Legends to Supplementary Figures:

Supplementary Figure 1. ***Time-course of locally administrated DAMGO on postoperative anti-hypersensitivity in adult and aged mice***

Incision-induced thermal (**A, C**) and mechanical (**B, D**) hypersensitivity were generated in adult (**A, B**) and aged (**C, D**) mice. At 1 day (for adults) and 1-3 days (for aged) post-surgery, operated hindpaws were injected with different dosages of DAMGO, and thermal (**A, C**) and mechanical (**B, D**) hypersensitivity were measured at 30, 60 (for some dosages) and 120 min post-DAMGO injection. Significance of DAMGO produced anti-hypersensitivity was compared against postoperative hypersensitivity reading (marked POP; 1-way ANOVA; ** $p<0.01$; ***$p<0.001$; n=5-8). Post-drug administration time points are indicated below X-axis. BL is pre-surgery baseline reading. Opioid dosages and mouse ages are indicated.

Supplementary Figure 2. ***Time-course of spinally administrated DAMGO on postoperative anti-hypersensitivity in adult and aged mice***

Incision-induced thermal (**A, C**) and mechanical (**B, D**) hypersensitivity were generated in adult (**A, B**) and aged (**C, D**) mice. At 1 day (for adults) and 1-3 days (for aged) post-surgery, different dosages of DAMGO were administered intrathecally, and thermal (**A, C**) and mechanical (**B, D**) hypersensitivity were measured at 30 and 120 min post-DAMGO injection. Significance of DAMGO produced anti-hypersensitivity was compared against postoperative hypersensitivity reading (marked POP). For thermal anti-hypersensitivity, statistics showed $p<0.001$ for all time points and DAMGO dosages (1-way ANOVA; n=5-8). Post-drug administration time points are indicated below X-axis. Opioid dosages and mouse ages are indicated.

Supplementary Figure 3. ***Time-course of locally administrated buprenorphine on postoperative anti-hypersensitivity in adult and aged mice***

Incision-induced thermal (**A, C**) and mechanical (**B, D**) hypersensitivity were generated in adult and aged mice. At 1 day (for adults) and 1-3 days (for aged) post-surgery, operated hindpaws were injected with different dosages of buprenorphine, and thermal (**A, C**) and mechanical (**B, D**) hypersensitivity were measured at 30 and 120 min post-buprenorphine injection. Significance of buprenorphine produced anti-hypersensitivity was compared against hypersensitivity reading (marked POP; 1-way ANOVA; NS – non-significant; *** $p<0.001$; n=5-8). Post-drug administration time points are indicated below X-axis. BL indicates the baseline pre-surgery reading. Opioid dosages and mouse ages are indicated.

Supplementary Figure 4. ***Time-course of locally administrated buprenorphine on postoperative anti-hypersensitivity in adult and aged mice***

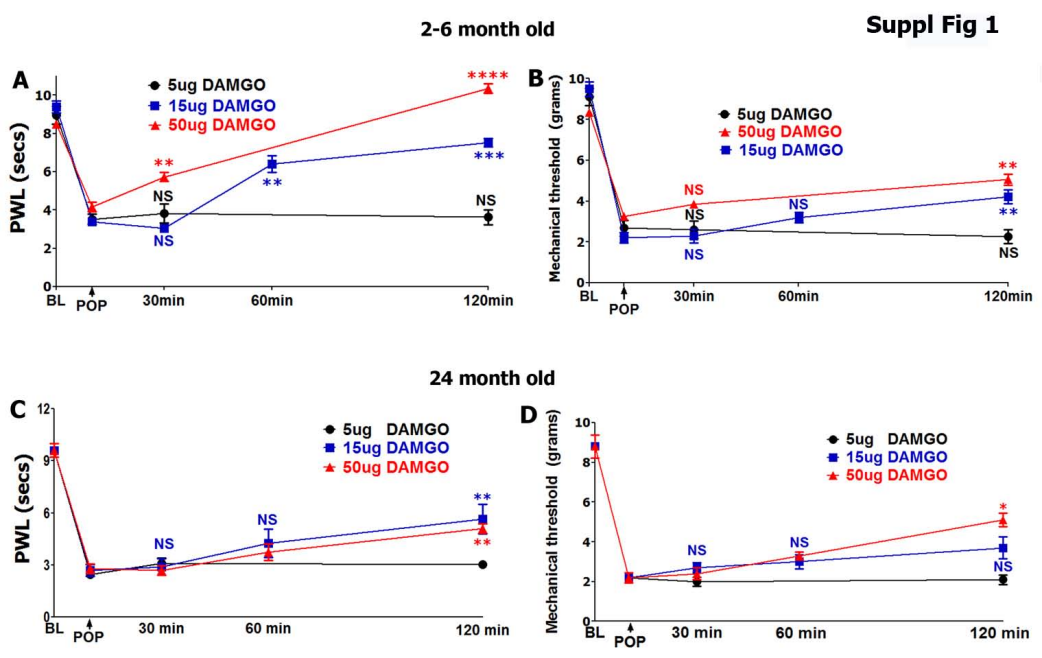
Incision-induced thermal (**A, C**) and mechanical (**B, D**) hypersensitivity were generated in adult and aged mice. At 1 day (for adults) and 1-3 days (for aged) post-surgery, different dosages of buprenorphine were intrathecally administrated, and thermal (**A, C**) and mechanical (**B, D**) hypersensitivity were evaluated at 30 and 120 min post-buprenorphine injection. Significance of buprenorphine produced anti-hypersensitivity was compared against hypersensitivity reading (marked POP; 1-way ANOVA; NS-non-significant; **$p<0.01$; ***$p<0.001$; ****$p<0.0001$; n=5-8). Post-drug administration time points are indicated below X-axis. Opioid dosages and mouse ages are indicated.

Supplementary Figure 5. ***Buprenorphine-induced locomotor activity in naive adult and aged mice***

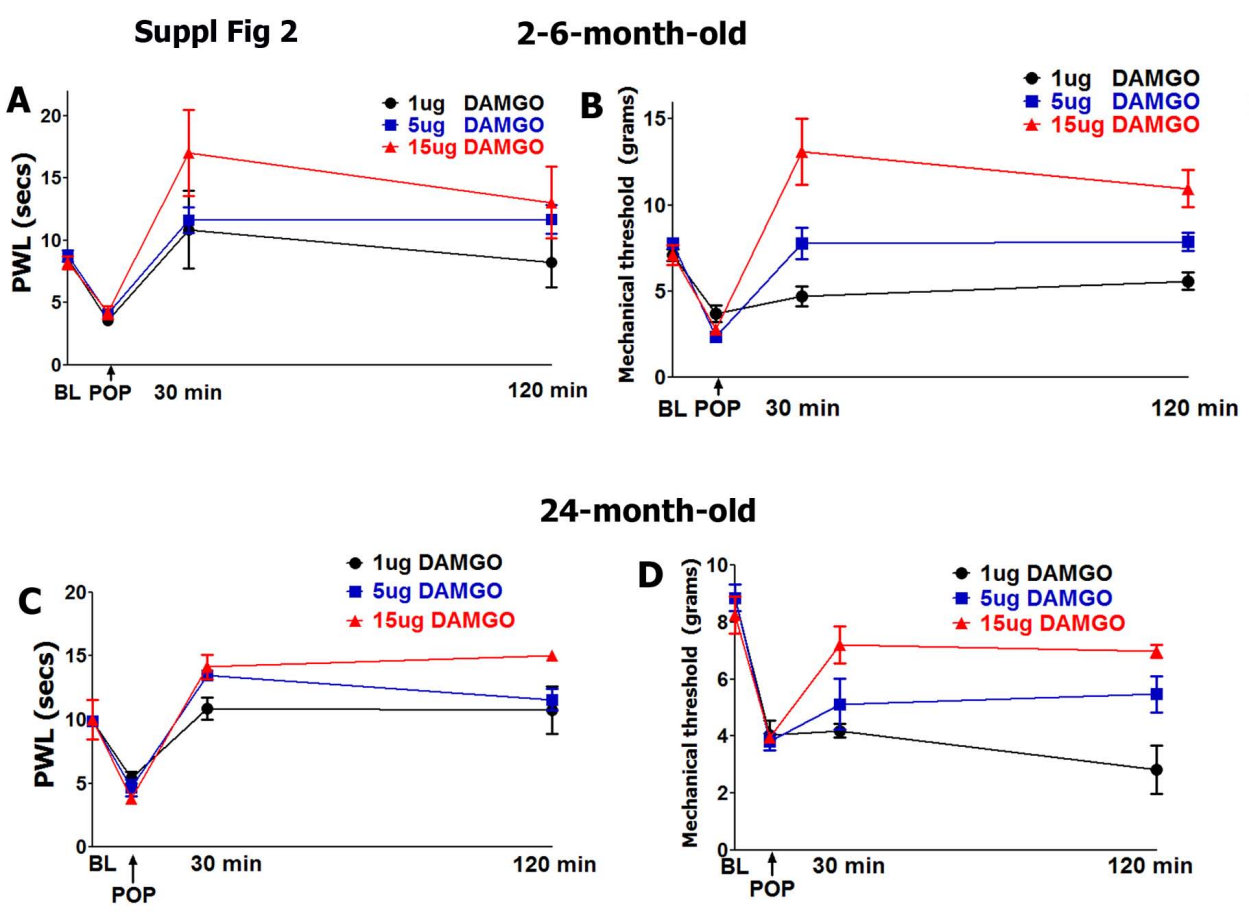
Buprenorphine-induced locomotor activities were measured as number of breaks of horizontal infrared beams per 30-min period in naïve adult (**A**) and aged (**C**) mice (n=4-6 per age group).

Overall locomotor activity during 2 h exposure to the activity chambers showed on panels (**B**) for adult and (**D**) for aged mice. Locomotor activities were measured after spinal administration of saline or different dosages of buprenorphine. During the initial 2-h exposure, saline (Sal) was administrated; and then 72h later, during a second 2-h exposure, buprenorphine (Bup) was administrated. Data of both sessions were obtained in the same animals. Buprenorphine dosages are indicated. For panels (**B**) and (**D**), statistic is 1-way ANOVA; * $p<0.05$.

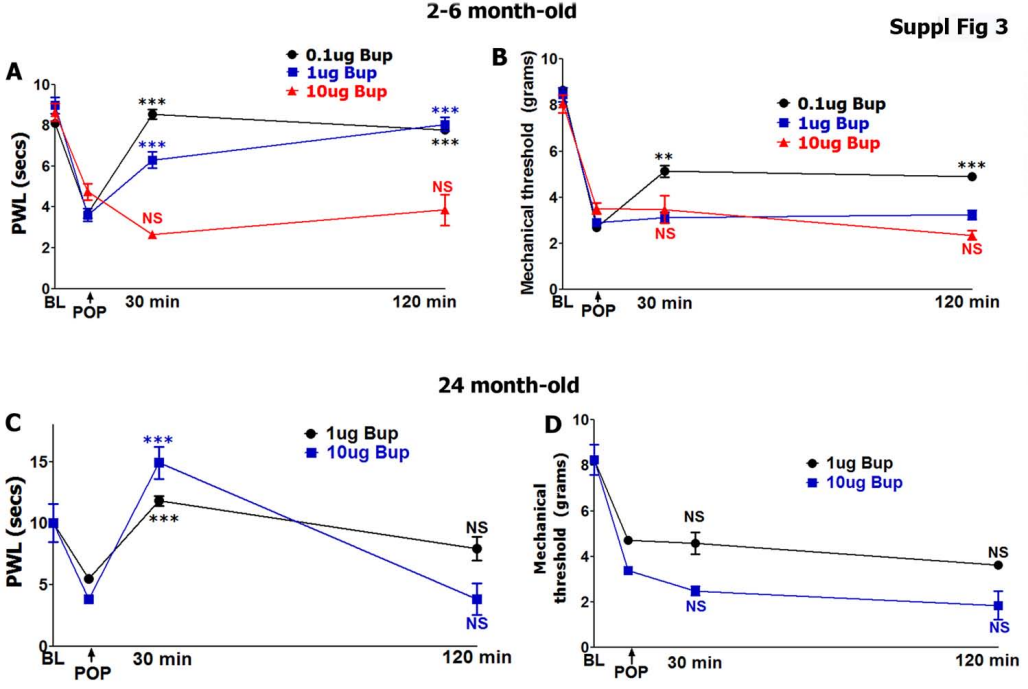
Suppl Fig 1

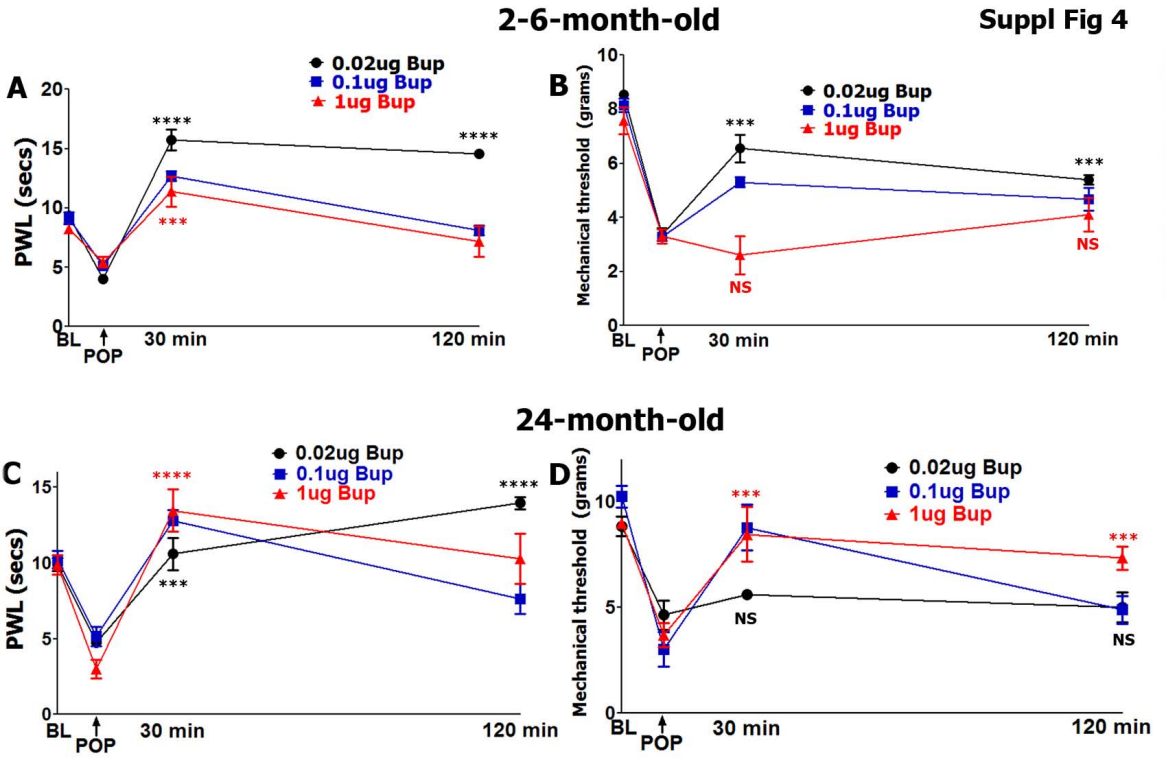

2-6 month old
A
5ug DAMGO
15ug DAMGO
50ug DAMGO
PWL (secs)
BL
POP
30min
60min
120min
****
**
***
NS
B
Mechanical threshold (grams)
24 month old
C
30 min
60 min
120 min
D

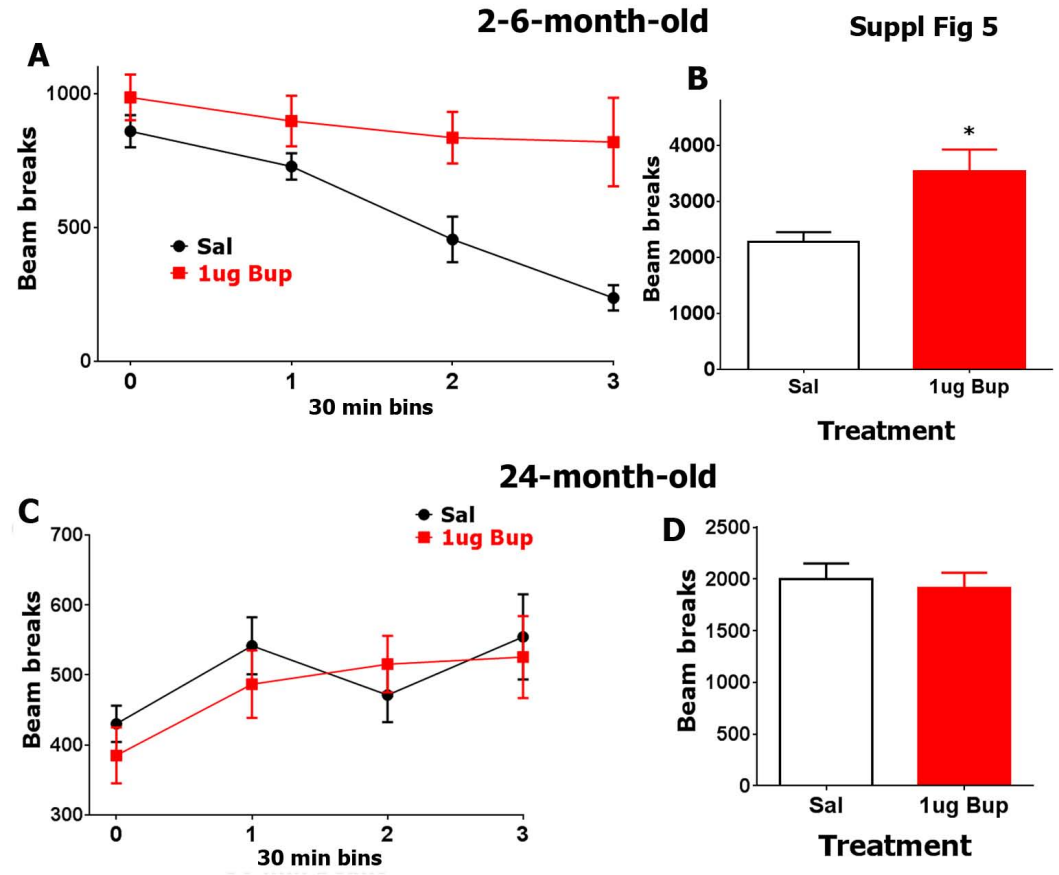
Suppl Fig 2


2-6-month-old
A
PWL (secs)
1ug DAMGO
5ug DAMGO
15ug DAMGO
BL POP
30 min
120 min
B
Mechanical threshold (grams)
1ug DAMGO
5ug DAMGO
15ug DAMGO
BL POP
30 min
120 min
24-month-old
C
PWL (secs)
1ug DAMGO
5ug DAMGO
15ug DAMGO
BL
POP
30 min
120 min
D
Mechanical threshold (grams)
1ug DAMGO
5ug DAMGO
15ug DAMGO
BL
POP
30 min
120 min

Suppl Fig 3


2-6 month-old
A
0.1ug Bup
1ug Bup
10ug Bup
PWL (secs)
***
***
***
***
NS
NS
BL
POP
30 min
120 min
B
Mechanical threshold (grams)
**
***
NS
NS
24 month-old
C
1ug Bup
10ug Bup
PWL (secs)
***
***
NS
NS
D
Mechanical threshold (grams)
NS
NS
NS
NS


2-6-month-old
A
B
0.02ug Bup
0.1ug Bup
1ug Bup
PWL (secs)
Mechanical threshold (grams)
BL
POP
30 min
120 min
****
***
NS
24-month-old
C
D


2-6-month-old
Suppl Fig 5
A
Beam breaks
1000
500
0
Sal
1ug Bup
0
1
2
3
30 min bins
B
Beam breaks
4000
3000
2000
1000
0
*
Sal
1ug Bup
Treatment
24-month-old
C
Sal
1ug Bup
Beam breaks
700
600
500
400
300
0
1
2
3
30 min bins
D
Beam breaks
2500
2000
1500
1000
500
0
Sal
1ug Bup
Treatment