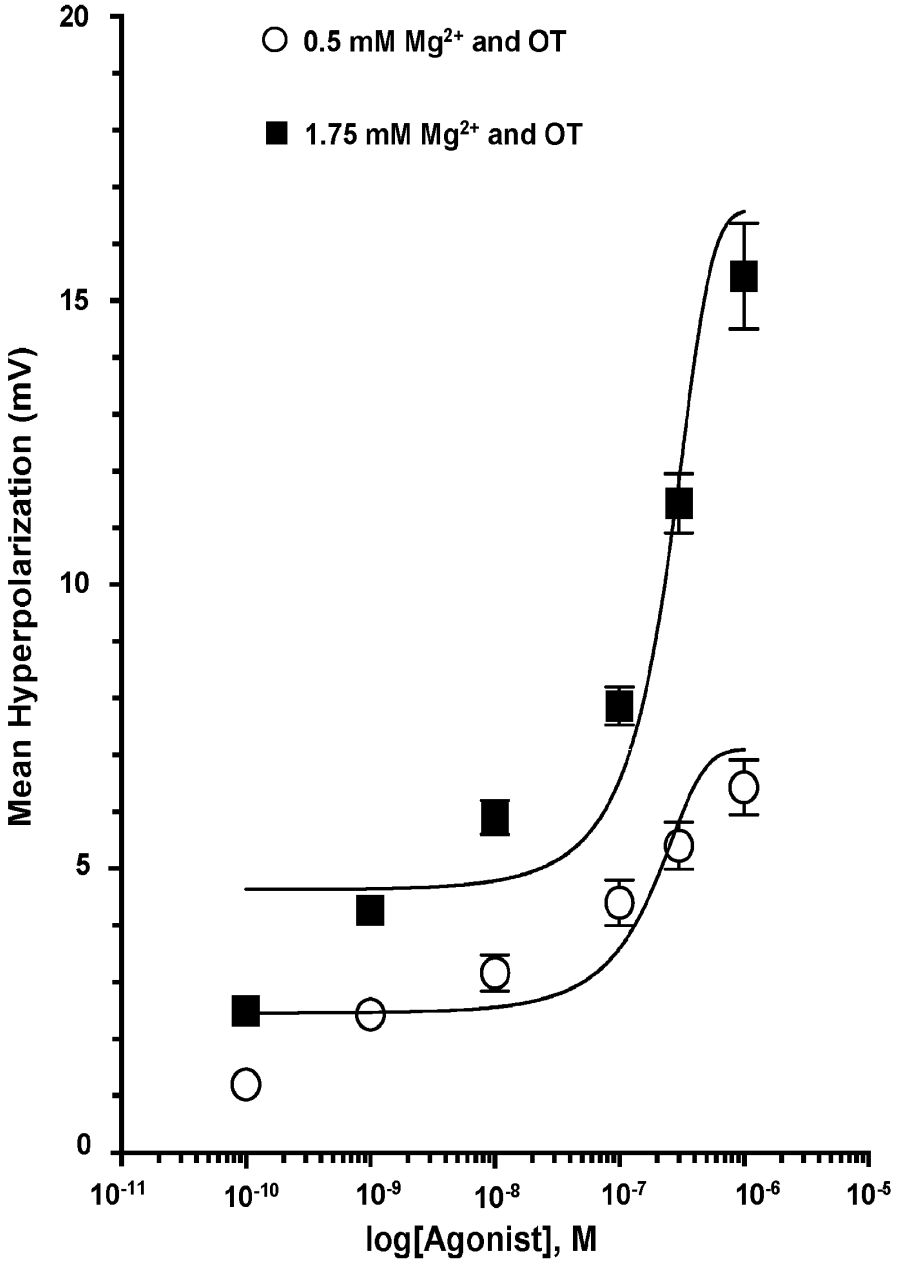
FIGURE 1


0.5 mM Mg2+ and OT
1.75 mM Mg2+ and OT
Mean Hyperpolarization (mV)
20
15
10
5
0
10-11
10-10
10-9
10-8
10-7
10-6
10-5
log[Agonist], M

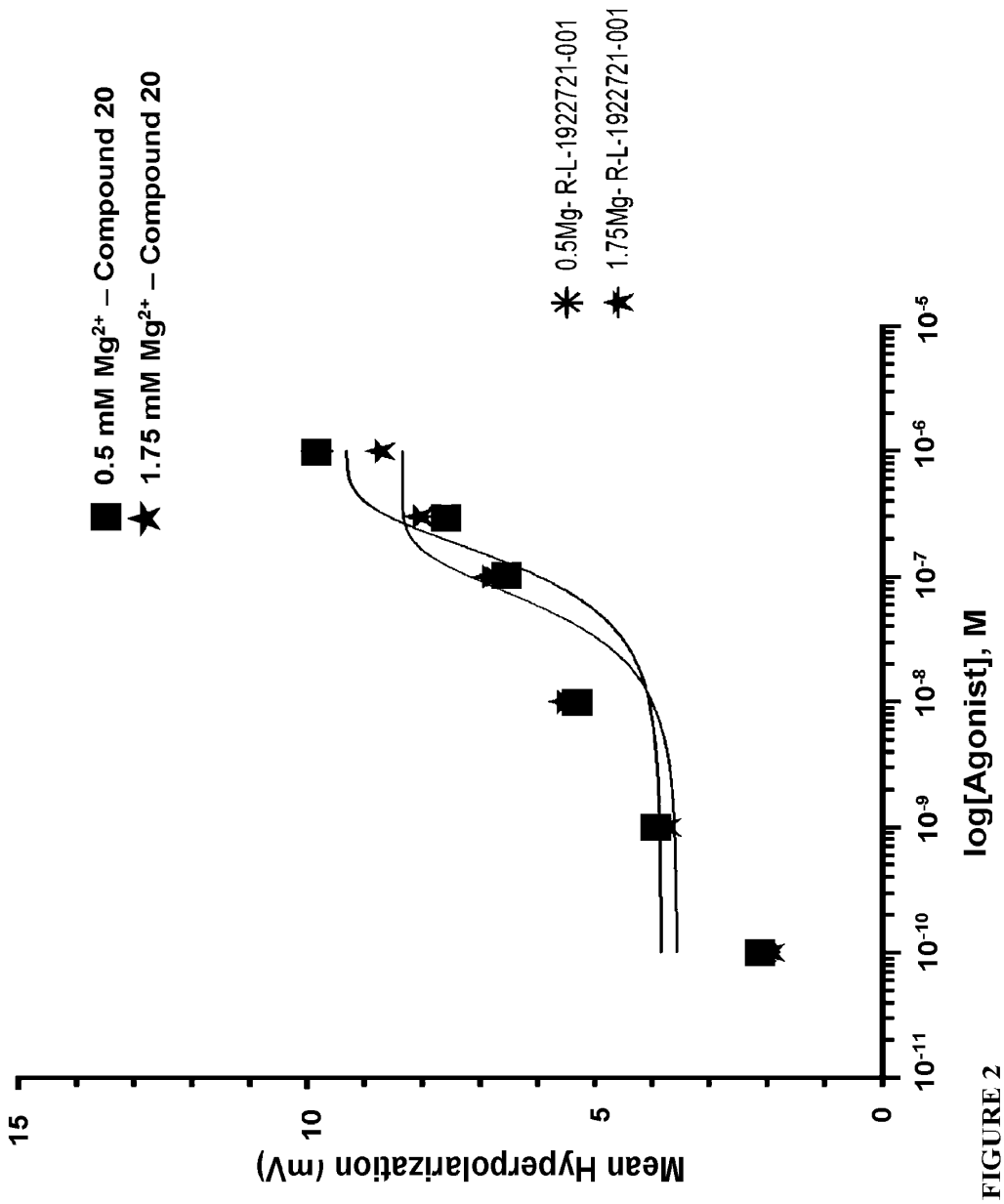

0.5 mM Mg2+ – Compound 20
1.75 mM Mg2+ – Compound 20
0.5Mg- R-L-1922721-001
1.75Mg- R-L-1922721-001
Mean Hyperpolarization (mV)
15
10
5
0
10-11
10-10
10-9
10-8
10-7
10-6
10-5
log[Agonist], M

FIGURE 2

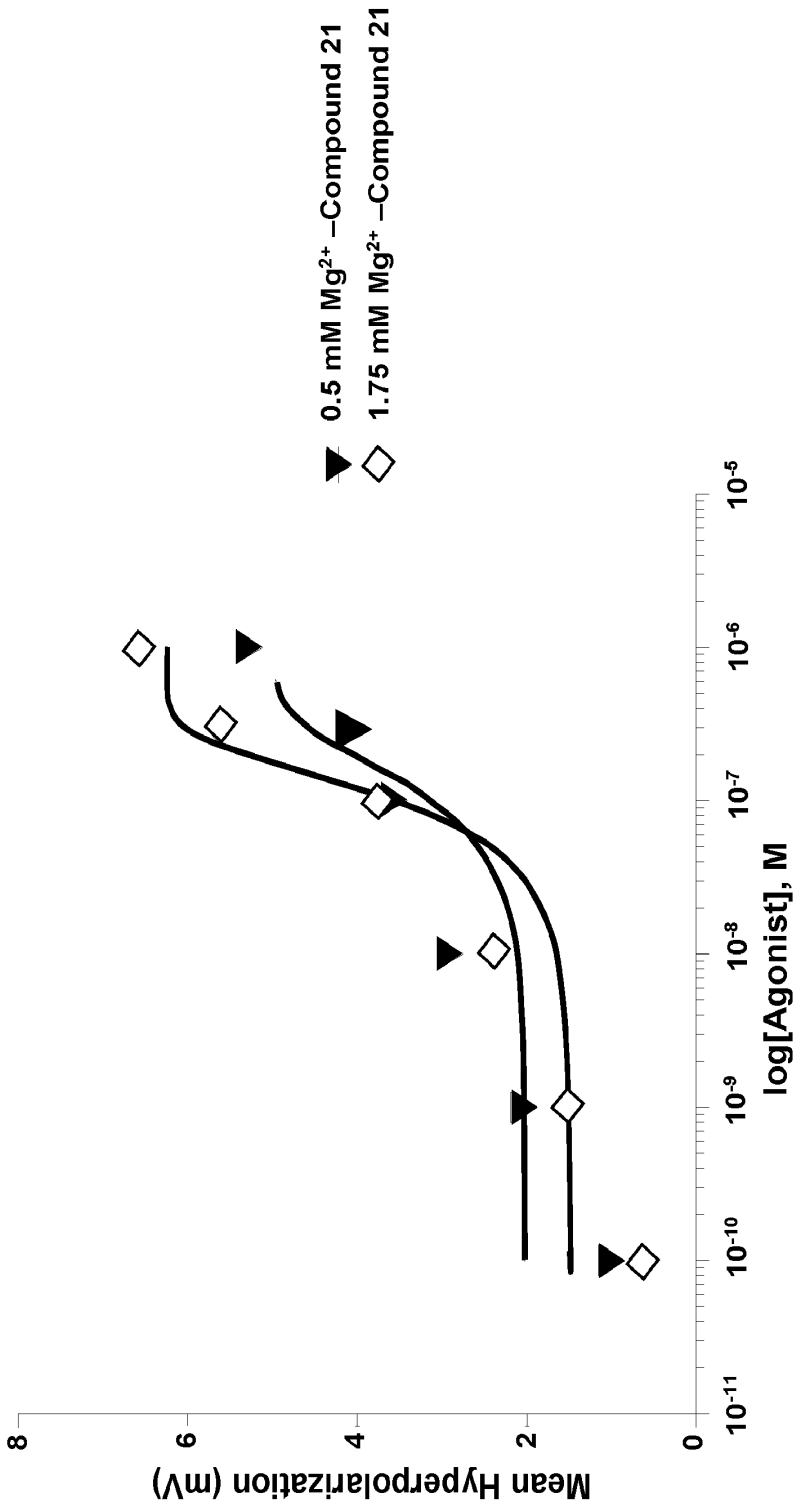

0.5 mM Mg2+ –Compound 21
1.75 mM Mg2+ –Compound 21
Mean Hyperpolarization (mV)
0
2
4
6
8
log[Agonist], M
10-11
10-10
10-9
10-8
10-7
10-6
10-5

FIGURE 3

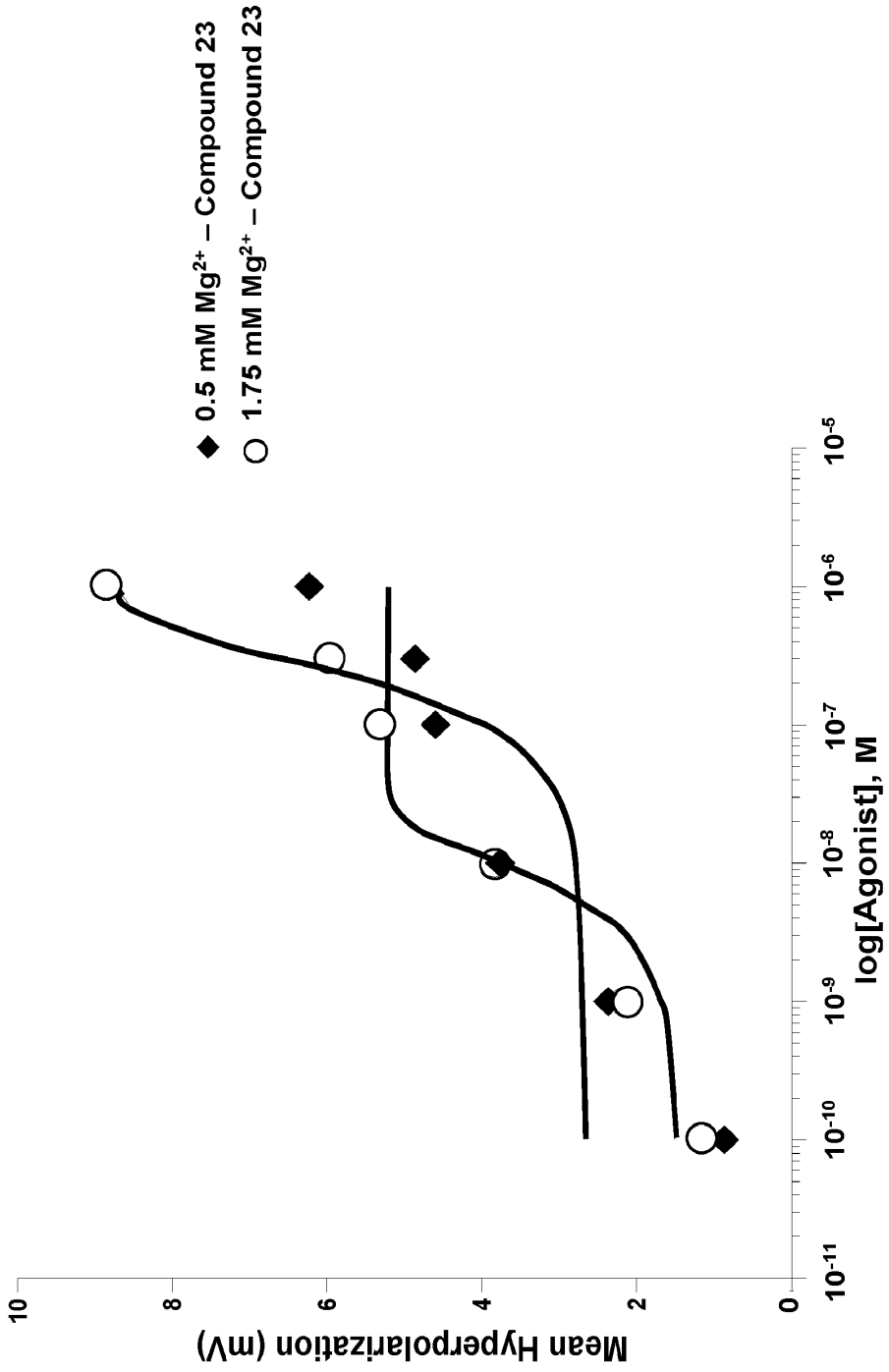

◆ 0.5 mM Mg2+ – Compound 23
○ 1.75 mM Mg2+ – Compound 23
Mean Hyperpolarization (mV)
0
2
4
6
8
10
10-11
10-10
10-9
10-8
10-7
10-6
10-5
log[Agonist], M

FIGURE 4

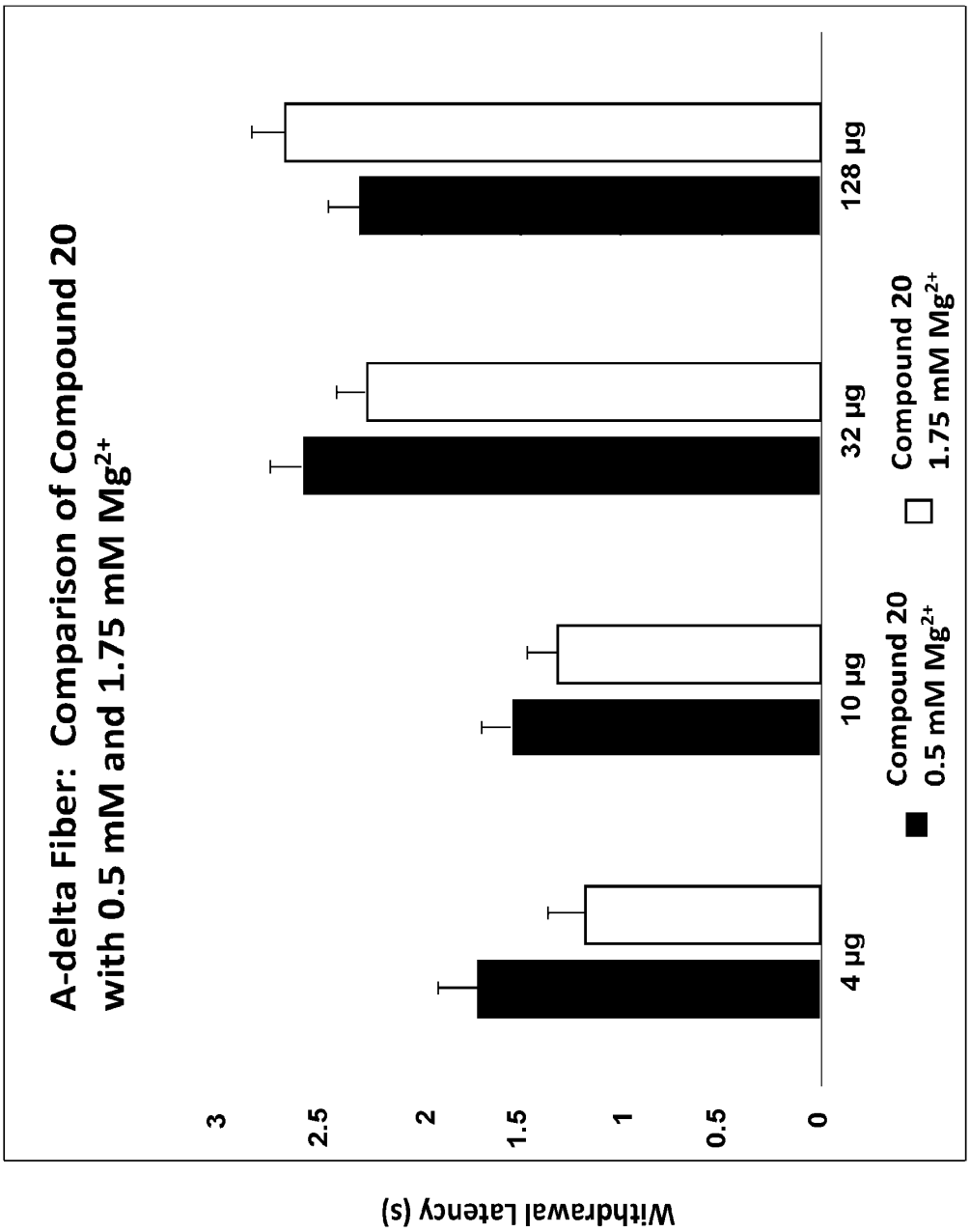

A-delta Fiber: Comparison of Compound 20
with 0.5 mM and 1.75 mM Mg2+
Withdrawal Latency (s)
0
0.5
1
1.5
2
2.5
3
4 µg
10 µg
32 µg
128 µg
Compound 20
0.5 mM Mg2+
Compound 20
1.75 mM Mg2+

FIGURE 5

FIGURE 6

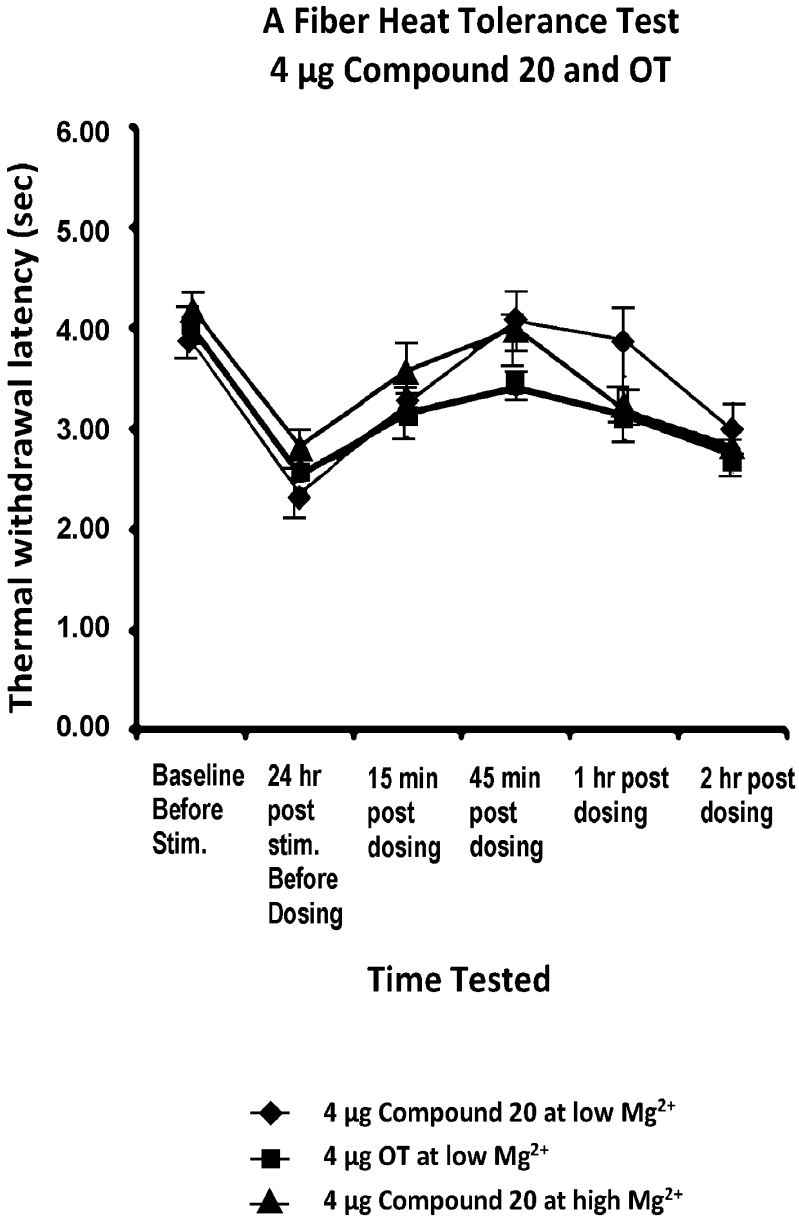

A Fiber Heat Tolerance Test
4 µg Compound 20 and OT
Thermal withdrawal latency (sec)
6.00
5.00
4.00
3.00
2.00
1.00
0.00
Baseline Before Stim.
24 hr post stim. Before Dosing
15 min post dosing
45 min post dosing
1 hr post dosing
2 hr post dosing
Time Tested
4 µg Compound 20 at low Mg2+
4 µg OT at low Mg2+
4 µg Compound 20 at high Mg2+

FIGURE 7

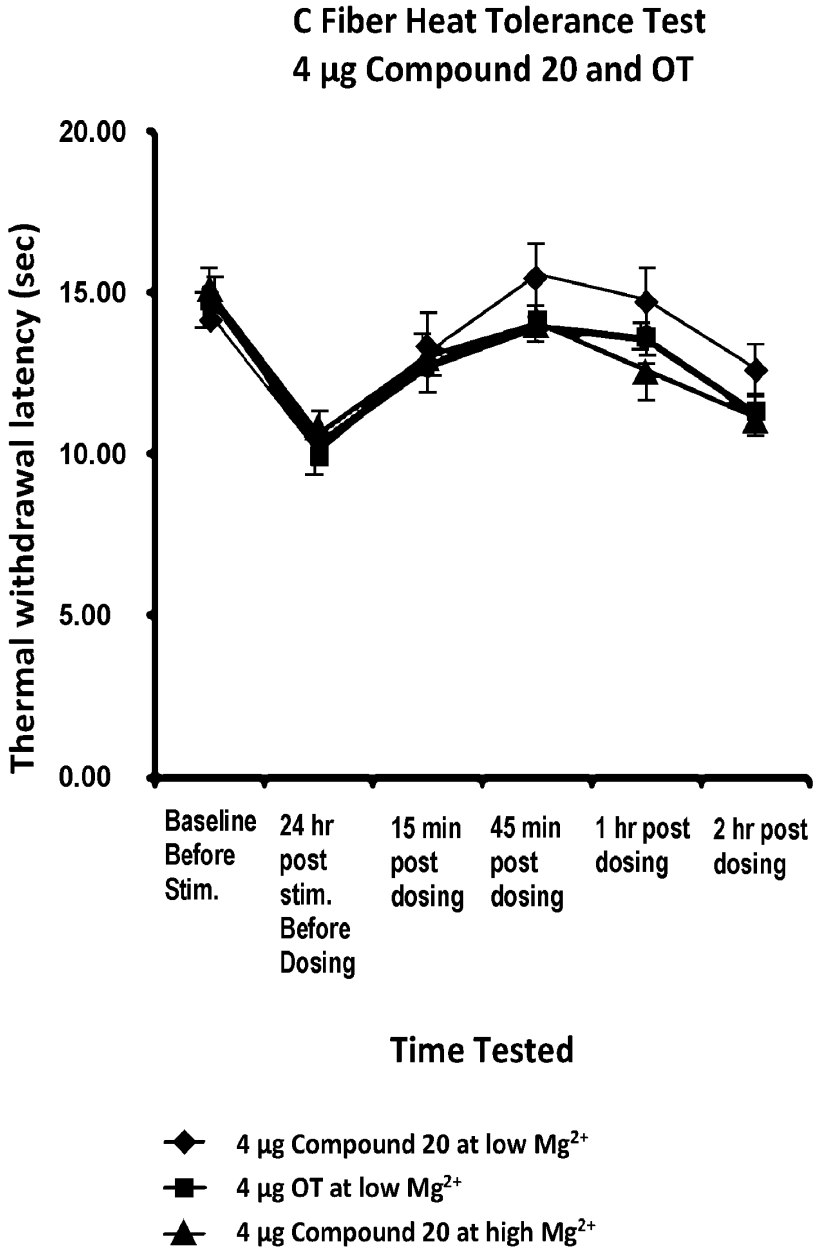

C Fiber Heat Tolerance Test
4 µg Compound 20 and OT
Thermal withdrawal latency (sec)
20.00
15.00
10.00
5.00
0.00
Baseline Before Stim.
24 hr post stim. Before Dosing
15 min post dosing
45 min post dosing
1 hr post dosing
2 hr post dosing
Time Tested
4 µg Compound 20 at low Mg2+
4 µg OT at low Mg2+
4 µg Compound 20 at high Mg2+

FIGURE 8

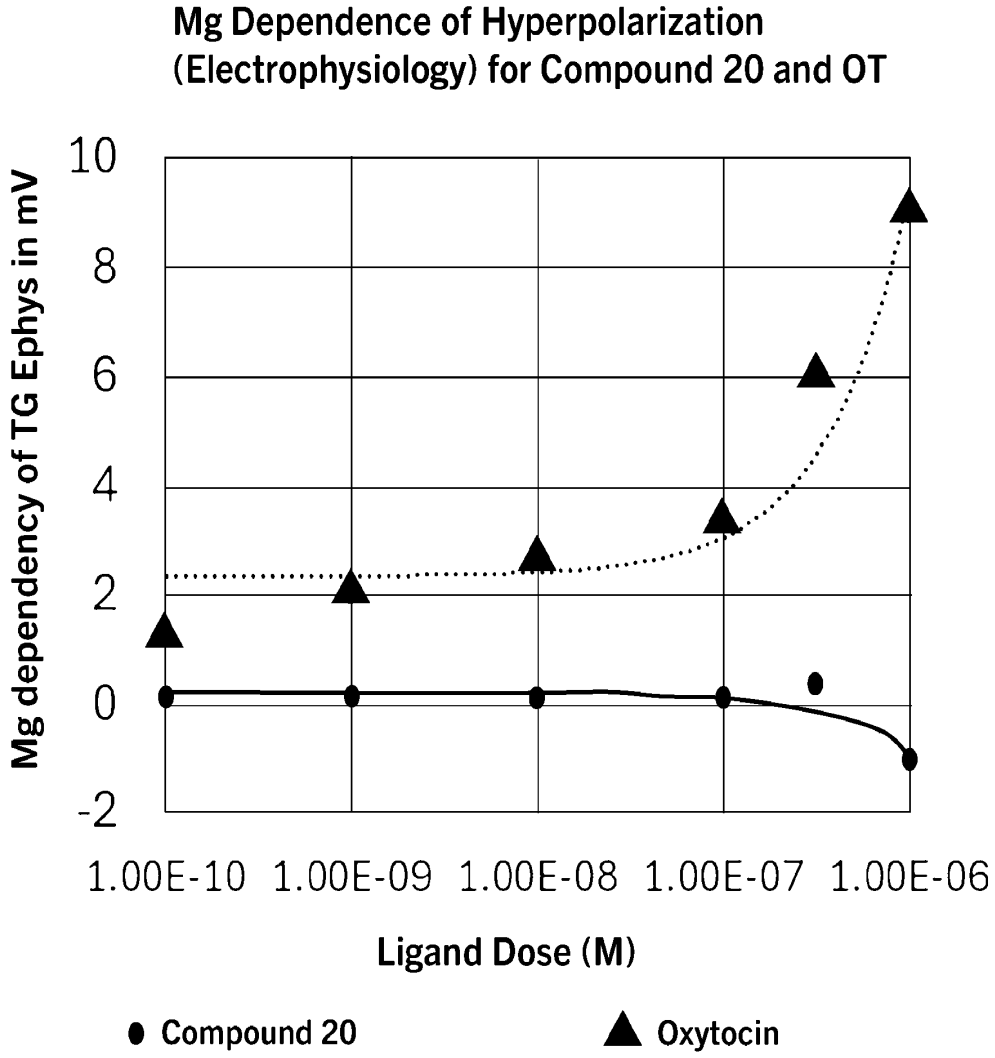
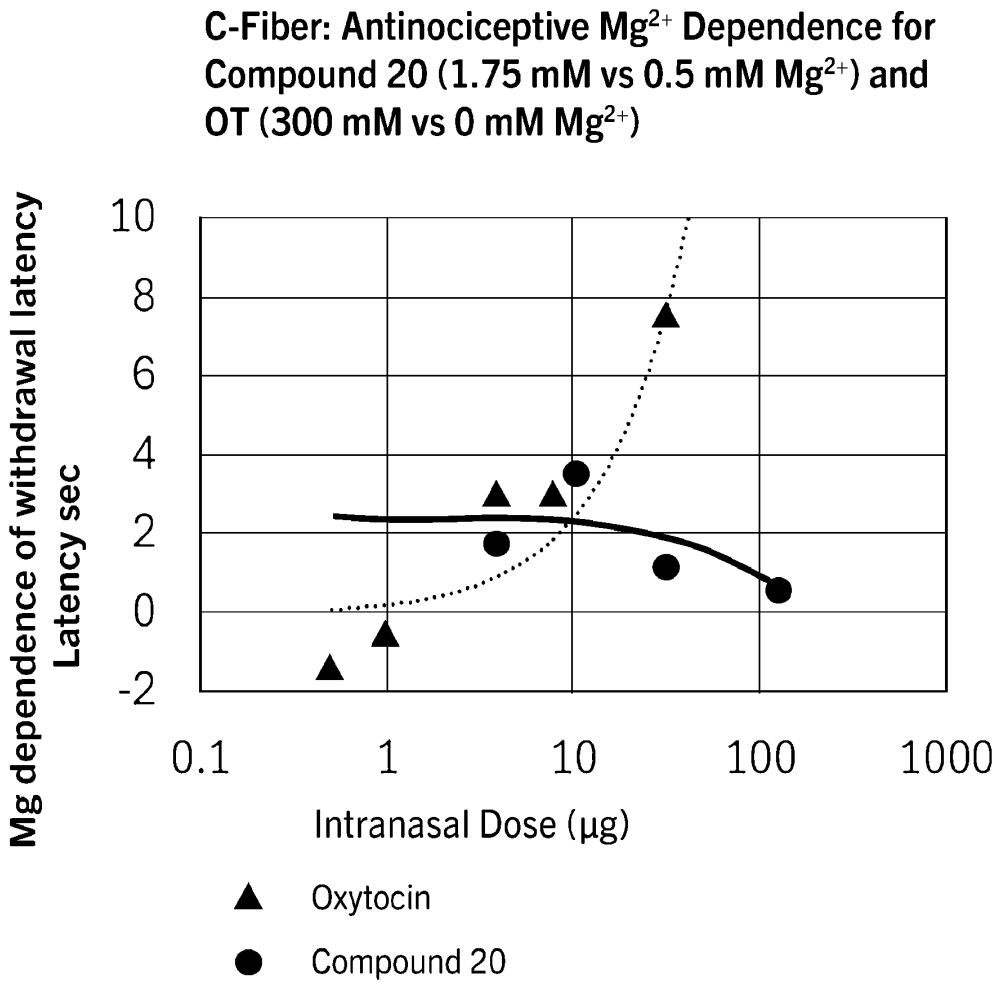

Mg Dependence of Hyperpolarization
(Electrophysiology) for Compound 20 and OT
Mg dependency of TG Ephys in mV
10
8
6
4
2
0
-2
1.00E-10
1.00E-09
1.00E-08
1.00E-07
1.00E-06
Ligand Dose (M)
Compound 20
Oxytocin

FIGURE 9


C-Fiber: Antinociceptive Mg2+ Dependence for Compound 20 (1.75 mM vs 0.5 mM Mg2+) and OT (300 mM vs 0 mM Mg2+)
Mg dependence of withdrawal latency
Latency sec
10
8
6
4
2
0
-2
0.1
1
10
100
1000
Intranasal Dose (µg)
Oxytocin
Compound 20