Figure 1

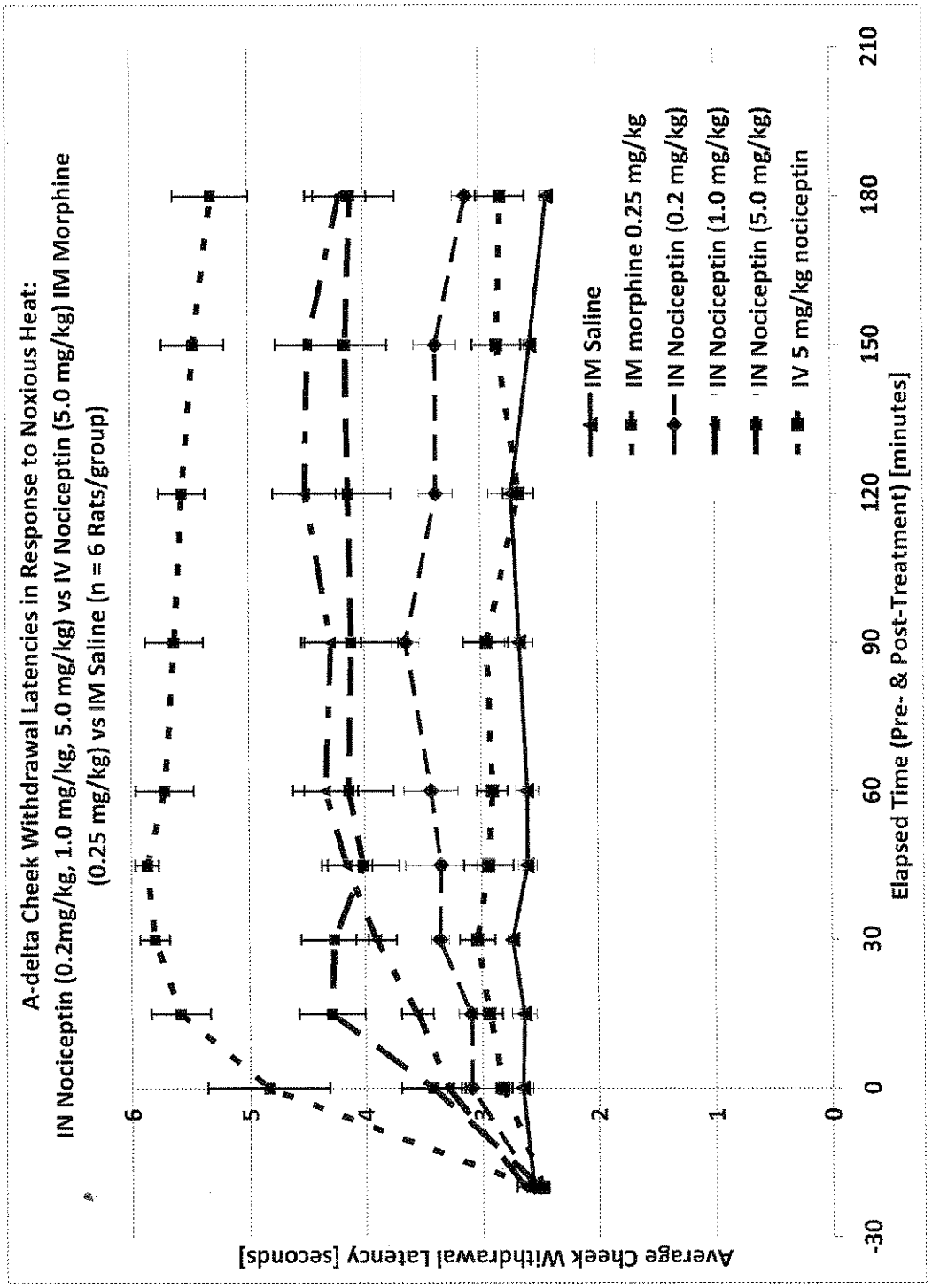

A-delta Cheek Withdrawal Latencies in Response to Noxious Heat:
IN Nociceptin (0.2mg/kg, 1.0 mg/kg, 5.0 mg/kg) vs IV Nociceptin (5.0 mg/kg) IM Morphine (0.25 mg/kg) vs IM Saline (n = 6 Rats/group)
Average Cheek Withdrawal Latency [seconds]
Elapsed Time (Pre- & Post-Treatment) [minutes]
-30
0
30
60
90
120
150
180
210
0
1
2
3
4
5
6
IM Saline
IM morphine 0.25 mg/kg
IN Nociceptin (0.2 mg/kg)
IN Nociceptin (1.0 mg/kg)
IN Nociceptin (5.0 mg/kg)
IV 5 mg/kg nociceptin

Figure 2

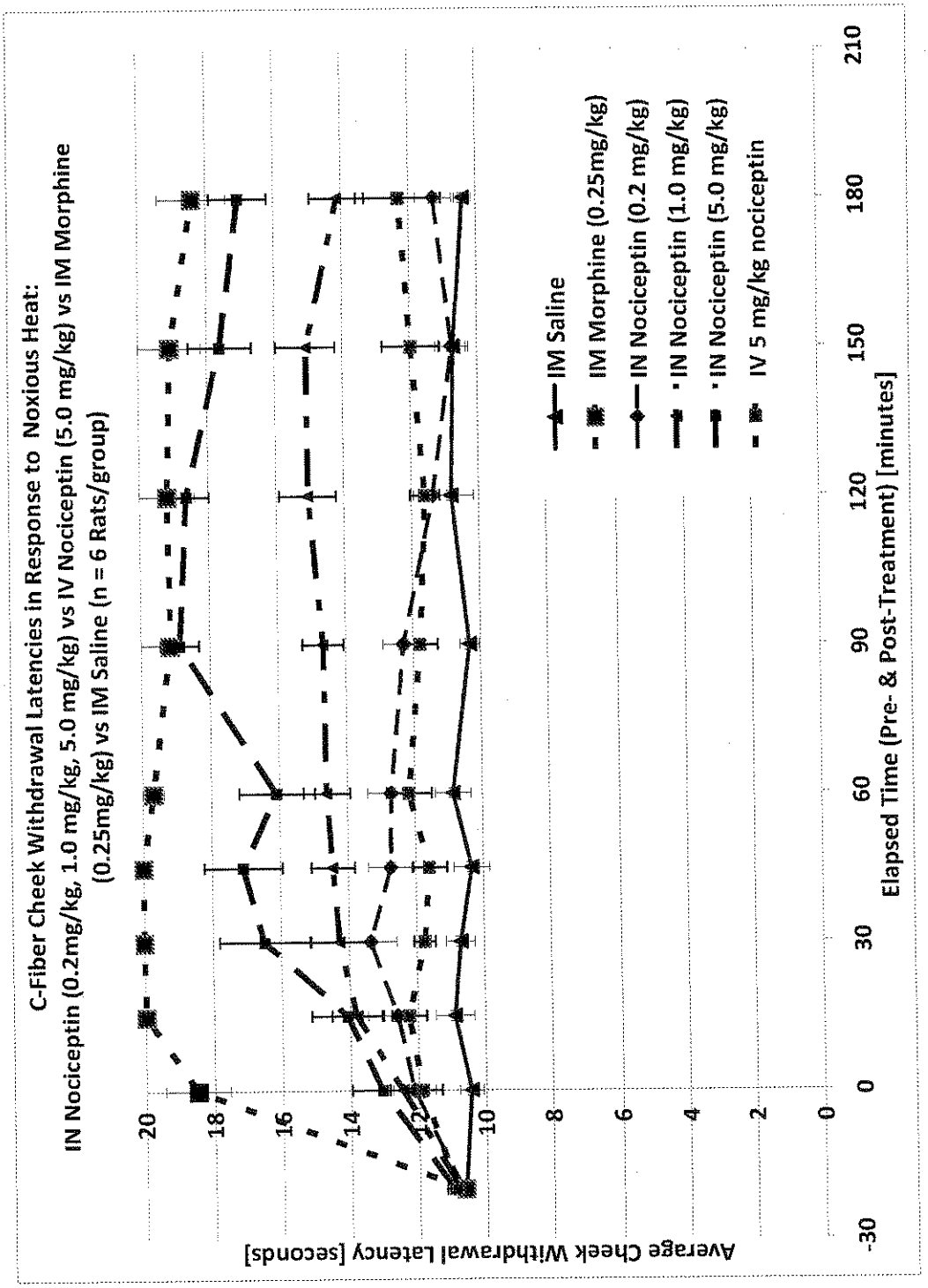

C-Fiber Cheek Withdrawal Latencies in Response to Noxious Heat:
IN Nociceptin (0.2mg/kg, 1.0 mg/kg, 5.0 mg/kg) vs IV Nociceptin (5.0 mg/kg) vs IM Morphine (0.25mg/kg) vs IM Saline (n = 6 Rats/group)
Average Cheek Withdrawal Latency [seconds]
Elapsed Time (Pre- & Post-Treatment) [minutes]
IM Saline
IM Morphine (0.25mg/kg)
IN Nociceptin (0.2 mg/kg)
IN Nociceptin (1.0 mg/kg)
IN Nociceptin (5.0 mg/kg)
IV 5 mg/kg nociceptin

Figure 3

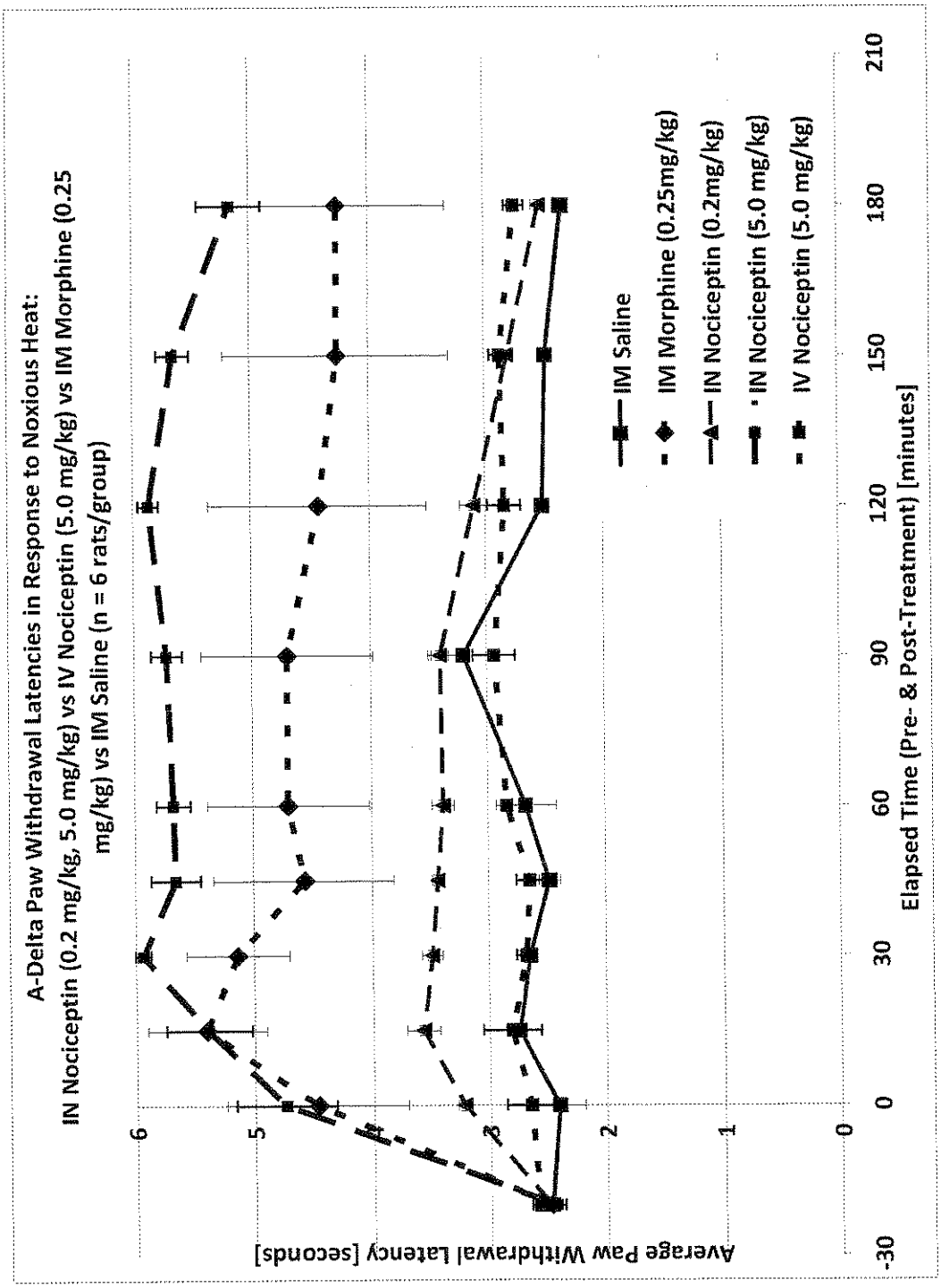

A-Delta Paw Withdrawal Latencies in Response to Noxious Heat:
IN Nociceptin (0.2 mg/kg, 5.0 mg/kg) vs IV Nociceptin (5.0 mg/kg) vs IM Morphine (0.25 mg/kg) vs IM Saline (n = 6 rats/group)
Average Paw Withdrawal Latency [seconds]
Elapsed Time (Pre- & Post-Treatment) [minutes]
IM Saline
IM Morphine (0.25mg/kg)
IN Nociceptin (0.2mg/kg)
IN Nociceptin (5.0 mg/kg)
IV Nociceptin (5.0 mg/kg)

Figure 4

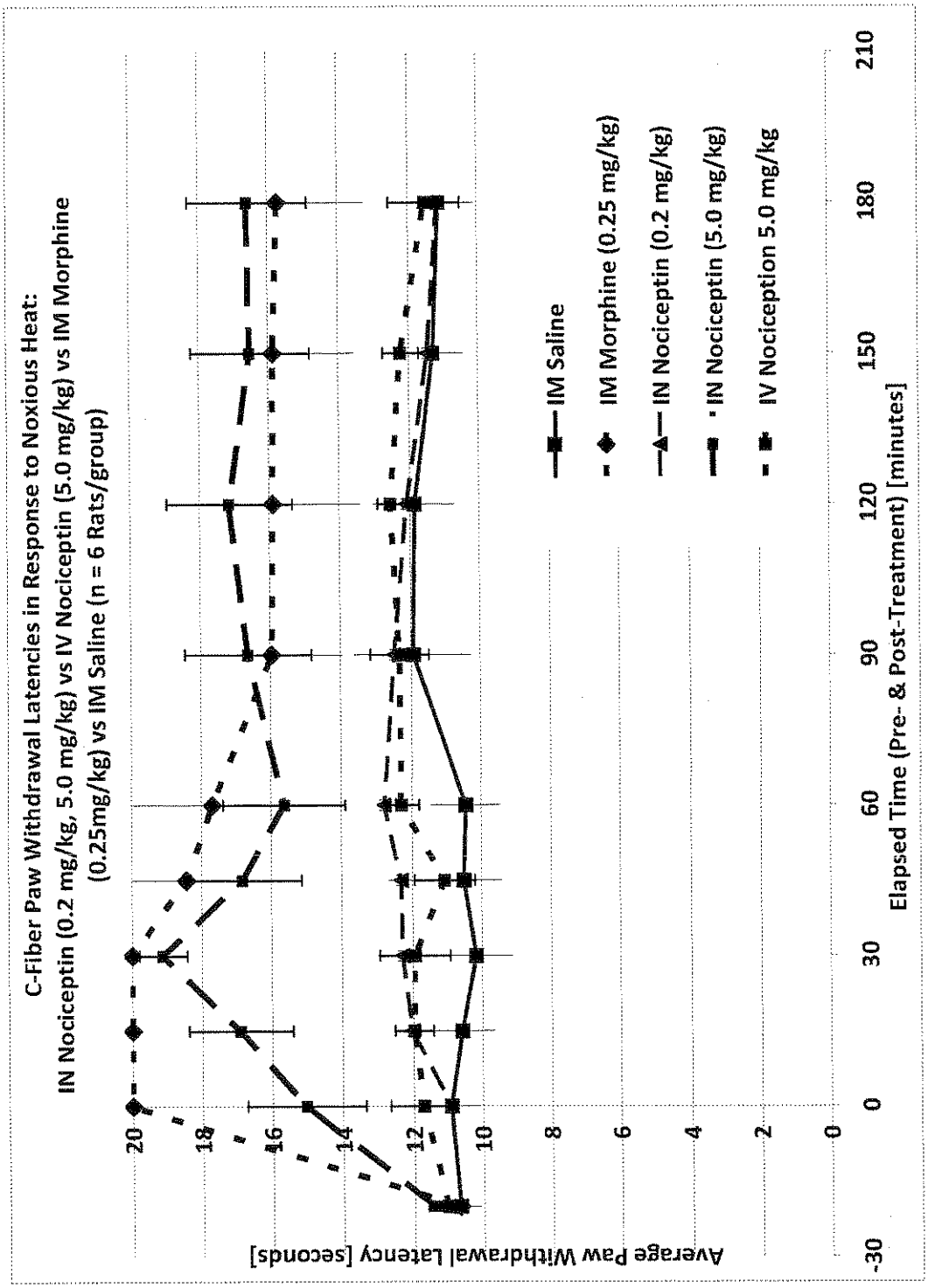

C-Fiber Paw Withdrawal Latencies in Response to Noxious Heat:
IN Nociceptin (0.2 mg/kg, 5.0 mg/kg) vs IV Nociceptin (5.0 mg/kg) vs IM Morphine (0.25mg/kg) vs IM Saline (n = 6 Rats/group)
Average Paw Withdrawal Latency [seconds]
Elapsed Time (Pre- & Post-Treatment) [minutes]
IM Saline
IM Morphine (0.25 mg/kg)
IN Nociceptin (0.2 mg/kg)
IN Nociceptin (5.0 mg/kg)
IV Nociception 5.0 mg/kg

Figure 5

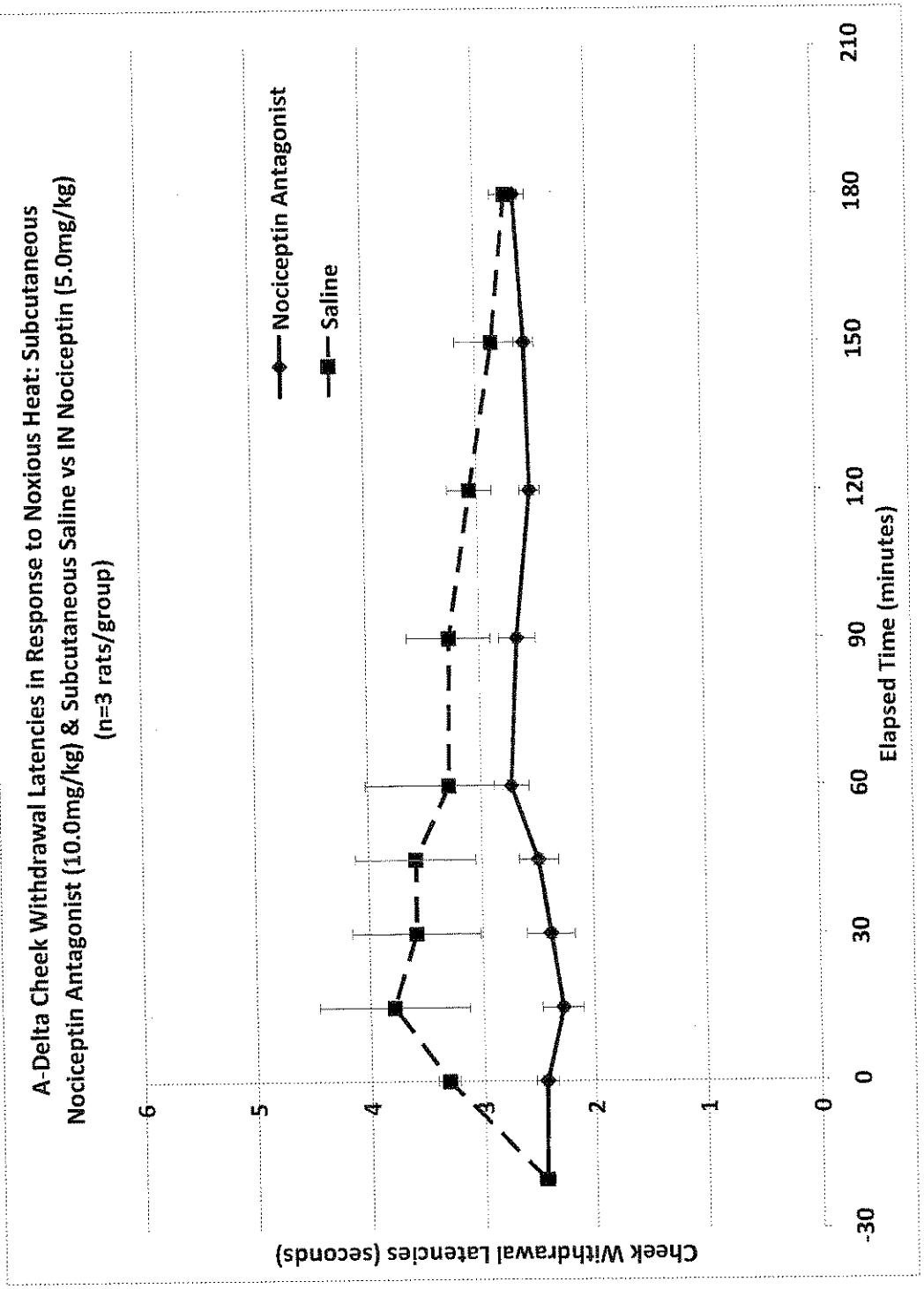

A-Delta Cheek Withdrawal Latencies in Response to Noxious Heat: Subcutaneous Nociceptin Antagonist (10.0mg/kg) & Subcutaneous Saline vs IN Nociceptin (5.0mg/kg)
(n=3 rats/group)
Nociceptin Antagonist
Saline
Cheek Withdrawal Latencies (seconds)
Elapsed Time (minutes)
-30
0
30
60
90
120
150
180
210
0
1
2
3
4
5
6

Figure 6

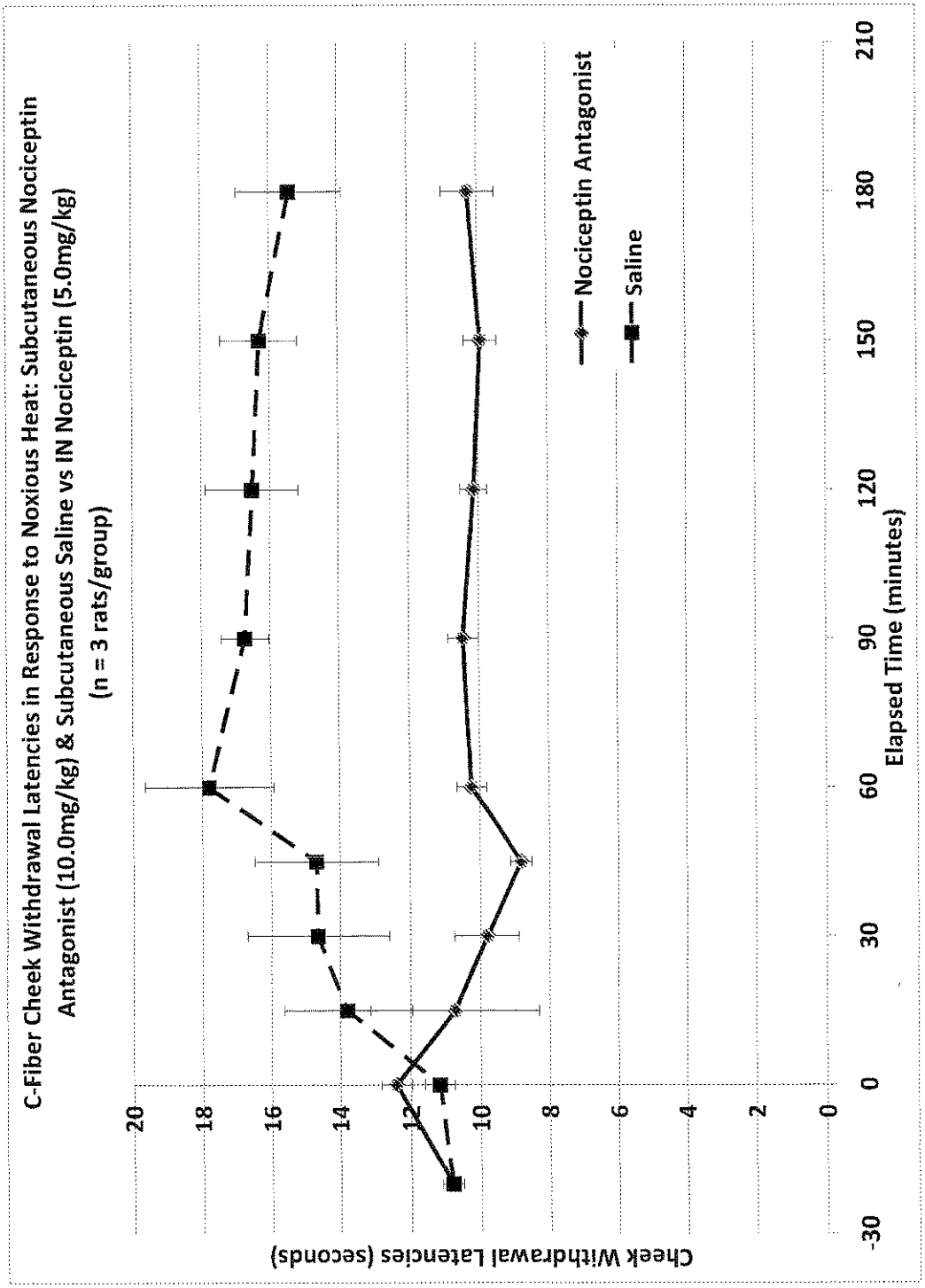

C-Fiber Cheek Withdrawal Latencies in Response to Noxious Heat: Subcutaneous Nociceptin Antagonist (10.0mg/kg) & Subcutaneous Saline vs IN Nociceptin (5.0mg/kg)
(n = 3 rats/group)
Cheek Withdrawal Latencies (seconds)
Elapsed Time (minutes)
Nociceptin Antagonist
Saline
20
18
16
14
12
10
8
6
4
2
0
-30
0
30
60
90
120
150
180
210

Figure 7

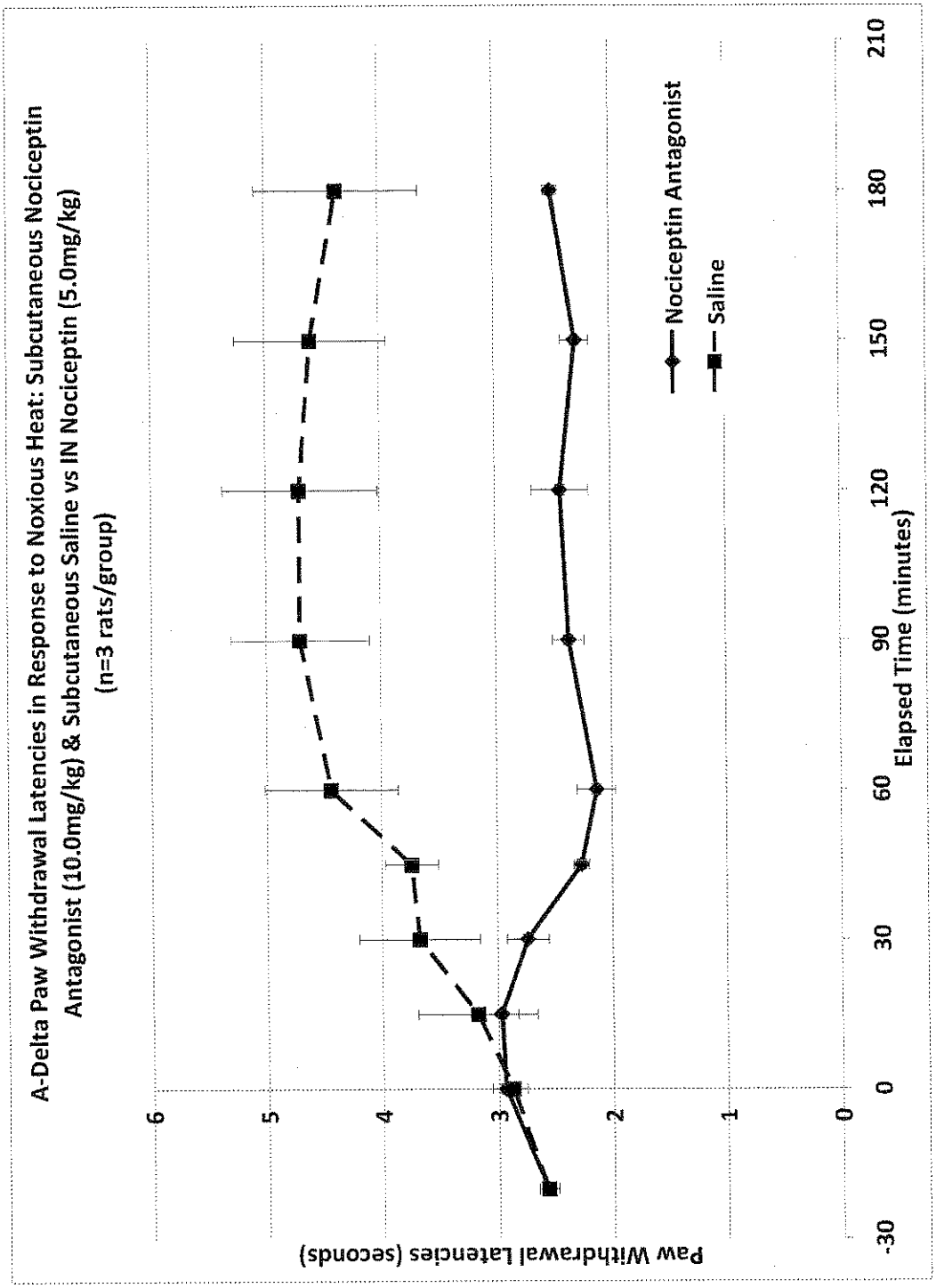

A-Delta Paw Withdrawal Latencies in Response to Noxious Heat: Subcutaneous Nociceptin Antagonist (10.0mg/kg) & Subcutaneous Saline vs IN Nociceptin (5.0mg/kg)
(n=3 rats/group)
Paw Withdrawal Latencies (seconds)
Elapsed Time (minutes)
Nociceptin Antagonist
Saline
-30
0
30
60
90
120
150
180
210
0
1
2
3
4
5
6

Figure 8

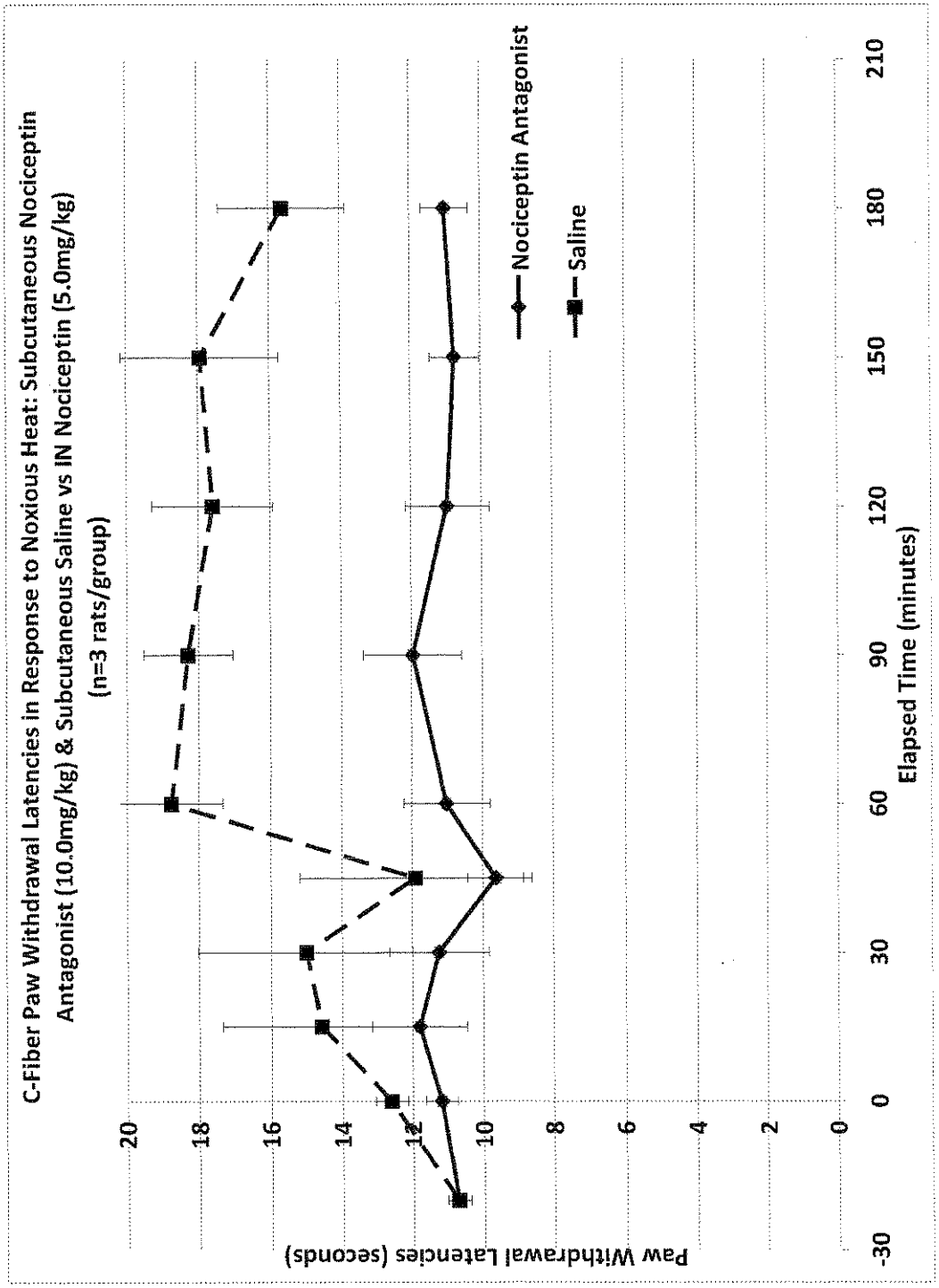

C-Fiber Paw Withdrawal Latencies in Response to Noxious Heat: Subcutaneous Nociceptin Antagonist (10.0mg/kg) & Subcutaneous Saline vs IN Nociceptin (5.0mg/kg)
(n=3 rats/group)
Paw Withdrawal Latencies (seconds)
20
18
16
14
12
10
8
6
4
2
0
-30
0
30
60
90
120
150
180
210
Elapsed Time (minutes)
Nociceptin Antagonist
Saline

Figure 9

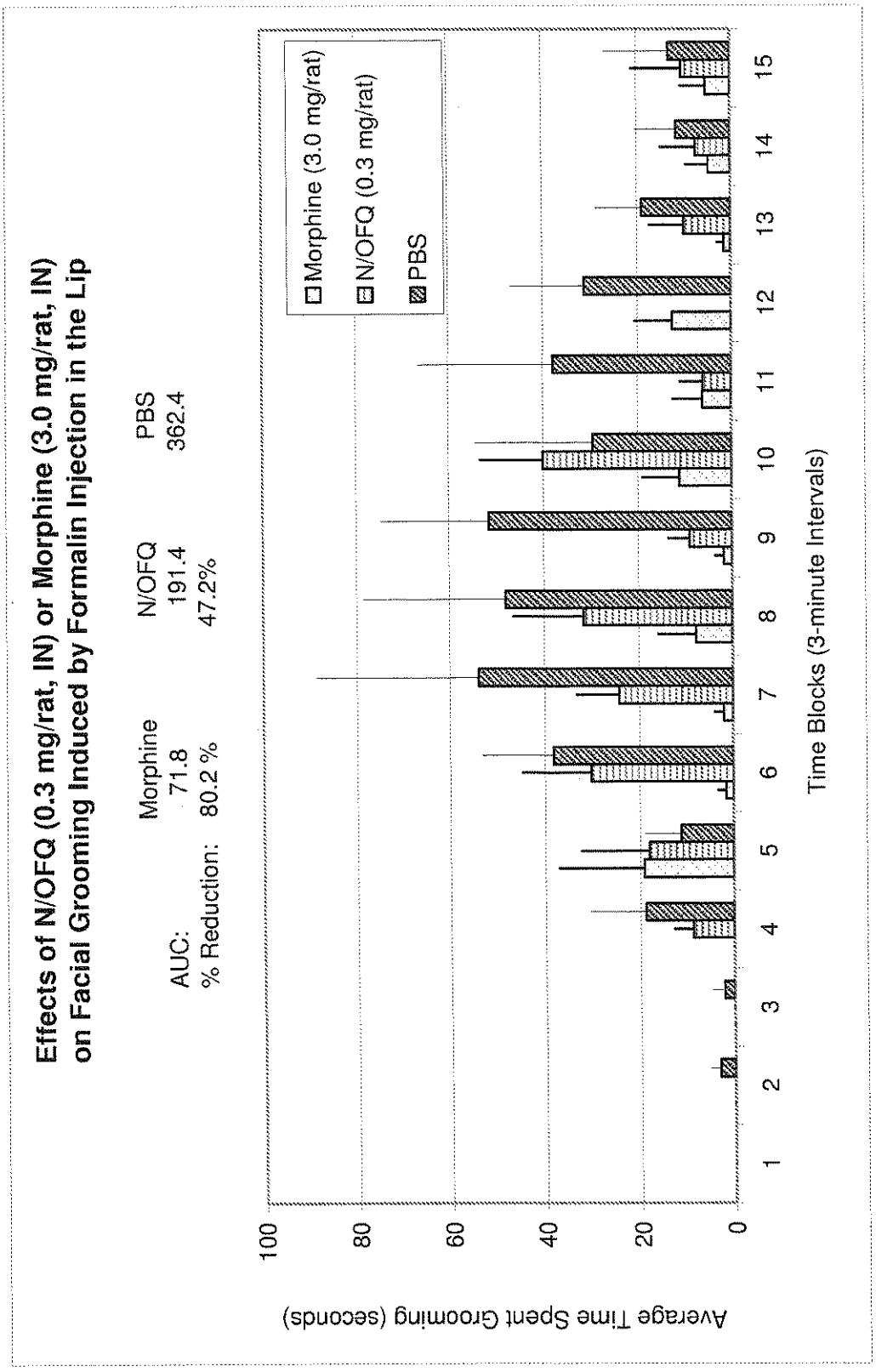

Effects of N/OFQ (0.3 mg/rat, IN) or Morphine (3.0 mg/rat, IN) on Facial Grooming Induced by Formalin Injection in the Lip
Morphine
N/OFQ
PBS
AUC:
71.8
191.4
362.4
% Reduction:
80.2 %
47.2%
Morphine (3.0 mg/rat)
N/OFQ (0.3 mg/rat)
PBS
Average Time Spent Grooming (seconds)
0
20
40
60
80
100
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
Time Blocks (3-minute Intervals)

Figure 10

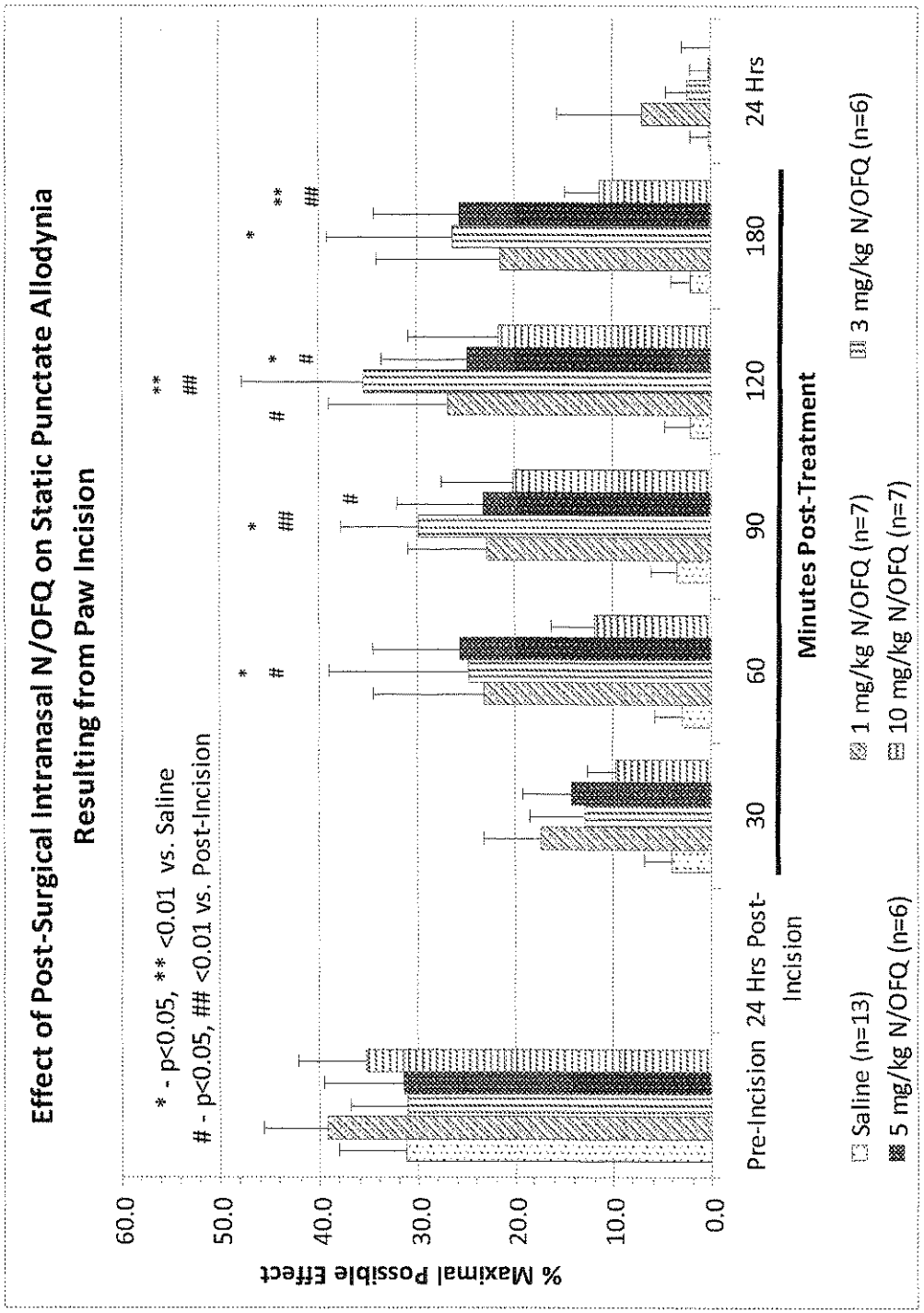

Effect of Post-Surgical Intranasal N/OFQ on Static Punctate Allodynia
Resulting from Paw Incision
* - p<0.05, ** <0.01 vs. Saline
# - p<0.05, ## <0.01 vs. Post-Incision
% Maximal Possible Effect
60.0
50.0
40.0
30.0
20.0
10.0
0.0
Pre-Incision
24 Hrs Post-Incision
30
60
90
120
180
24 Hrs
Minutes Post-Treatment
Saline (n=13)
1 mg/kg N/OFQ (n=7)
3 mg/kg N/OFQ (n=6)
5 mg/kg N/OFQ (n=6)
10 mg/kg N/OFQ (n=7)

Figure 11

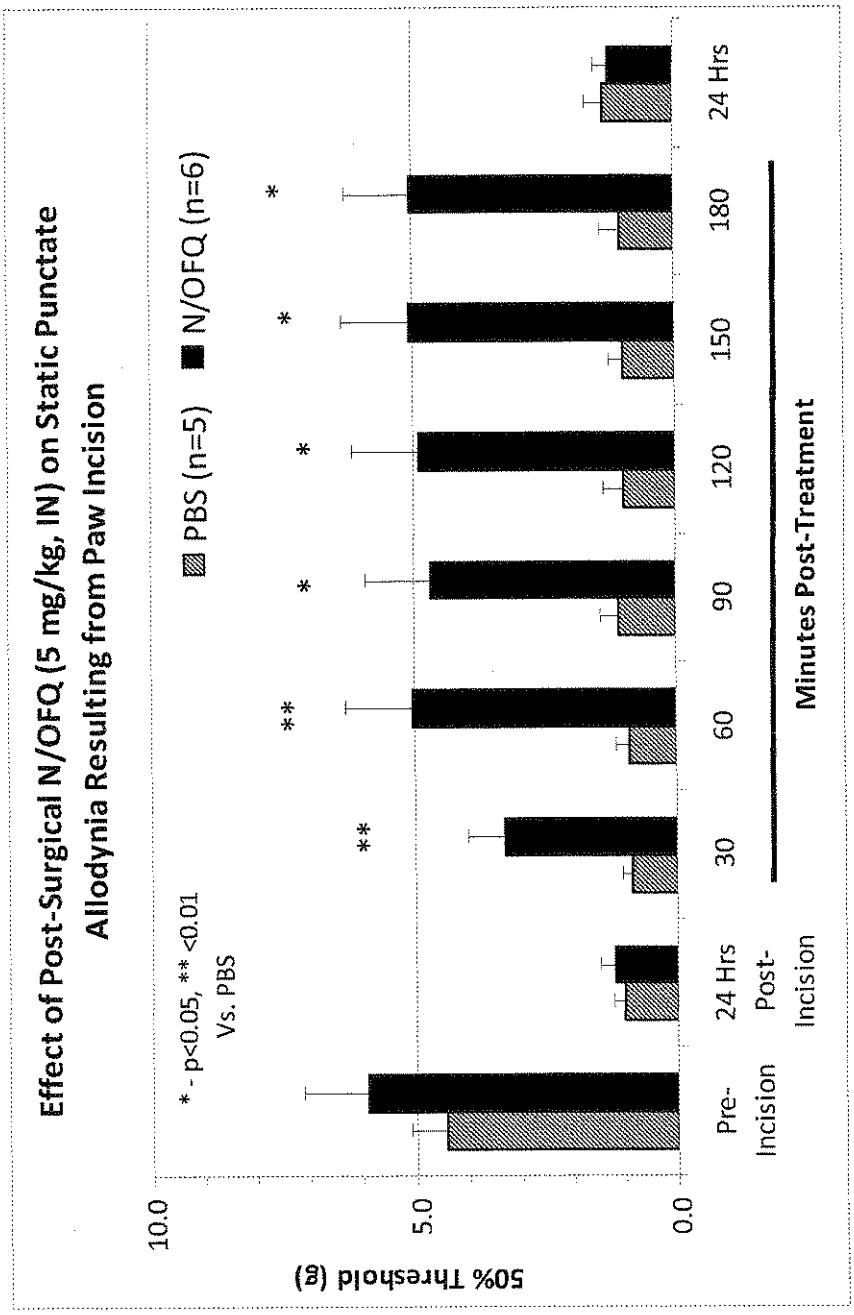

Effect of Post-Surgical N/OFQ (5 mg/kg, IN) on Static Punctate Allodynia Resulting from Paw Incision
* - p<0.05, ** <0.01 Vs. PBS
PBS (n=5)
N/OFQ (n=6)
50% Threshold (g)
10.0
5.0
0.0
Pre-Incision
24 Hrs Post-Incision
30
60
90
120
150
180
24 Hrs
Minutes Post-Treatment

Figure 12

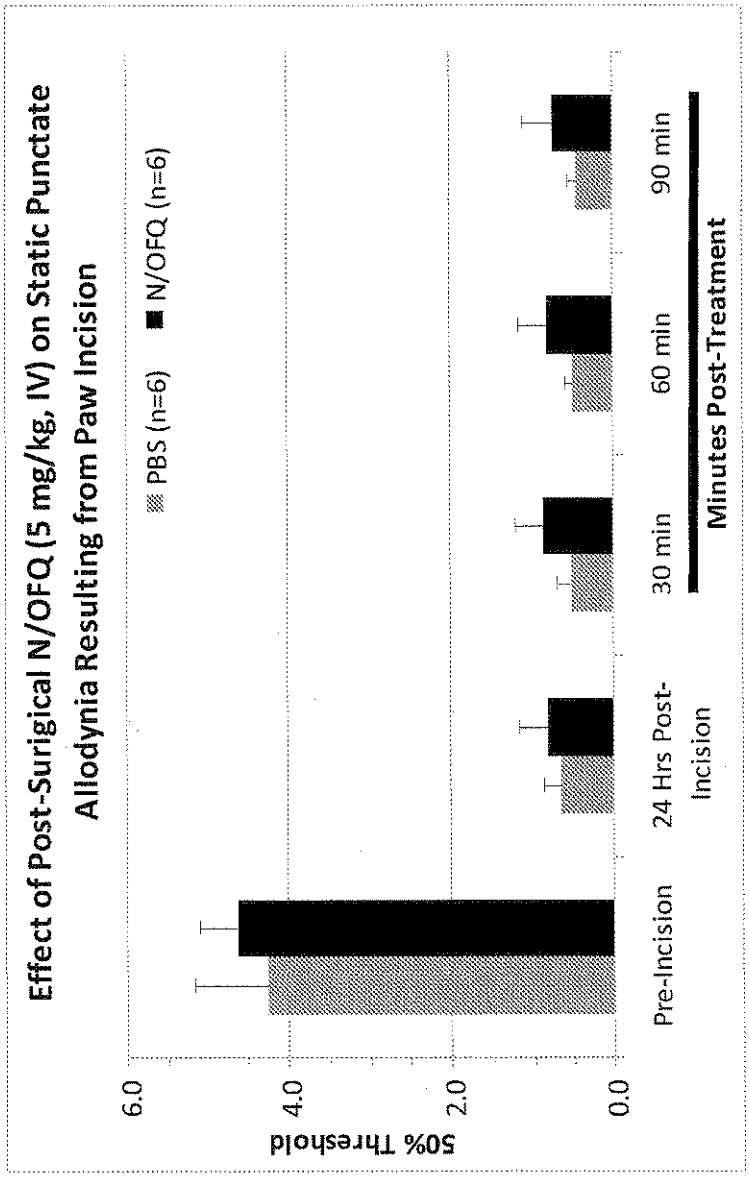

Effect of Post-Surigical N/OFQ (5 mg/kg, IV) on Static Punctate Allodynia Resulting from Paw Incision
PBS (n=6)
N/OFQ (n=6)
50% Threshold
6.0
4.0
2.0
0.0
Pre-Incision
24 Hrs Post-Incision
30 min
60 min
90 min
Minutes Post-Treatment

Figure 13

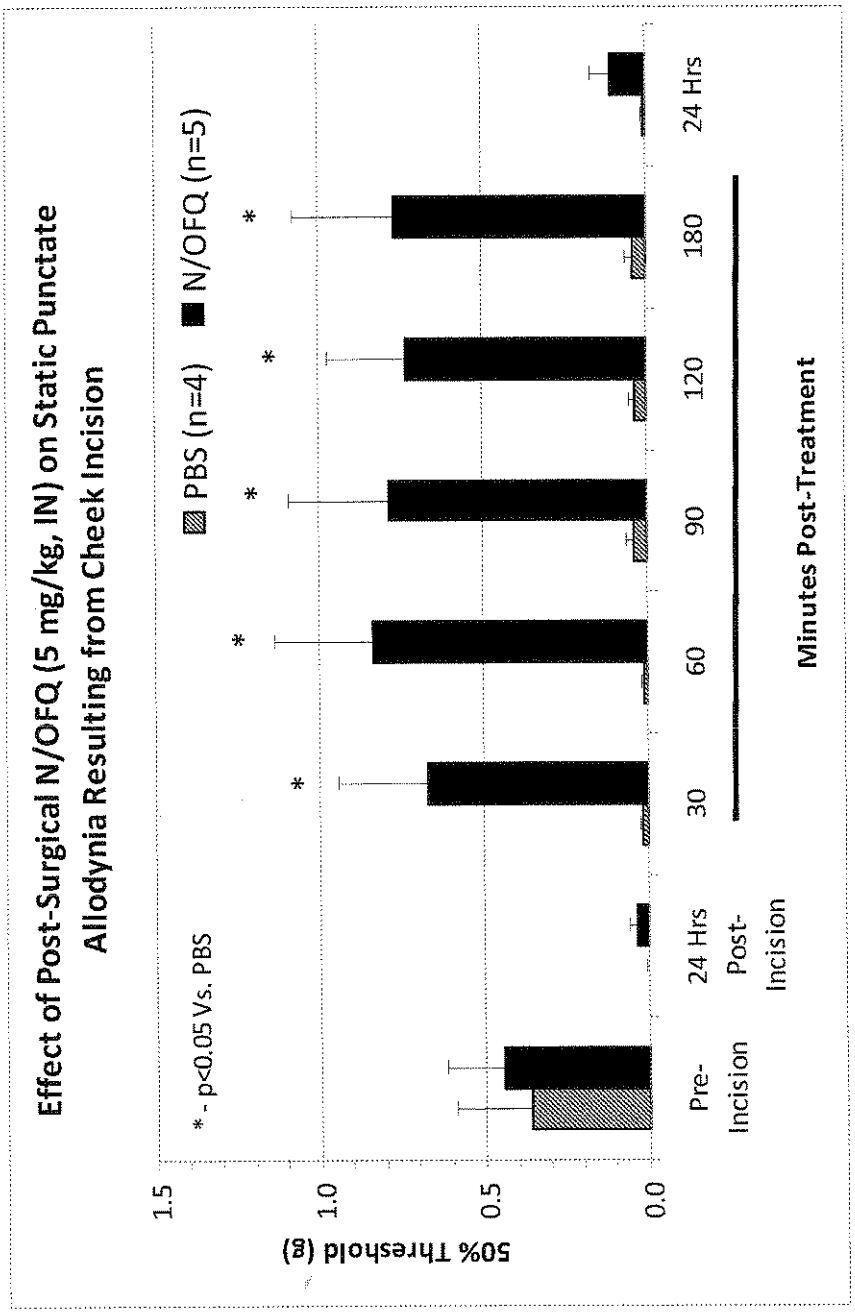

Effect of Post-Surgical N/OFQ (5 mg/kg, IN) on Static Punctate Allodynia Resulting from Cheek Incision
* - p<0.05 Vs. PBS
PBS (n=4)
N/OFQ (n=5)
50% Threshold (g)
1.5
1.0
0.5
0.0
Pre-Incision
24 Hrs Post-Incision
30
60
90
120
180
24 Hrs
Minutes Post-Treatment

Figure 14

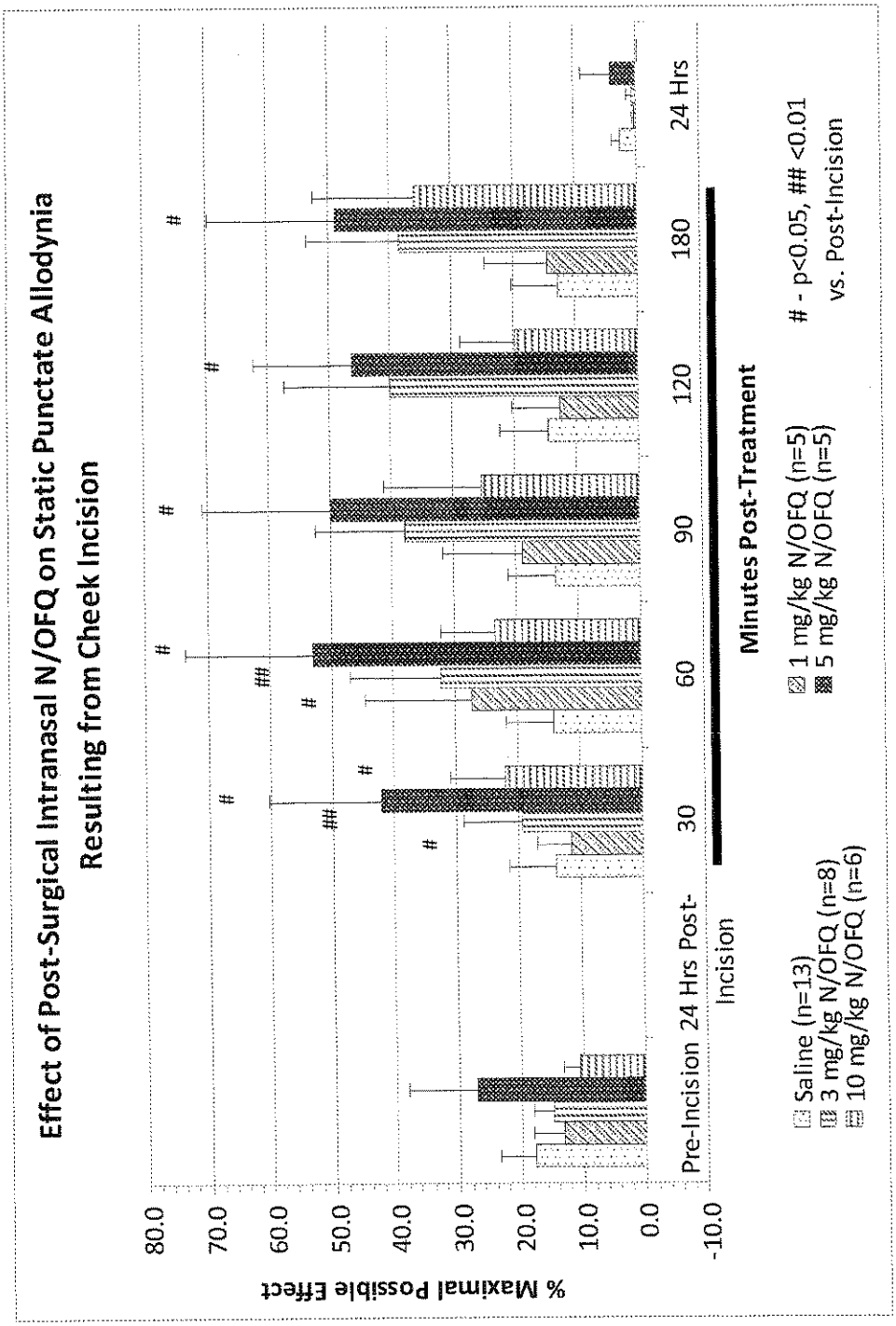

Effect of Post-Surgical Intranasal N/OFQ on Static Punctate Allodynia
Resulting from Cheek Incision
% Maximal Possible Effect
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
-10.0
Pre-Incision
24 Hrs Post-Incision
30
60
90
120
180
24 Hrs
Minutes Post-Treatment
Saline (n=13)
3 mg/kg N/OFQ (n=8)
10 mg/kg N/OFQ (n=6)
1 mg/kg N/OFQ (n=5)
5 mg/kg N/OFQ (n=5)
- p<0.05, ## <0.01
vs. Post-Incision

Figure 15

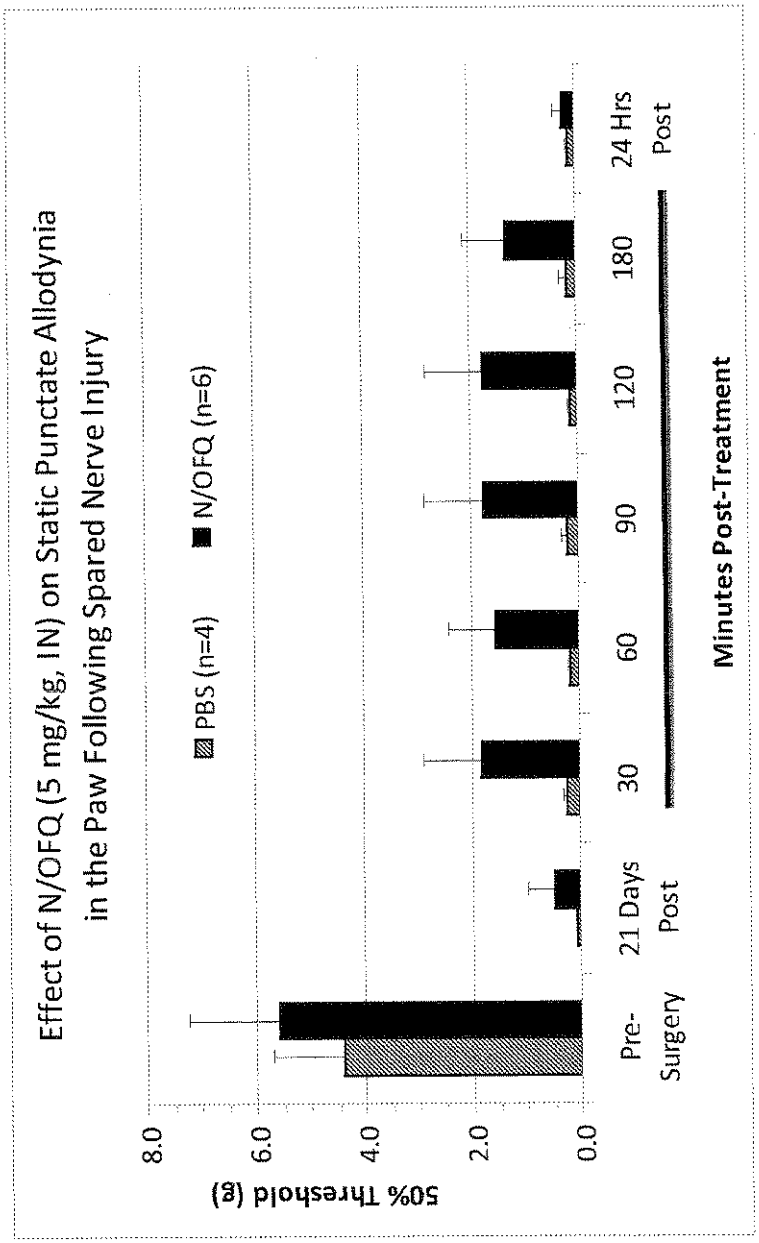
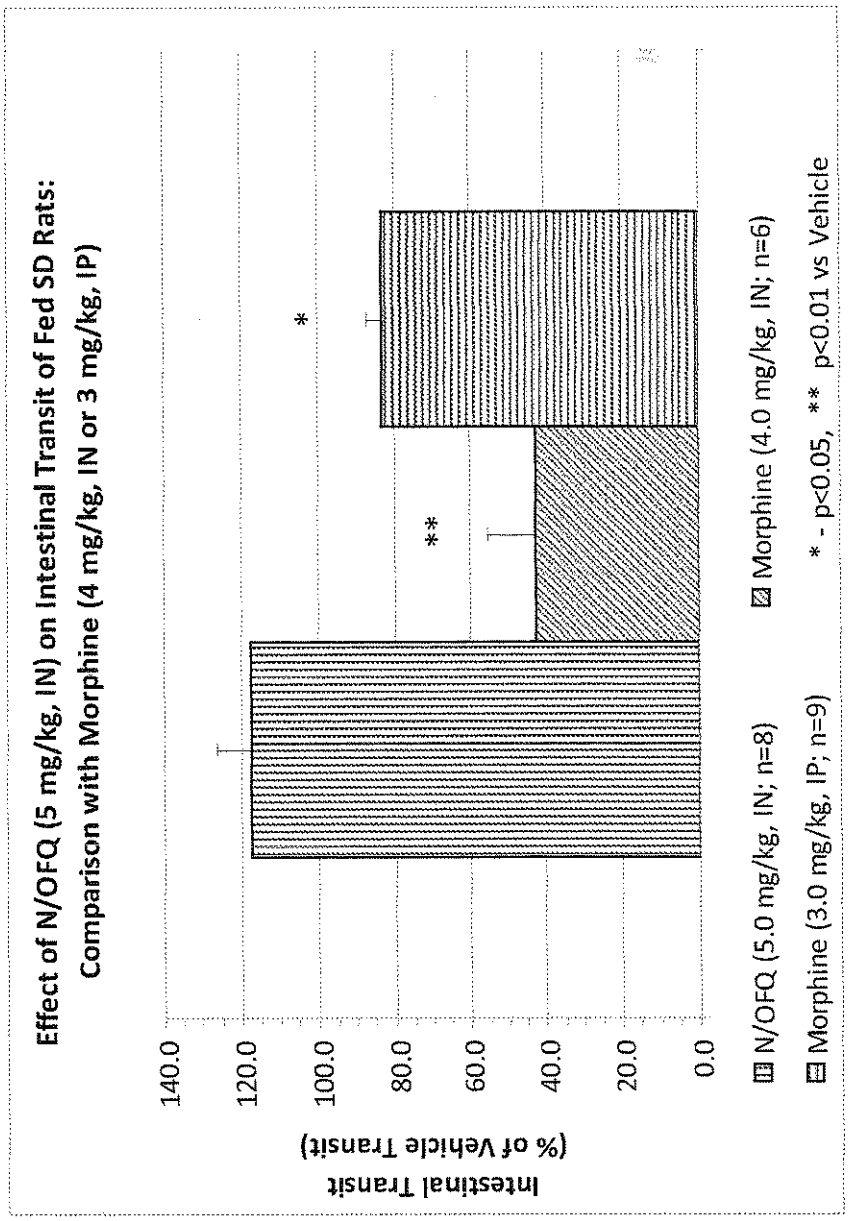

Effect of N/OFQ (5 mg/kg, IN) on Static Punctate Allodynia in the Paw Following Spared Nerve Injury
PBS (n=4)
N/OFQ (n=6)
50% Threshold (g)
8.0
6.0
4.0
2.0
0.0
Pre-Surgery
21 Days Post
30
60
90
120
180
24 Hrs Post
Minutes Post-Treatment

Figure 16


Effect of N/OFQ (5 mg/kg, IN) on Intestinal Transit of Fed SD Rats:
Comparison with Morphine (4 mg/kg, IN or 3 mg/kg, IP)
Intestinal Transit
(% of Vehicle Transit)
140.0
120.0
100.0
80.0
60.0
40.0
20.0
0.0
*
**
N/OFQ (5.0 mg/kg, IN; n=8)
Morphine (4.0 mg/kg, IN; n=6)
Morphine (3.0 mg/kg, IP; n=9)
* - p<0.05, ** p<0.01 vs Vehicle