Fig. 1

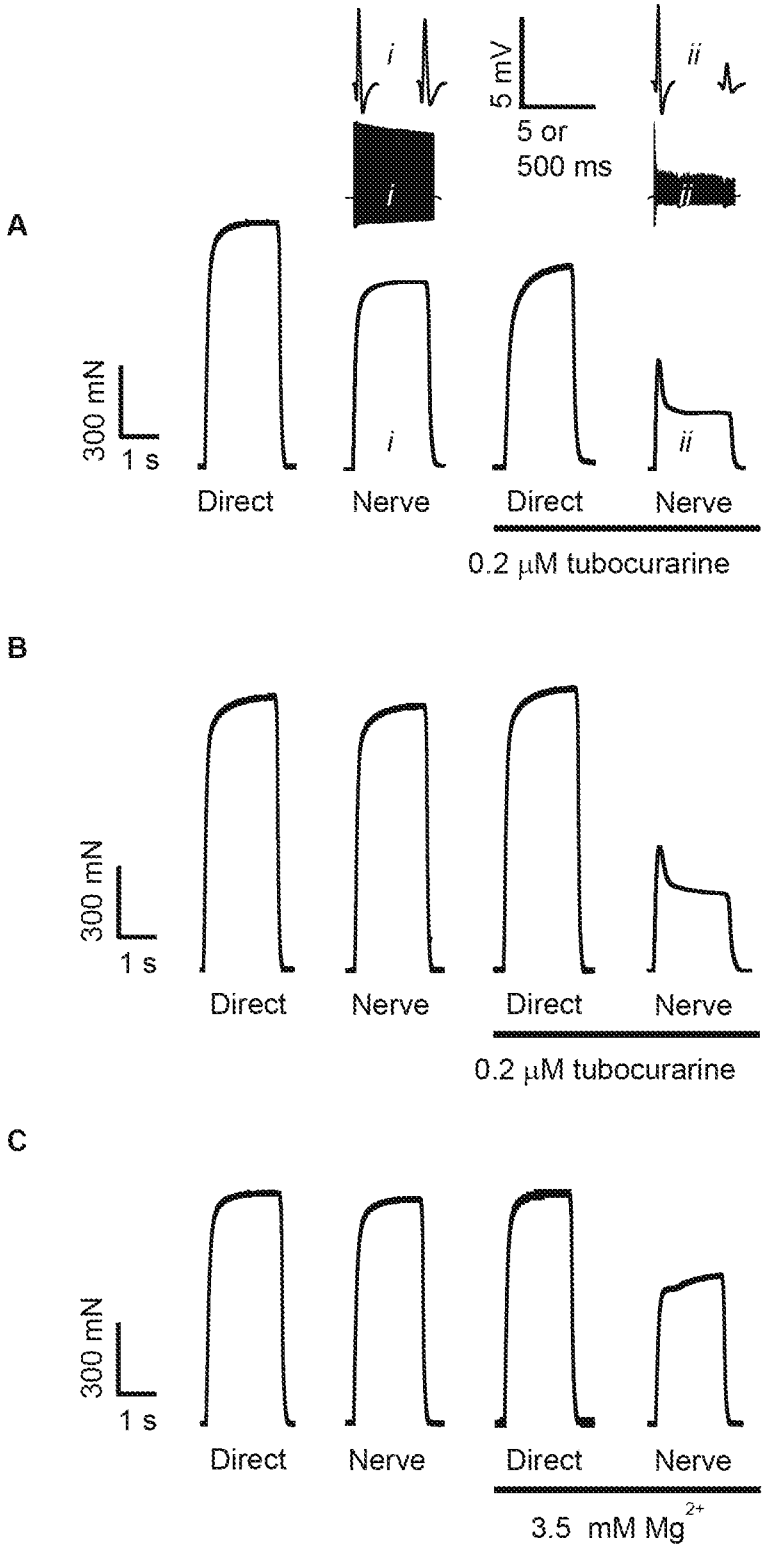

A
i
ii
5 mV
5 or
500 ms
300 mN
1 s
Direct
Nerve
Direct
Nerve
0.2 μM tubocurarine
B
300 mN
1 s
Direct
Nerve
Direct
Nerve
0.2 μM tubocurarine
C
300 mN
1 s
Direct
Nerve
Direct
Nerve
3.5 mM Mg2+

Fig. 2

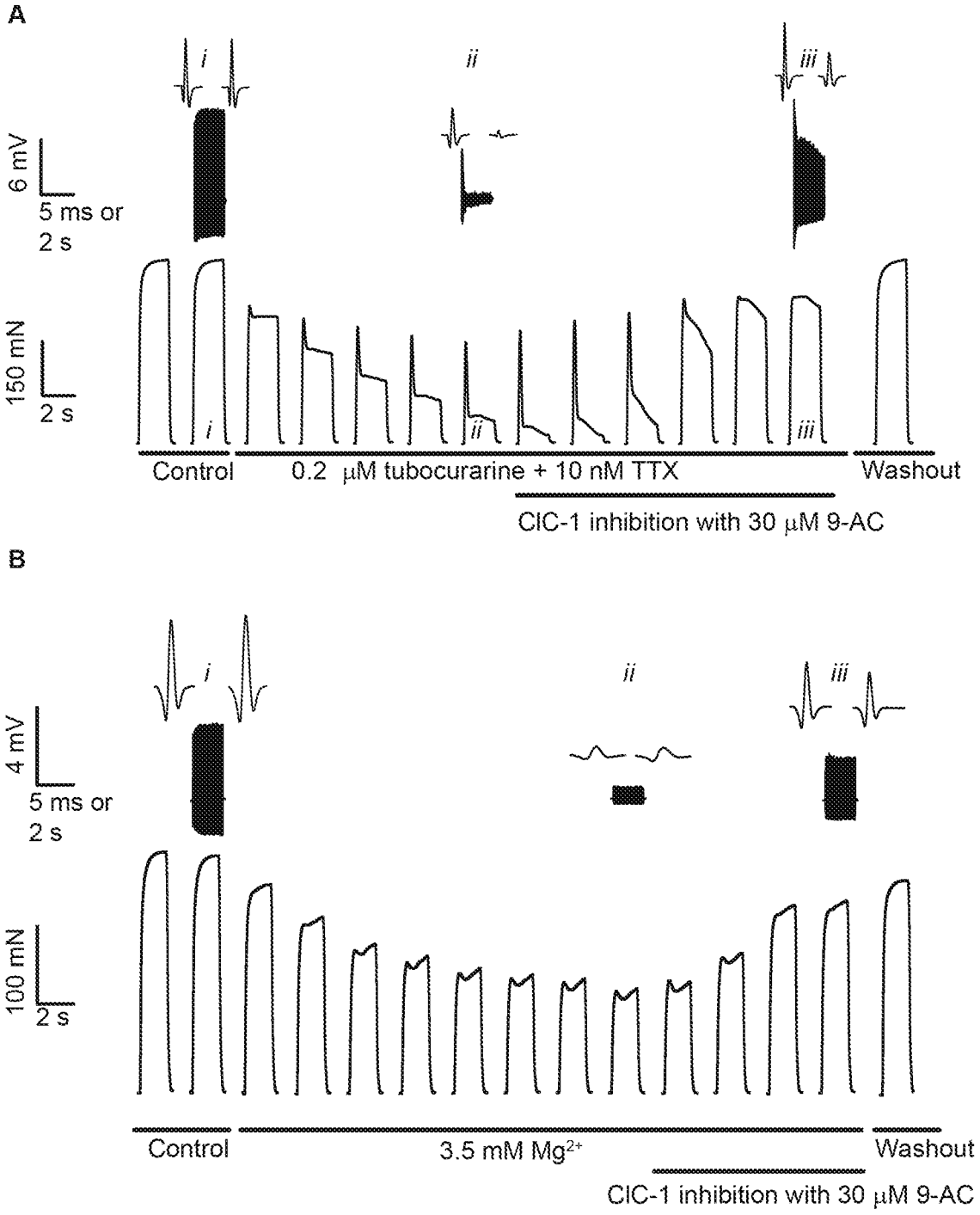

A
i
ii
iii
6 mV
5 ms or
2 s
150 mN
2 s
Control
0.2 μM tubocurarine + 10 nM TTX
Washout
ClC-1 inhibition with 30 μM 9-AC
B
4 mV
5 ms or
2 s
100 mN
2 s
Control
3.5 mM Mg2+
Washout
ClC-1 inhibition with 30 μM 9-AC

Fig. 3.

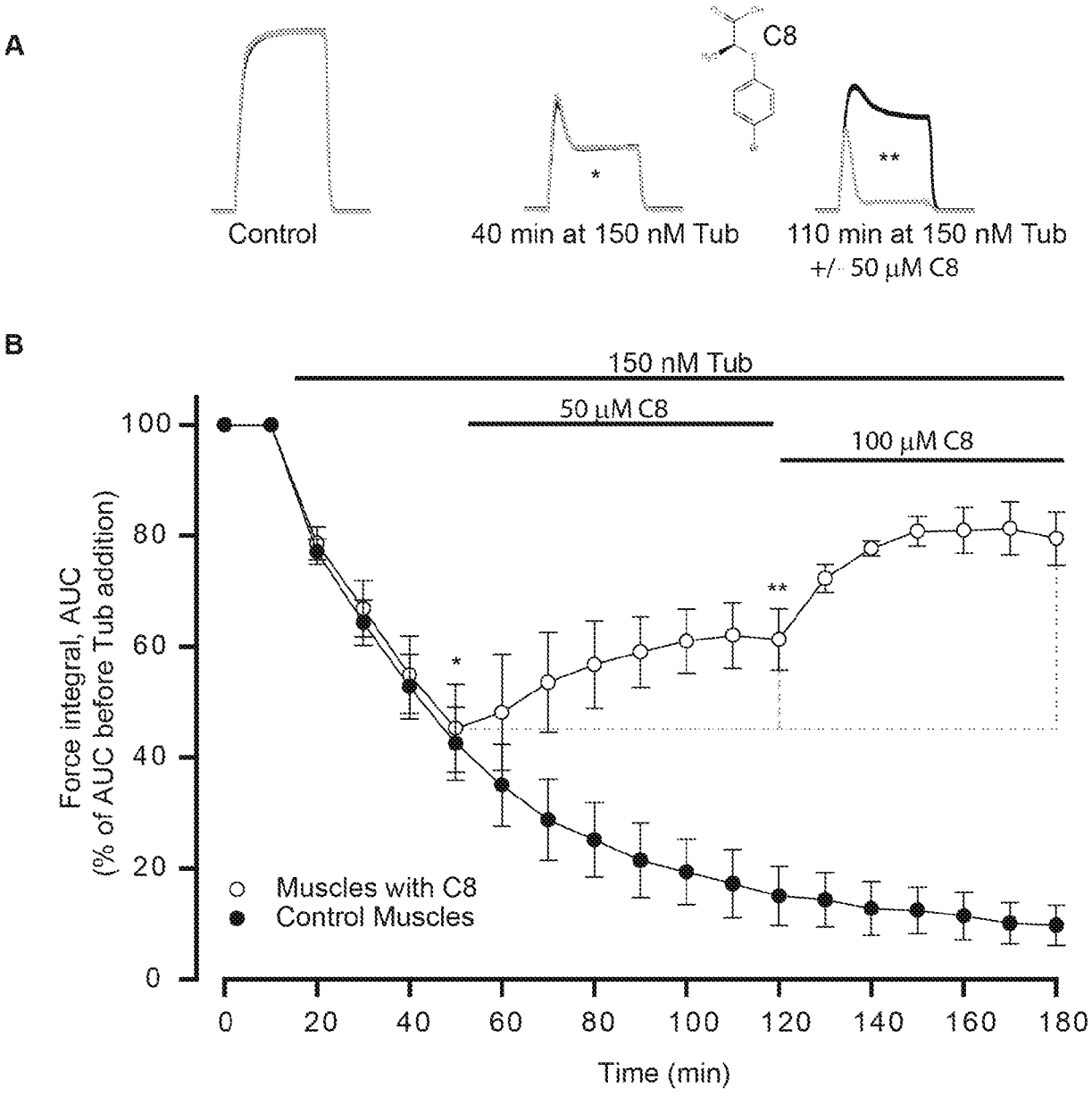

A
C8
*
**
Control
40 min at 150 nM Tub
110 min at 150 nM Tub
+/- 50 µM C8
B
150 nM Tub
50 µM C8
100 µM C8
Force integral, AUC
(% of AUC before Tub addition)
100
80
60
40
20
0
*
**
Muscles with C8
Control Muscles
0
20
40
60
80
100
120
140
160
180
Time (min)

Fig. 4

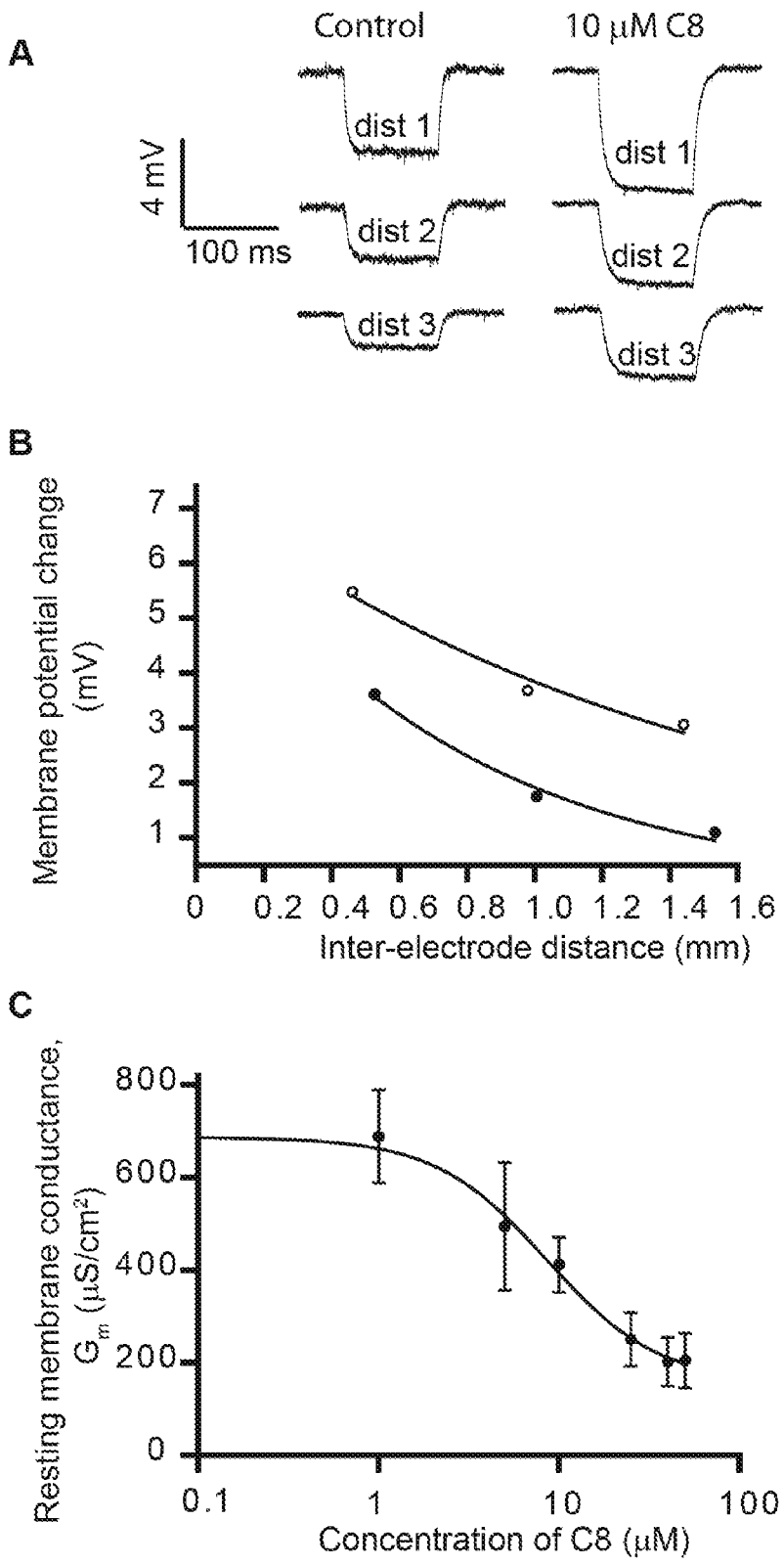

A
Control
10 μM C8
dist 1
dist 2
dist 3
4 mV
100 ms
B
Membrane potential change (mV)
Inter-electrode distance (mm)
C
Resting membrane conductance, G_m (μS/cm²)
Concentration of C8 (μM)

Fig. 5

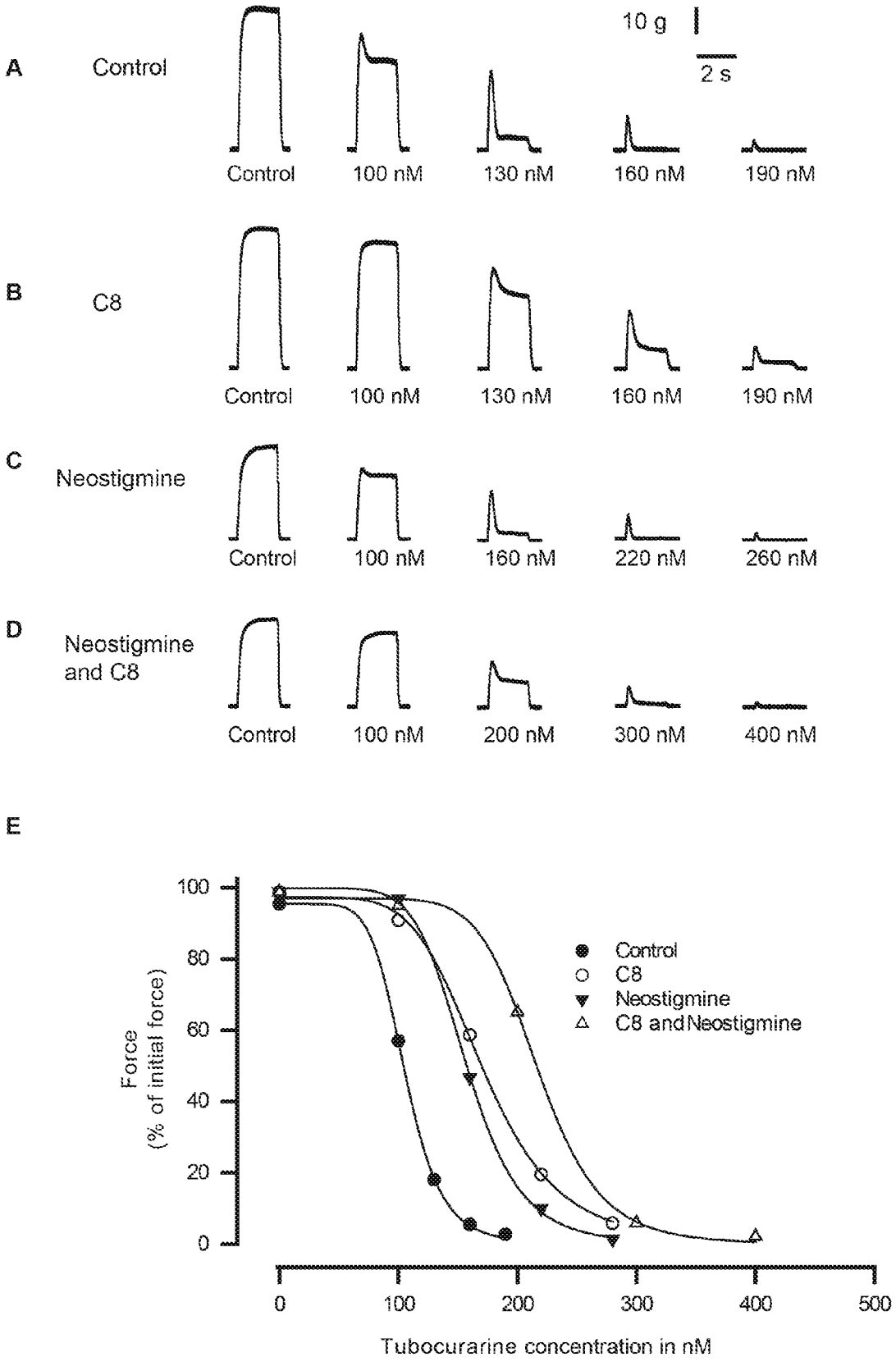

A
Control
10 g
2 s
Control
100 nM
130 nM
160 nM
190 nM
B
C8
Control
100 nM
130 nM
160 nM
190 nM
C
Neostigmine
Control
100 nM
160 nM
220 nM
260 nM
D
Neostigmine
and C8
Control
100 nM
200 nM
300 nM
400 nM
E
Force
(% of initial force)
100
80
60
40
20
0
Control
C8
Neostigmine
C8 and Neostigmine
0
100
200
300
400
500
Tubocurarine concentration in nM

Fig. 6

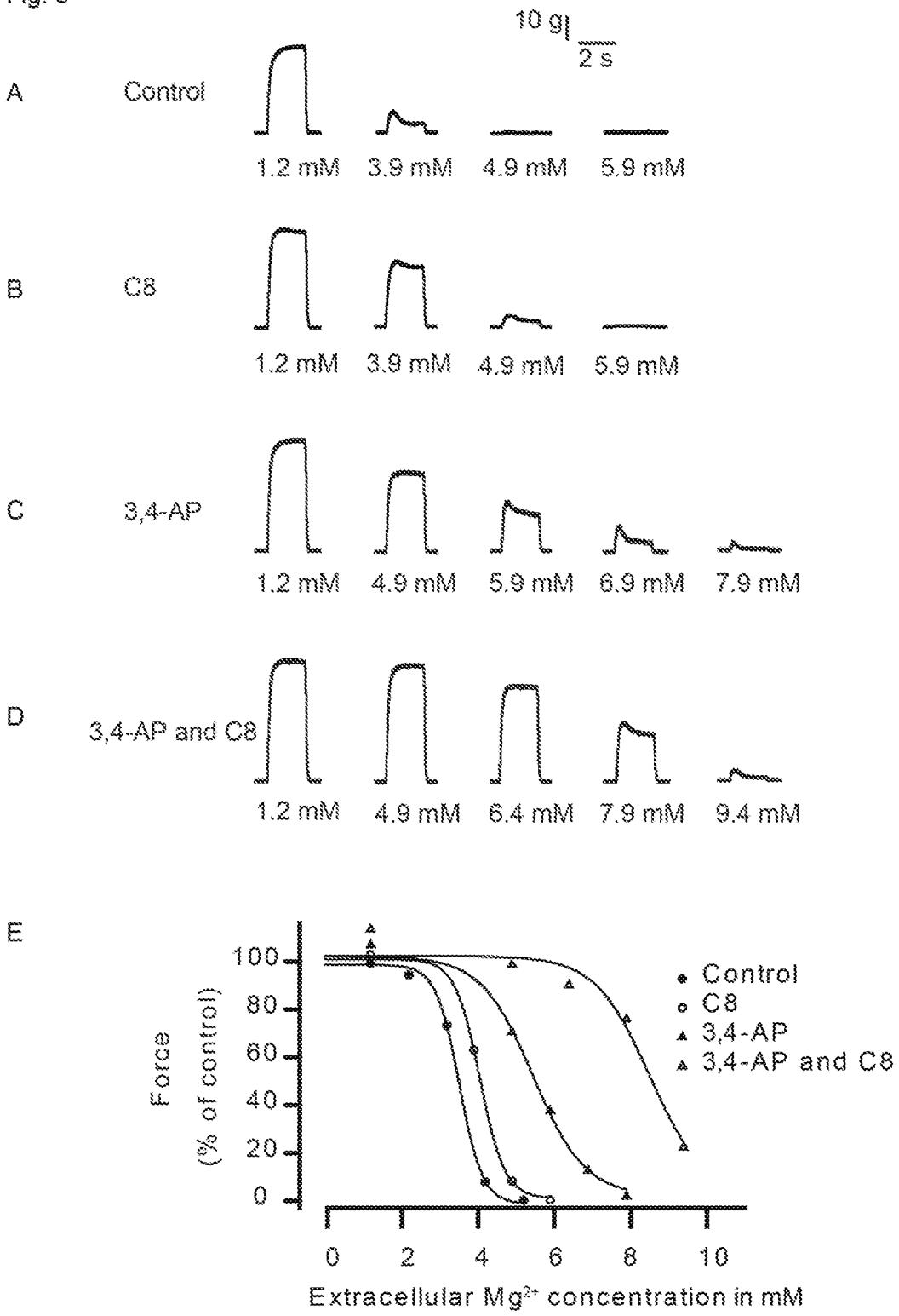

10 g
2 s
A
Control
1.2 mM
3.9 mM
4.9 mM
5.9 mM
B
C8
1.2 mM
3.9 mM
4.9 mM
5.9 mM
C
3,4-AP
1.2 mM
4.9 mM
5.9 mM
6.9 mM
7.9 mM
D
3,4-AP and C8
1.2 mM
4.9 mM
6.4 mM
7.9 mM
9.4 mM
E
Force
(% of control)
100
80
60
40
20
0
0
2
4
6
8
10
Extracellular Mg2+ concentration in mM
Control
C8
3,4-AP
3,4-AP and C8

Fig. 7

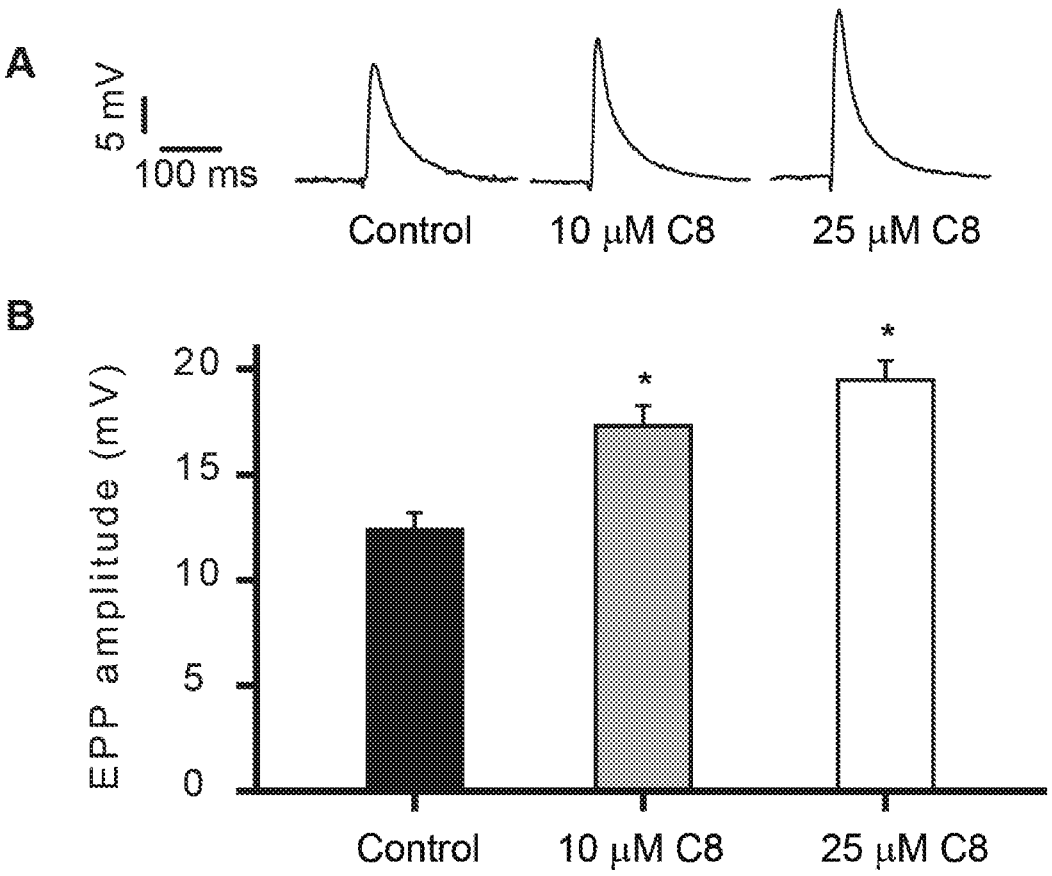
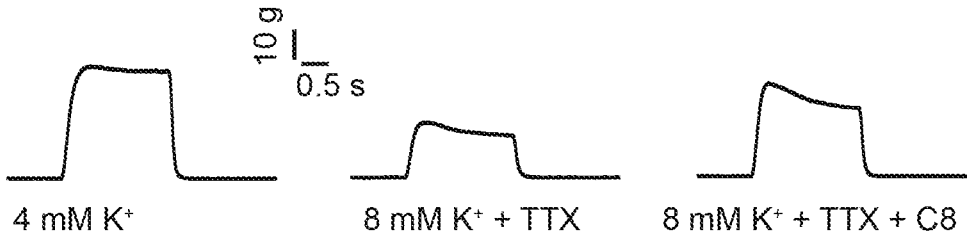

A
5 mV
100 ms
Control
10 μM C8
25 μM C8
B
EPP amplitude (mV)
20
15
10
5
0
*
*
Control
10 μM C8
25 μM C8

Fig. 8

A


10 g
0.5 s
4 mM K+
8 mM K+ + TTX
8 mM K+ + TTX + C8

B

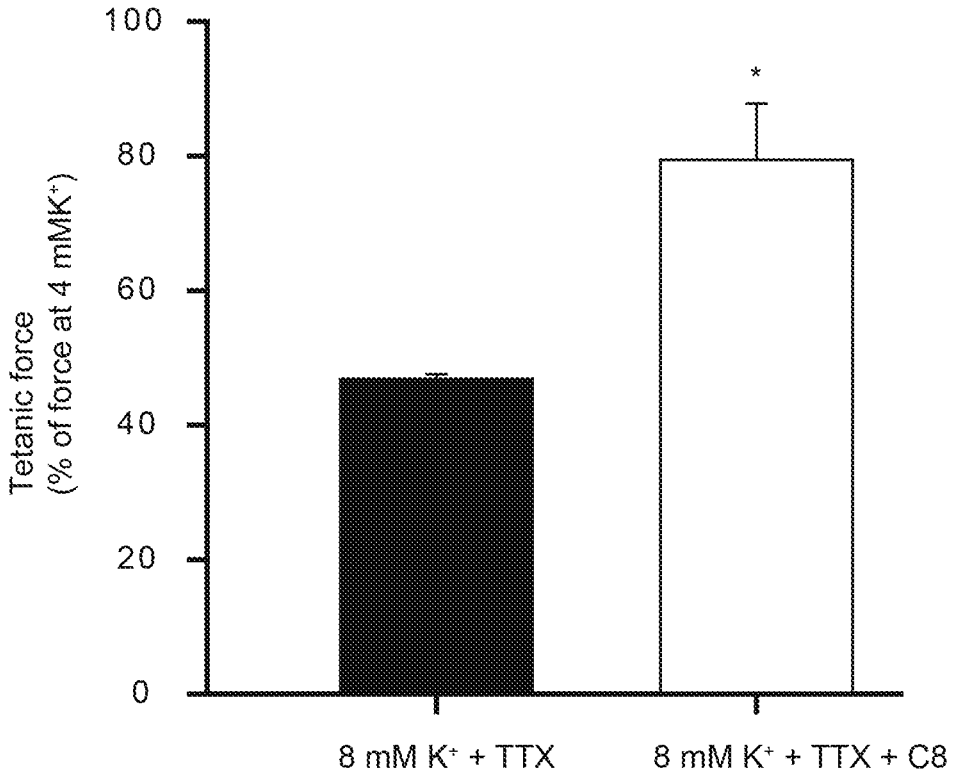

100
80
60
40
20
0
Tetanic force
(% of force at 4 mMK+)
*
8 mM K+ + TTX
8 mM K+ + TTX + C8

Fig. 9

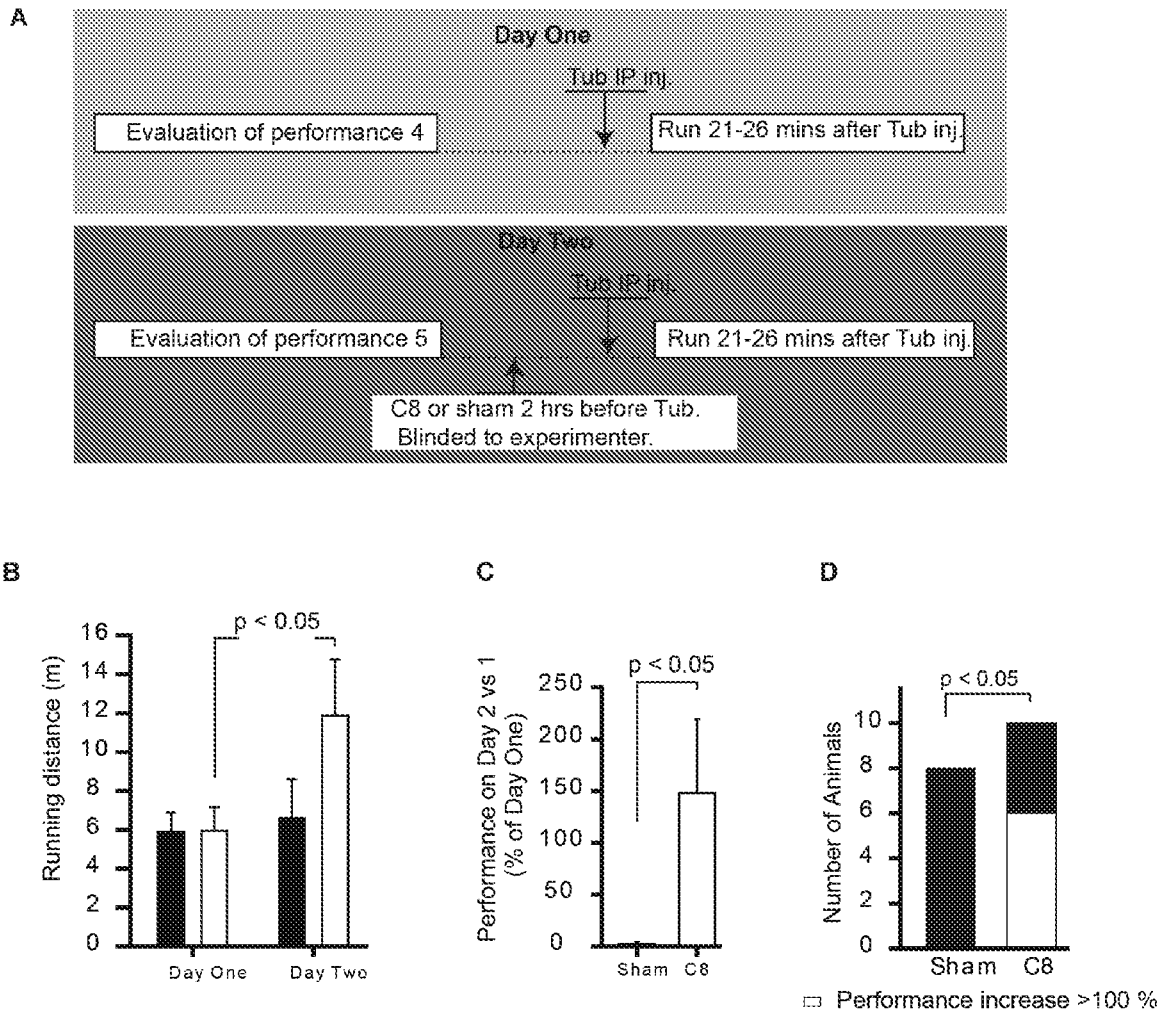
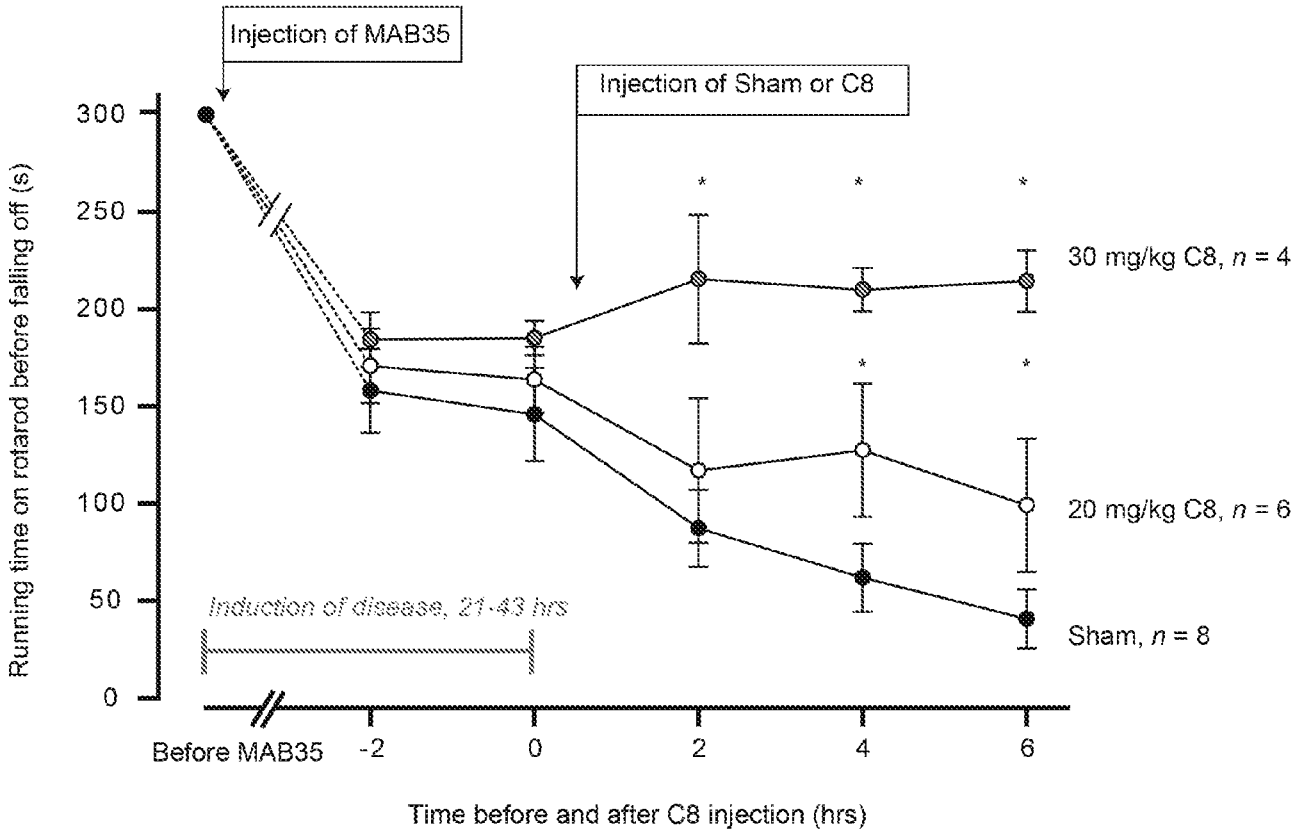

A
Day One
Tub IP inj.
Evaluation of performance 4
Run 21-26 mins after Tub inj.
Day Two
Tub IP inj.
Evaluation of performance 5
Run 21-26 mins after Tub inj.
C8 or sham 2 hrs before Tub.
Blinded to experimenter.
B
p < 0.05
Running distance (m)
16
14
12
10
8
6
4
2
0
Day One
Day Two
C
p < 0.05
Performance on Day 2 vs 1 (% of Day One)
250
200
150
100
50
0
Sham
C8
D
p < 0.05
Number of Animals
10
8
6
4
2
0
Sham
C8
Performance increase >100 %

Fig. 10


Injection of MAB35
Injection of Sham or C8
Running time on rotarod before falling off (s)
300
250
200
150
100
50
0
*
*
*
*
*
30 mg/kg C8, n = 4
20 mg/kg C8, n = 6
Sham, n = 8
Induction of disease, 21-43 hrs
Before MAB35
-2
0
2
4
6
Time before and after C8 injection (hrs)