
Day 1					
Lamina I	100% ± 24.8	90.7 ± 6.3	*48.4 ± 12.1* $^{**, \#\#}$	108.1 ± 4.8	*70.8 ± 11.0* $^{\#}$
Lamina II	100% ± 31.6	91.1 ± 10.8	*57.3 ± 13.8* $^{*, \#\#}$	108.9 ± 5.3	74.9 ± 17.2
Lamina III	100% ± 37.6	121.3 ± 27.8	*64.9 ± 20.4* *	142.4 ± 8.1 $^{\#}$	102.9 ± 28.0
Day 9					
Lamina I	100% ± 6.0	90.7 ± 7.9	191.2 ± 12.3 $^{***, \#\#\#}$	94.4 ± 4.1	90.1 ± 5.4
Lamina II	100% ± 7.2	*83.0 ± 6.6* $^{\#}$	159.1 ± 7.6 $^{**, \#\#}$	*88.1 ± 4.1* $^{\#}$	*81.9 ± 4.5* $^{\#}$
Lamina III	100% ± 7.0	*80.4 ± 7.1* $^{\#}$	147.4 ± 6.7 $^{**, \#\#}$	*86.6 ± 3.9* $^{\#}$	*79.5 ± 4.2* $^{\#}$

Supplemental Digital Content 6. Virus-mediated change in enkephalin immunoreactivity (Enk-ir) and mu opioid receptor immunoreactivity (mOR-ir) in lamina I, II, and III of the dorsal horn of the lumbar spinal cord (mean ± SD).

Days indicate time after infection with control virus (hsvCON), herpes simplex virus vectors that encode the mu opioid receptor (hsvMOR), preproenkephalin (hsvPPE), or both (hsvMOR+PPE) on day 7 post-L5 spinal nerve ligation or infection with hsvCON on day 7 post-sham surgery (Sham). Statistically significant (P<0.05) decreases in expression are indicated in italics.

vs. sham; # significant at $P<0.05$; ## significant at $P<0.01$; ### significant at $P<0.001$

* vs. control virus-treated (hsvCON);* significant at $P<0.05$; ** significant at $P<0.01$; *** significant at $P<0.001$