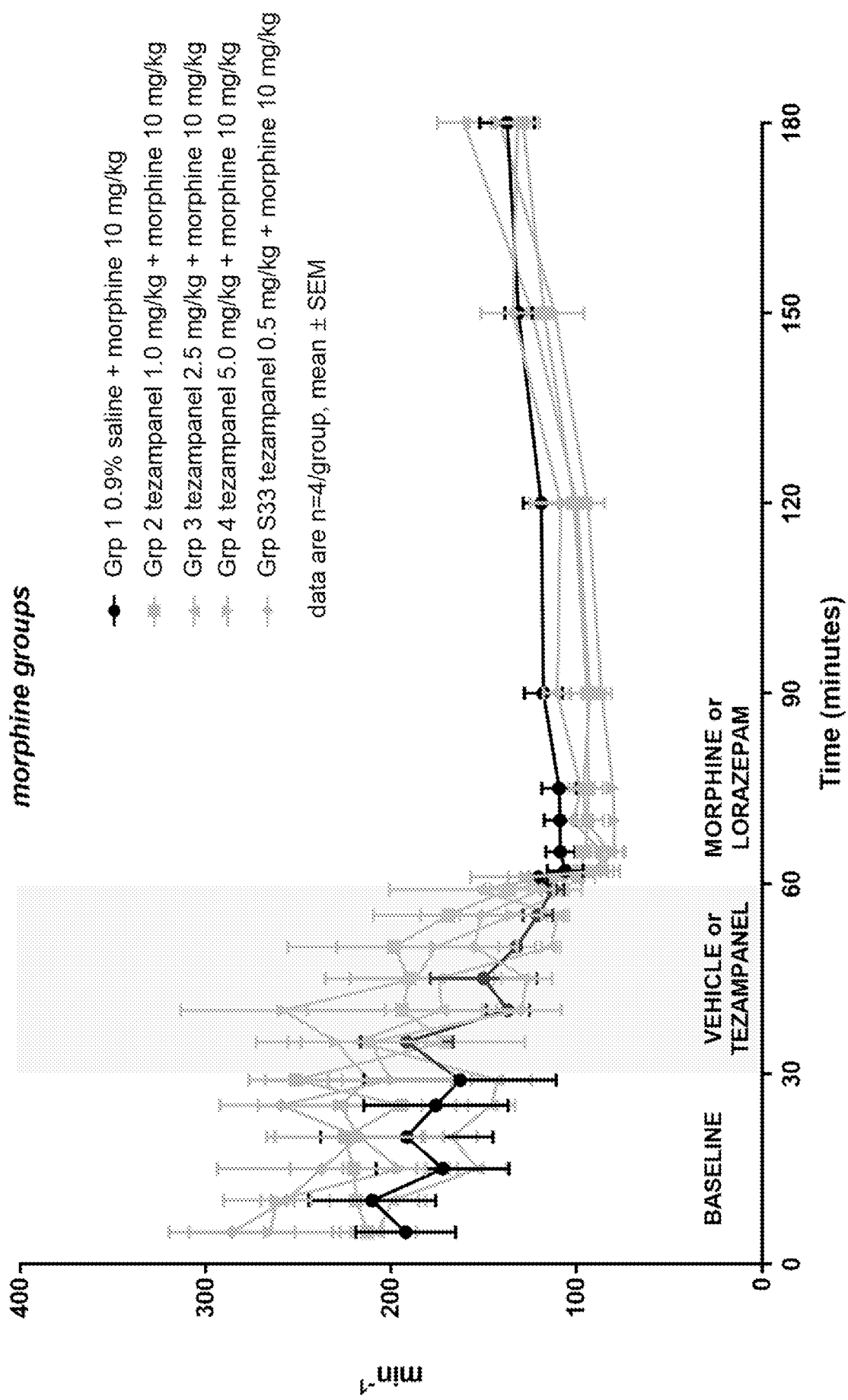

Respiratory Rate
morphine groups
Grp 1 0.9% saline + morphine 10 mg/kg
Grp 2 tezampanel 1.0 mg/kg + morphine 10 mg/kg
Grp 3 tezampanel 2.5 mg/kg + morphine 10 mg/kg
Grp 4 tezampanel 5.0 mg/kg + morphine 10 mg/kg
Grp S33 tezampanel 0.5 mg/kg + morphine 10 mg/kg
data are n=4/group, mean ± SEM
min-1
400
300
200
100
0
0
30
60
90
120
150
180
Time (minutes)
BASELINE
VEHICLE or TEZAMPANEL
MORPHINE or LORAZEPAM

Figure 1A

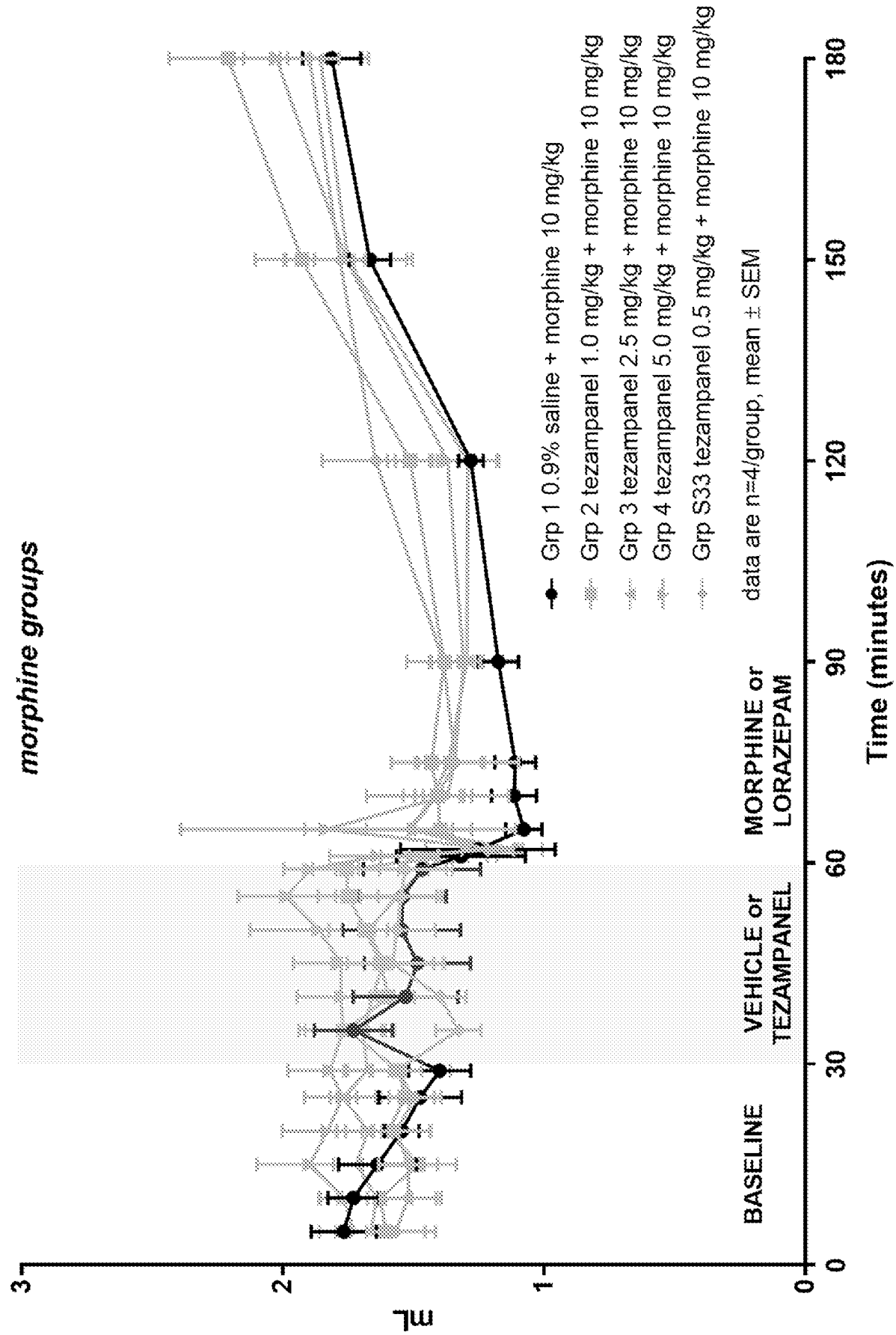

Tidal Volume
morphine groups
mL
3
2
1
0
0
30
60
90
120
150
180
Time (minutes)
BASELINE
VEHICLE or TEZAMPANEL
MORPHINE or LORAZEPAM
Grp 1 0.9% saline + morphine 10 mg/kg
Grp 2 tezampanel 1.0 mg/kg + morphine 10 mg/kg
Grp 3 tezampanel 2.5 mg/kg + morphine 10 mg/kg
Grp 4 tezampanel 5.0 mg/kg + morphine 10 mg/kg
Grp S33 tezampanel 0.5 mg/kg + morphine 10 mg/kg
data are n=4/group, mean ± SEM

Figure 1B

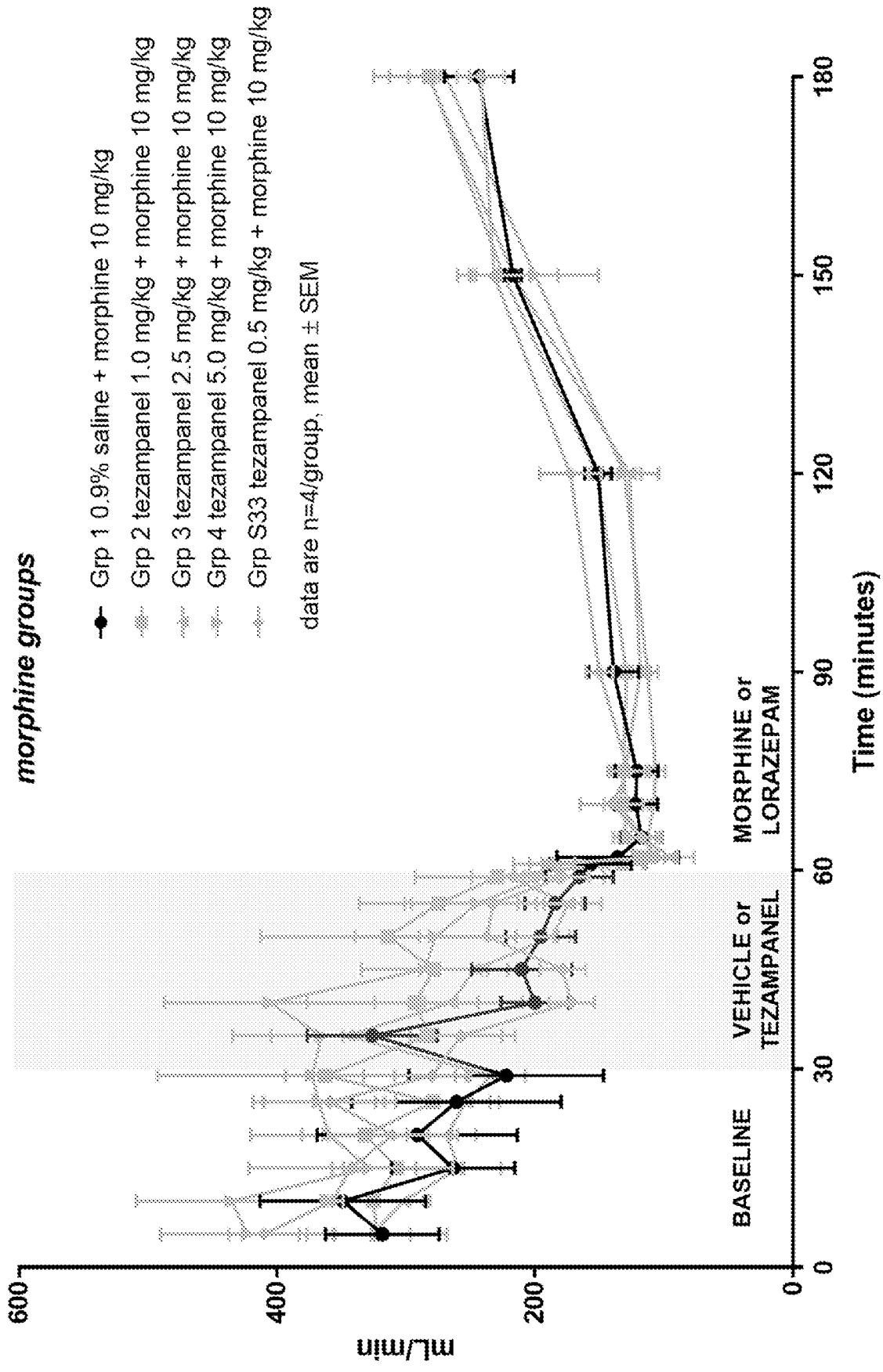

Minute Volume
morphine groups
Grp 1 0.9% saline + morphine 10 mg/kg
Grp 2 tezampanel 1.0 mg/kg + morphine 10 mg/kg
Grp 3 tezampanel 2.5 mg/kg + morphine 10 mg/kg
Grp 4 tezampanel 5.0 mg/kg + morphine 10 mg/kg
Grp S33 tezampanel 0.5 mg/kg + morphine 10 mg/kg
data are n=4/group, mean ± SEM
mL/min
600
400
200
0
0
30
60
90
120
150
180
Time (minutes)
BASELINE
VEHICLE or TEZAMPANEL
MORPHINE or LORAZEPAM

Figure 1C

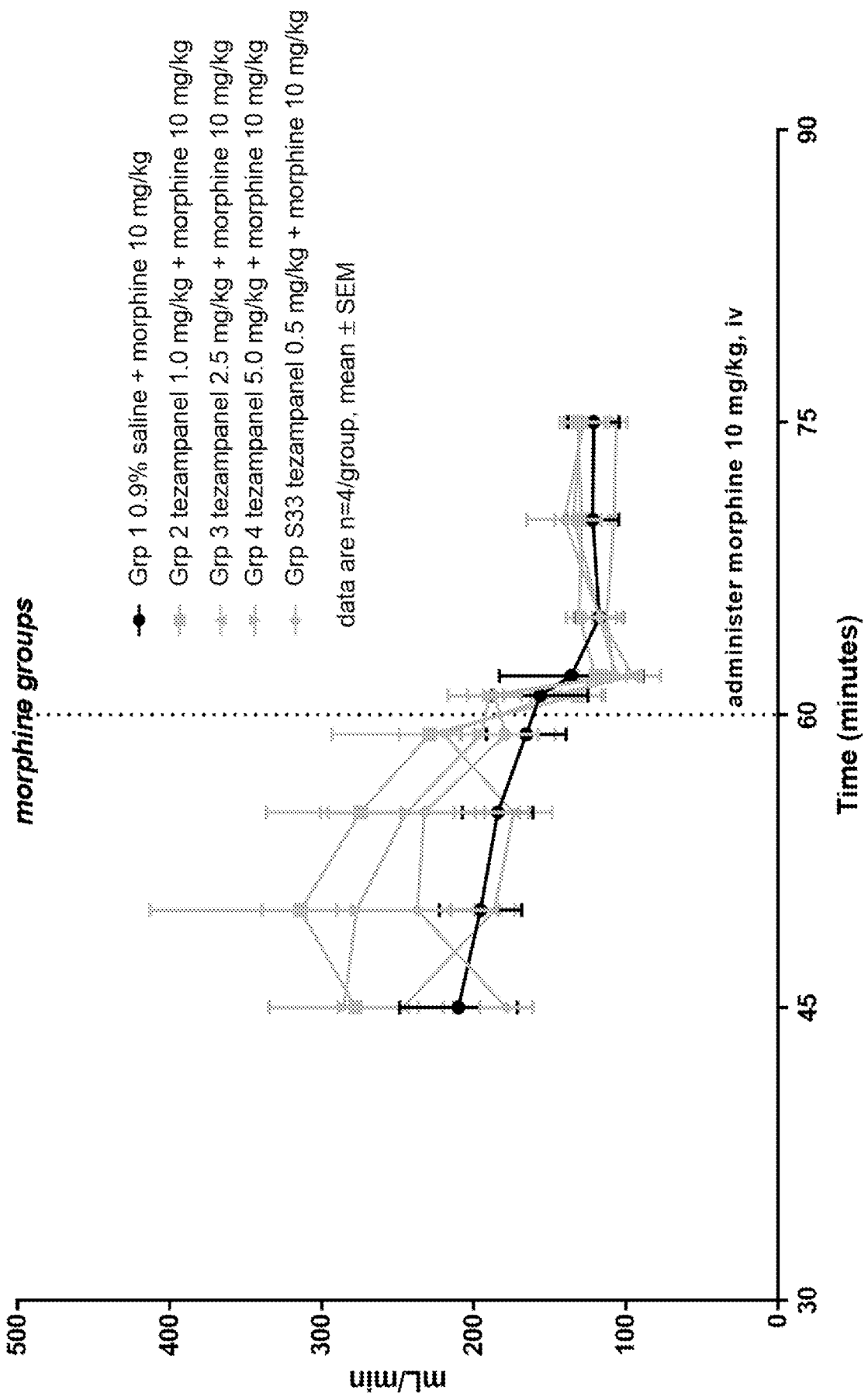

Minute Volume
morphine groups
Grp 1 0.9% saline + morphine 10 mg/kg
Grp 2 tezampanel 1.0 mg/kg + morphine 10 mg/kg
Grp 3 tezampanel 2.5 mg/kg + morphine 10 mg/kg
Grp 4 tezampanel 5.0 mg/kg + morphine 10 mg/kg
Grp S33 tezampanel 0.5 mg/kg + morphine 10 mg/kg
data are n=4/group, mean ± SEM
administer morphine 10 mg/kg, iv
mL/min
Time (minutes)
500
400
300
200
100
0
30
45
60
75
90

Figure 1D

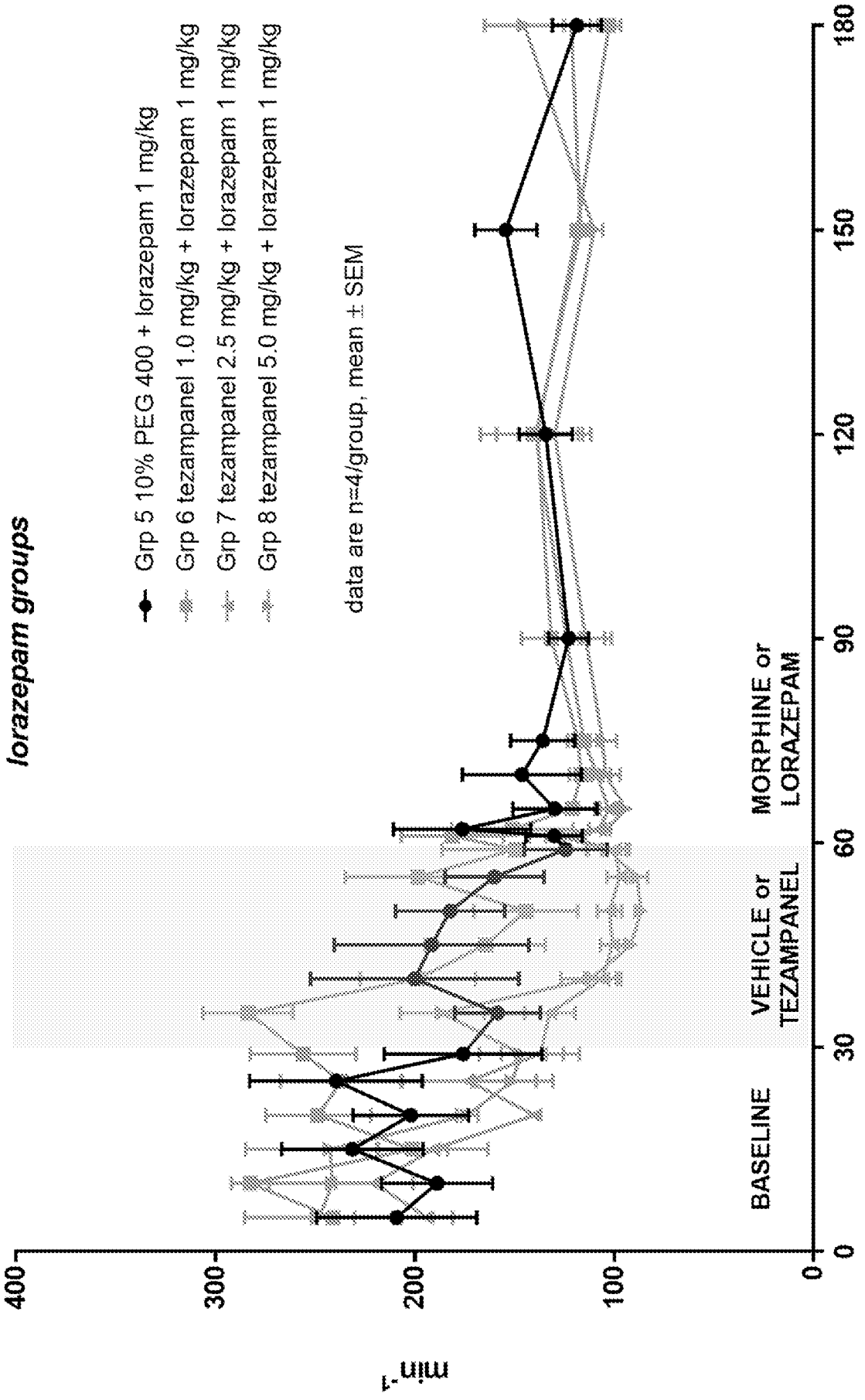

Respiratory Rate
lorazepam groups
Grp 5 10% PEG 400 + lorazepam 1 mg/kg
Grp 6 tezampanel 1.0 mg/kg + lorazepam 1 mg/kg
Grp 7 tezampanel 2.5 mg/kg + lorazepam 1 mg/kg
Grp 8 tezampanel 5.0 mg/kg + lorazepam 1 mg/kg
data are n=4/group, mean ± SEM
BASELINE
VEHICLE or TEZAMPANEL
MORPHINE or LORAZEPAM
min-1
Time (minutes)
0
100
200
300
400
0
30
60
90
120
150
180

Figure 2A

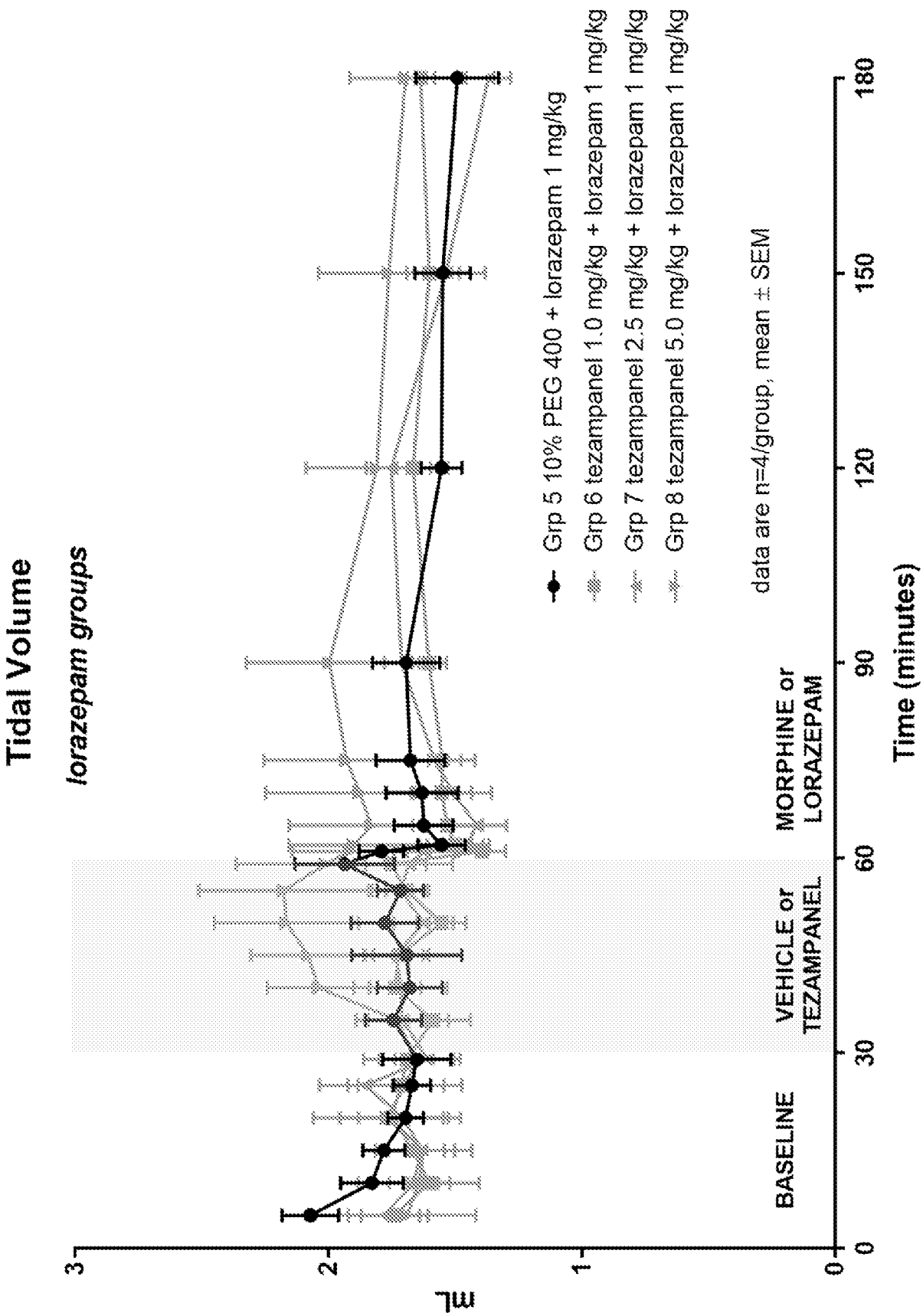

Tidal Volume
lorazepam groups
mL
3
2
1
0
0
30
60
90
120
150
180
Time (minutes)
BASELINE
VEHICLE or TEZAMPANEL
MORPHINE or LORAZEPAM
Grp 5 10% PEG 400 + lorazepam 1 mg/kg
Grp 6 tezampanel 1.0 mg/kg + lorazepam 1 mg/kg
Grp 7 tezampanel 2.5 mg/kg + lorazepam 1 mg/kg
Grp 8 tezampanel 5.0 mg/kg + lorazepam 1 mg/kg
data are n=4/group, mean ± SEM

Figure 2B

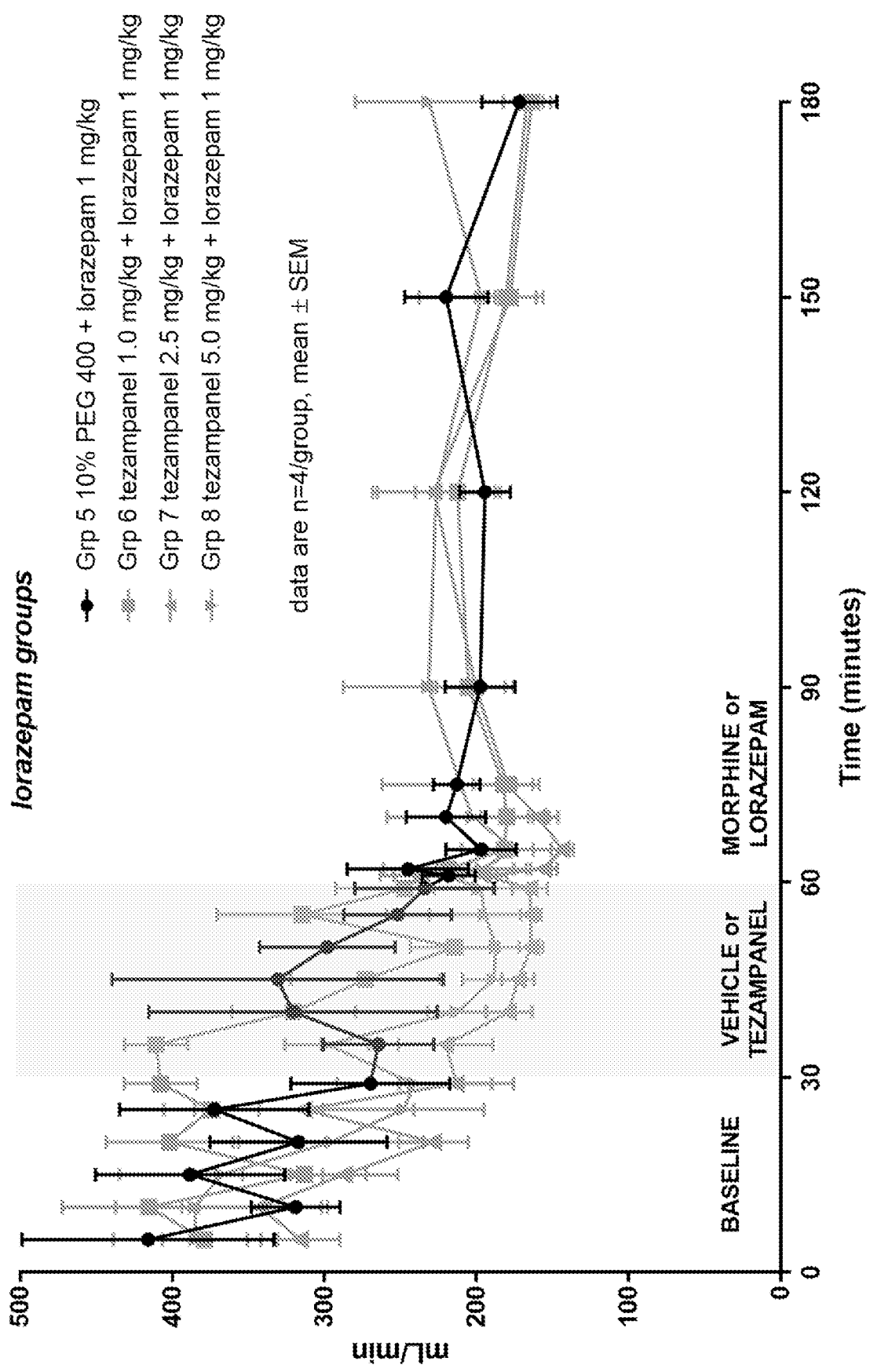

Minute Volume
lorazepam groups
Grp 5 10% PEG 400 + lorazepam 1 mg/kg
Grp 6 tezampanel 1.0 mg/kg + lorazepam 1 mg/kg
Grp 7 tezampanel 2.5 mg/kg + lorazepam 1 mg/kg
Grp 8 tezampanel 5.0 mg/kg + lorazepam 1 mg/kg
data are n=4/group, mean ± SEM
mL/min
500
400
300
200
100
0
BASELINE
VEHICLE or TEZAMPANEL
MORPHINE or LORAZEPAM
0
30
60
90
120
150
180
Time (minutes)

Figure 2C

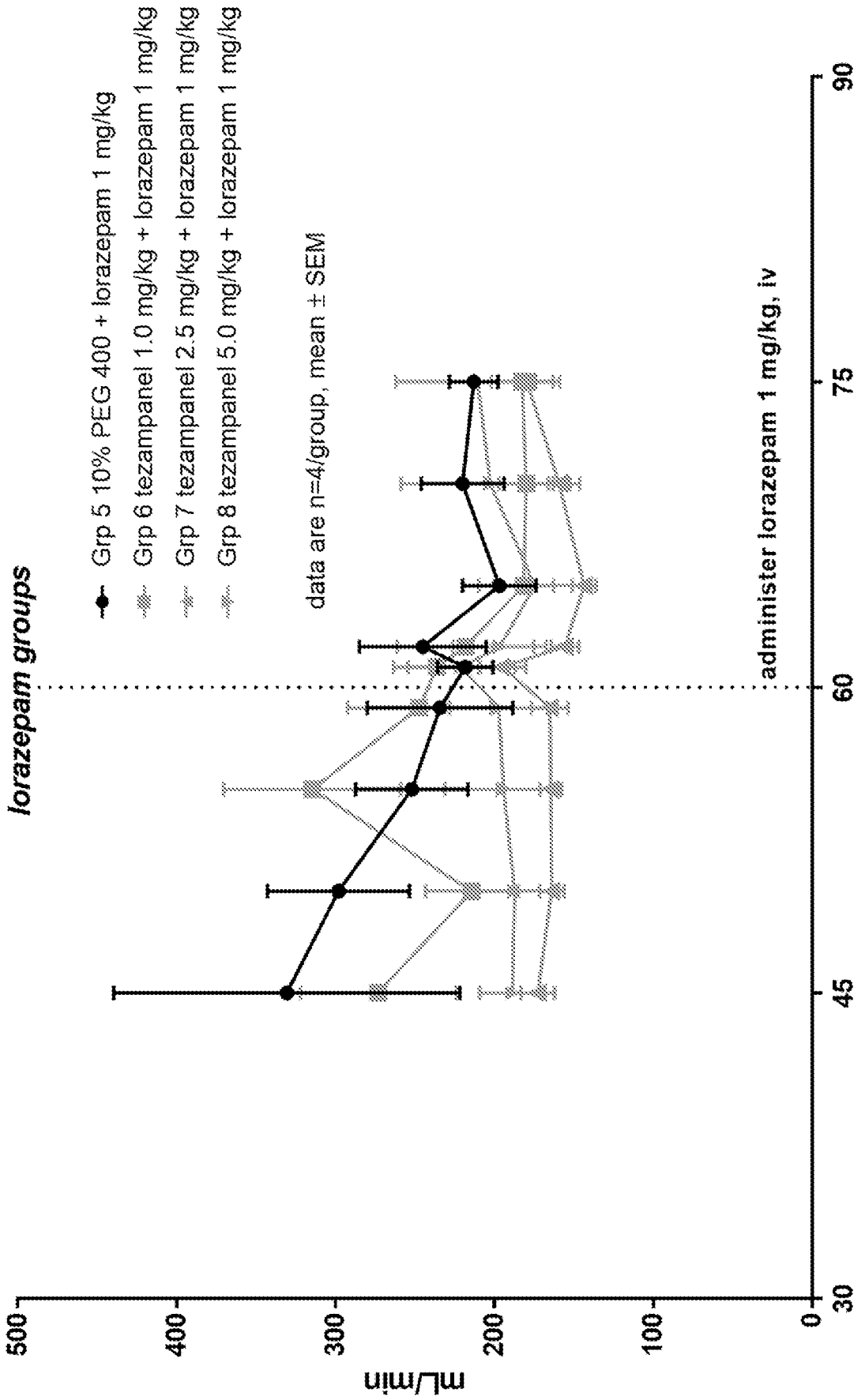

Minute Volume
lorazepam groups
Grp 5 10% PEG 400 + lorazepam 1 mg/kg
Grp 6 tezampanel 1.0 mg/kg + lorazepam 1 mg/kg
Grp 7 tezampanel 2.5 mg/kg + lorazepam 1 mg/kg
Grp 8 tezampanel 5.0 mg/kg + lorazepam 1 mg/kg
data are n=4/group, mean ± SEM
administer lorazepam 1 mg/kg, iv
mL/min
500
400
300
200
100
0
30
45
60
75
90
Time (minutes)

Figure 2D

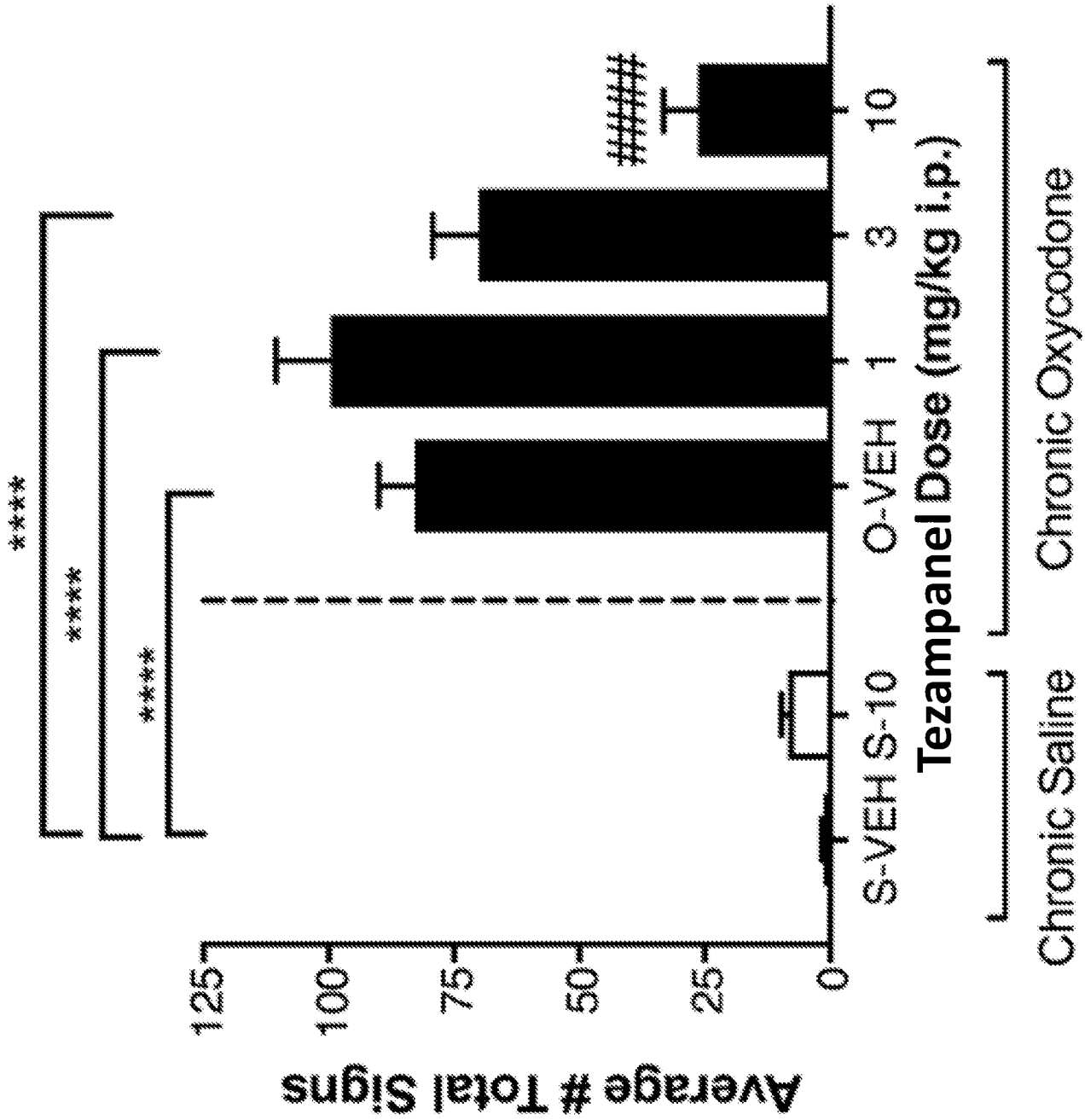

Average # Total Signs
125
100
75
50
25
0
S-VEH
S-10
O-VEH
1
3
10
Tezampanel Dose (mg/kg i.p.)
Chronic Saline
Chronic Oxycodone
****
****
****
#####

Figure 3A

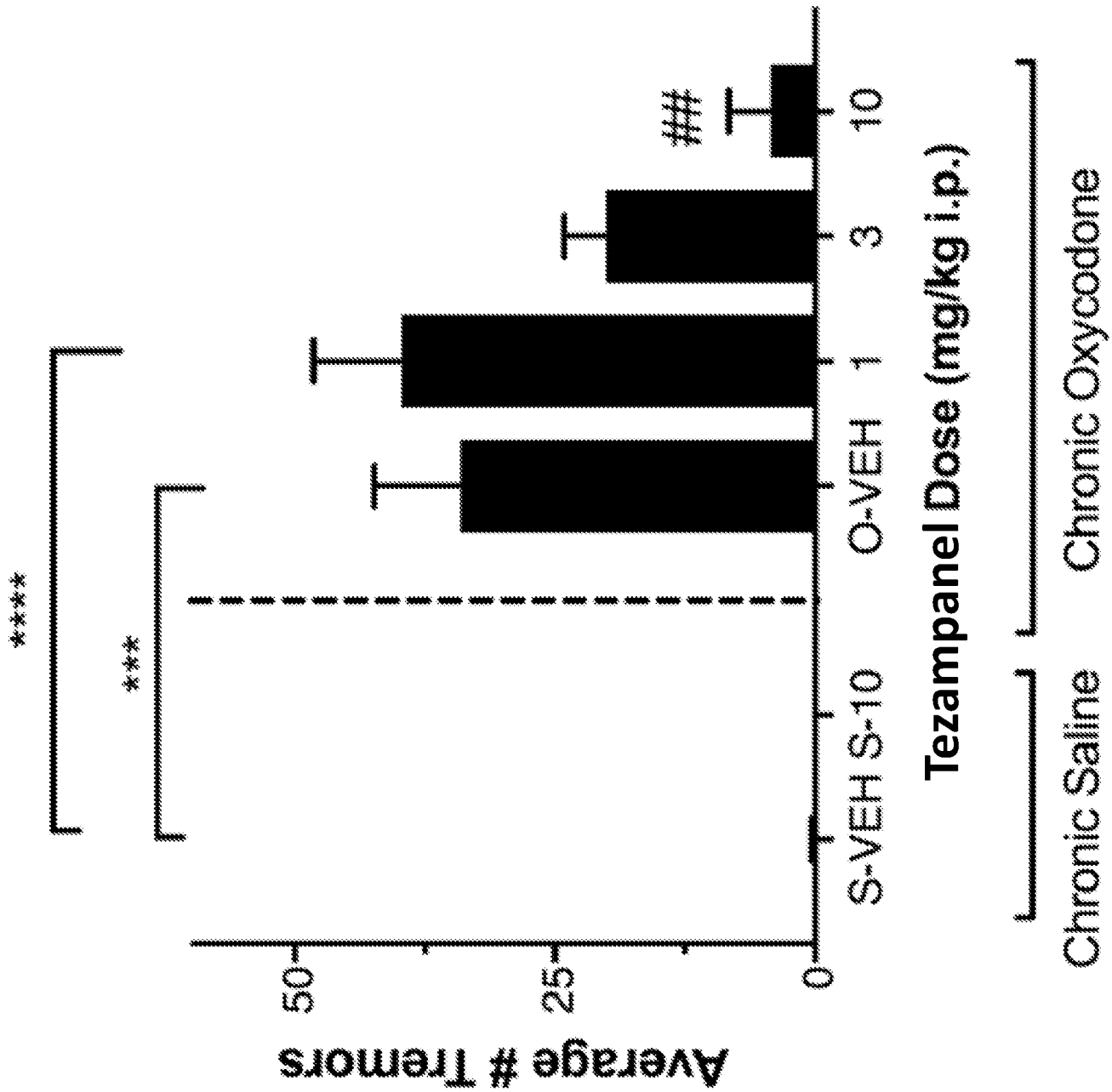

Average # Tremors
50
25
0
S-VEH
S-10
O-VEH
1
3
10
Tezampanel Dose (mg/kg i.p.)
Chronic Saline
Chronic Oxycodone
****
***
##

Figure 3B

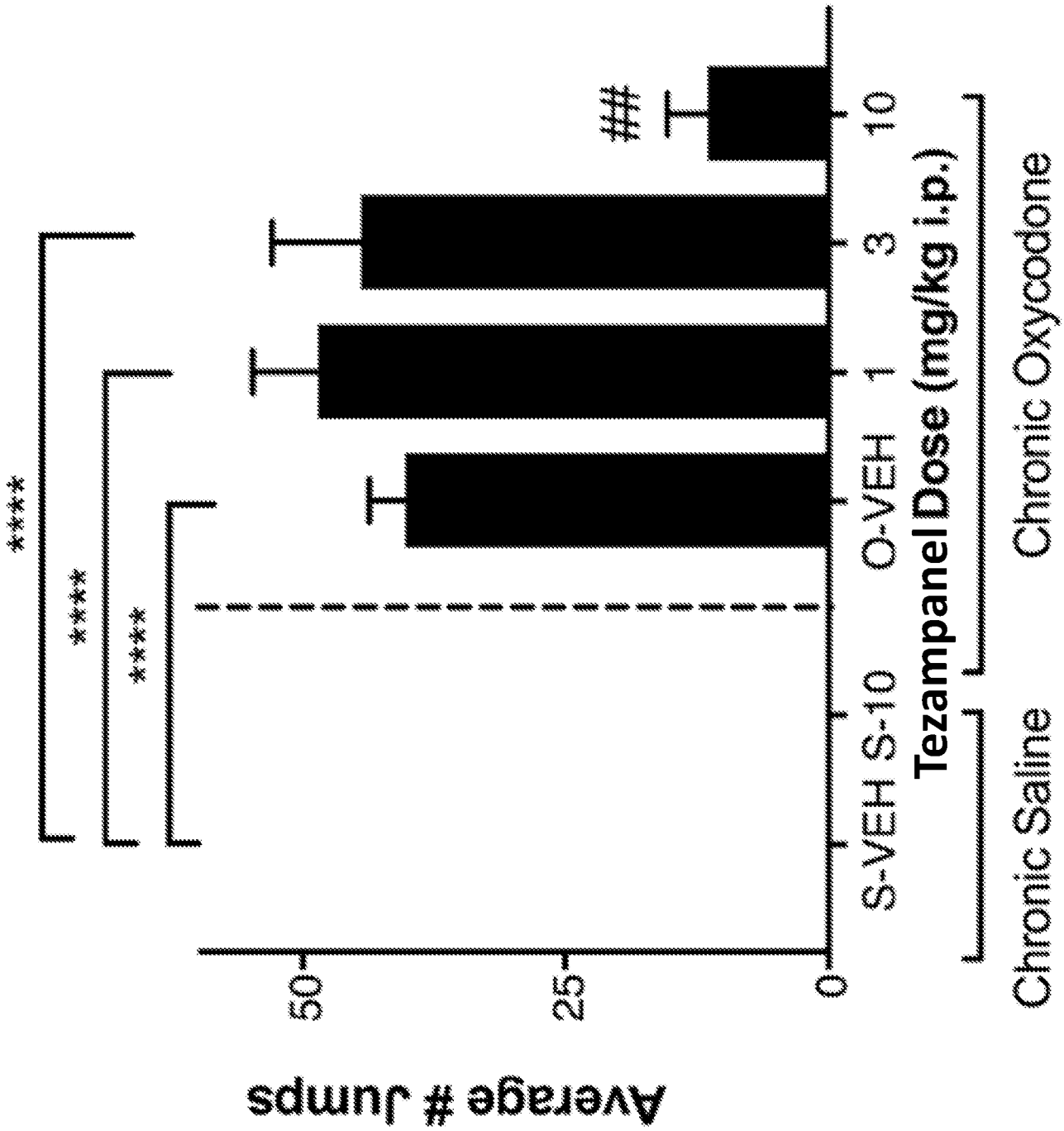

Average # Jumps
0
25
50
S-VEH
S-10
O-VEH
1
3
10
Tezampanel Dose (mg/kg i.p.)
Chronic Saline
Chronic Oxycodone
****
****
****
##

Figure 3C

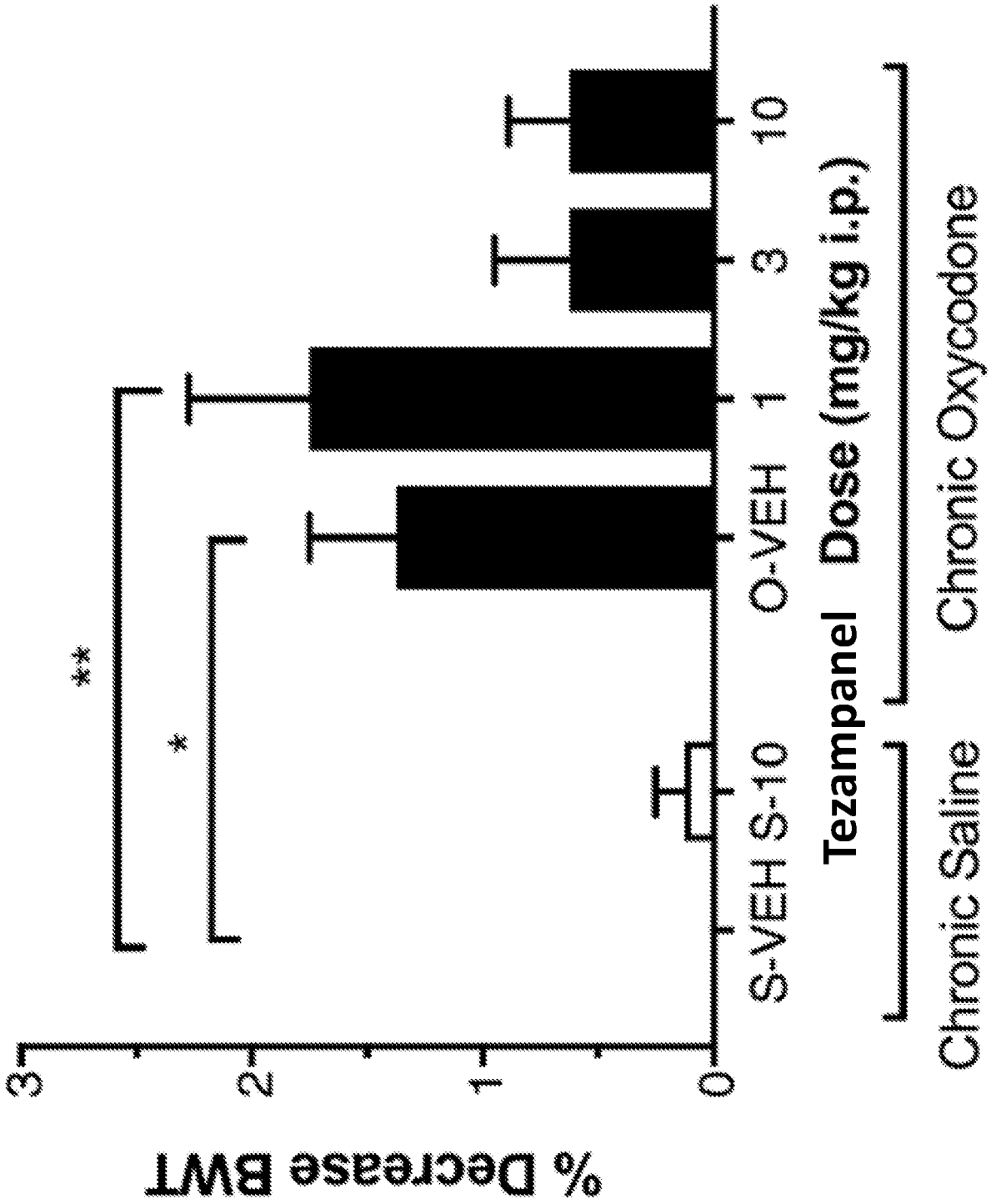

% Decrease BWT
3
2
1
0
**
*
S-VEH S-10 O-VEH 1 3 10
Tezampanel Dose (mg/kg i.p.)
Chronic Saline
Chronic Oxycodone

Figure 3D

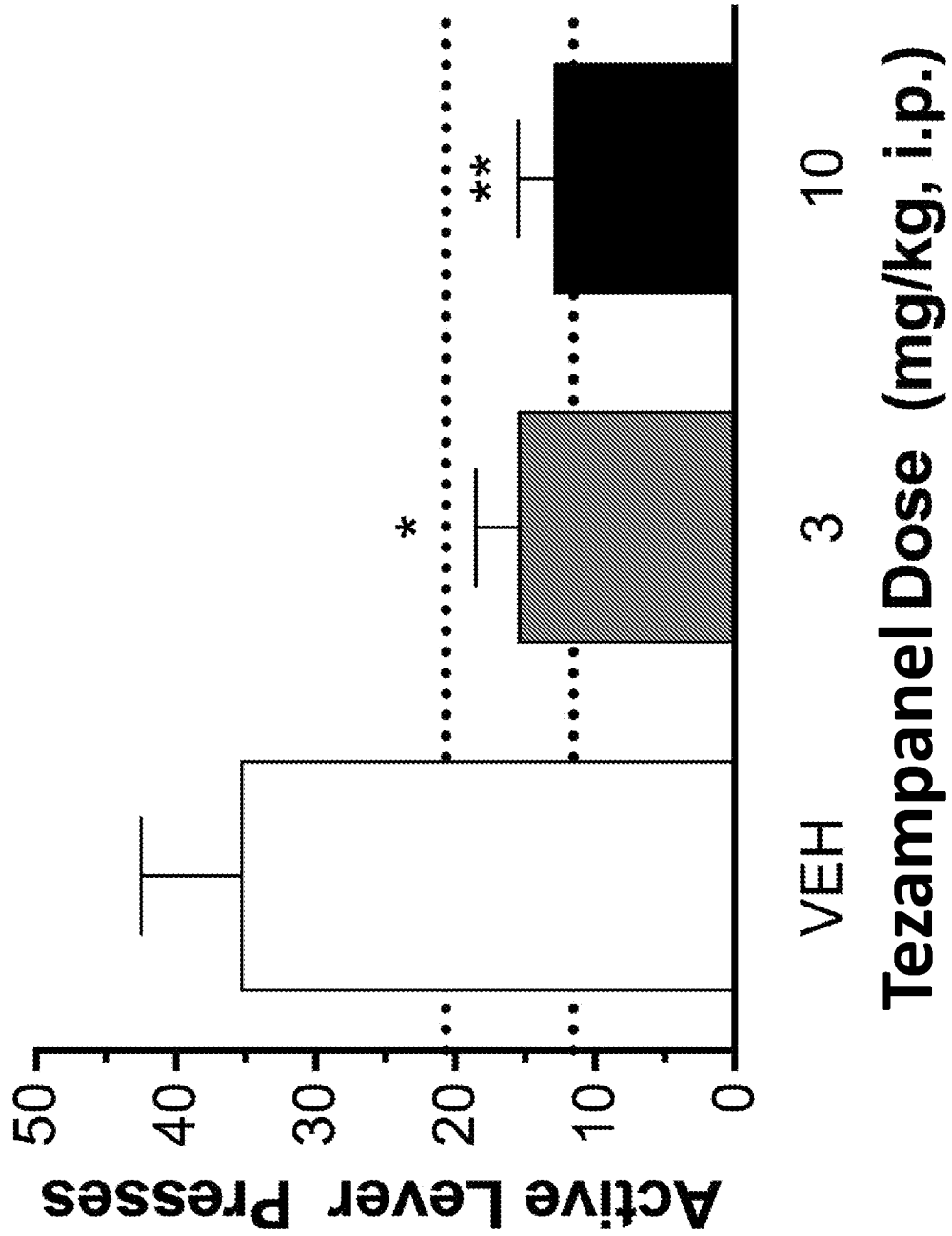

Active Lever Presses
50
40
30
20
10
0
*
**
VEH
3
10
Tezampanel Dose (mg/kg, i.p.)

Figure 4A

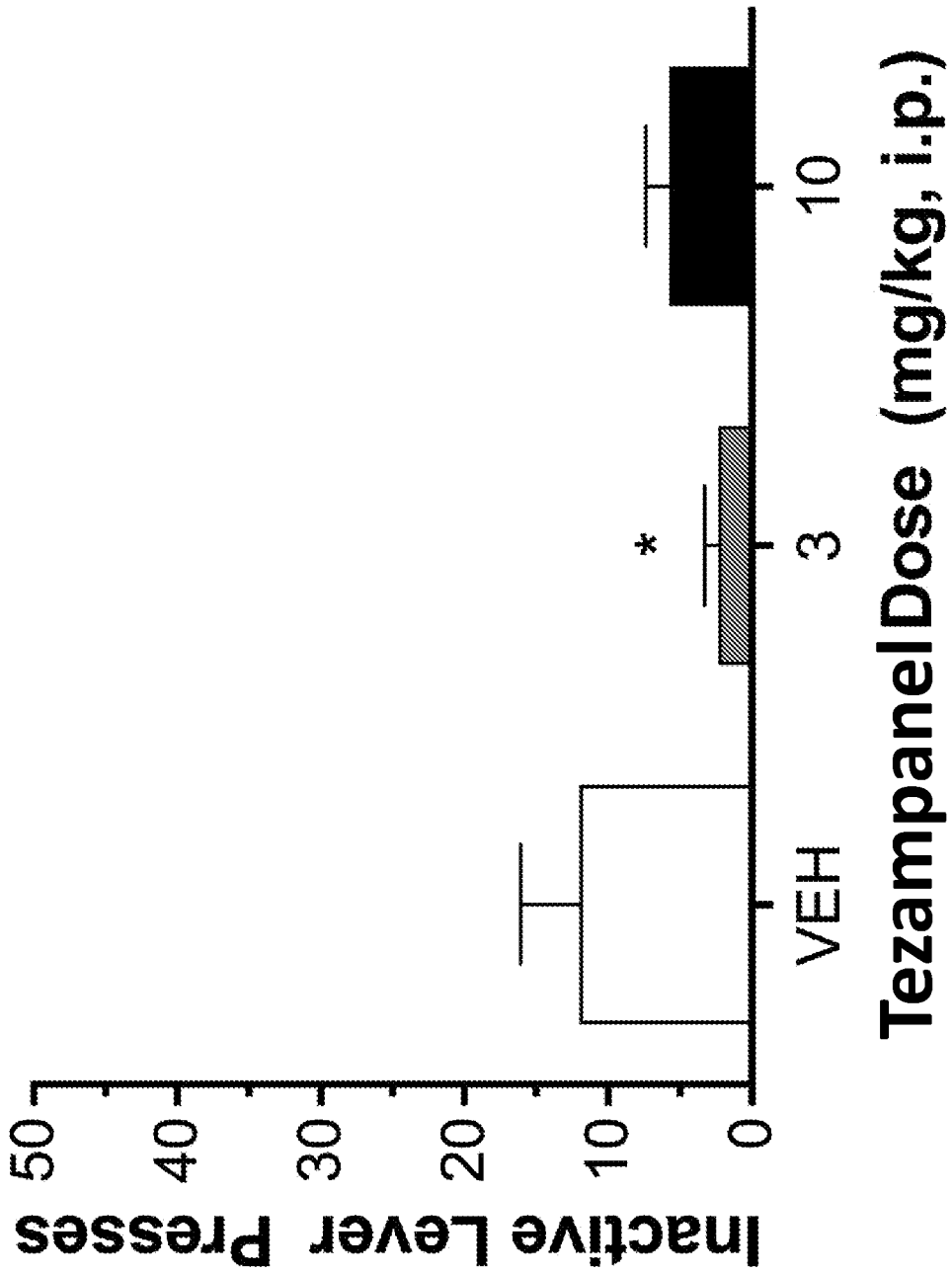

Inactive Lever Presses
0
10
20
30
40
50
VEH
*
3
10
Tezampanel Dose (mg/kg, i.p.)

Figure 4B