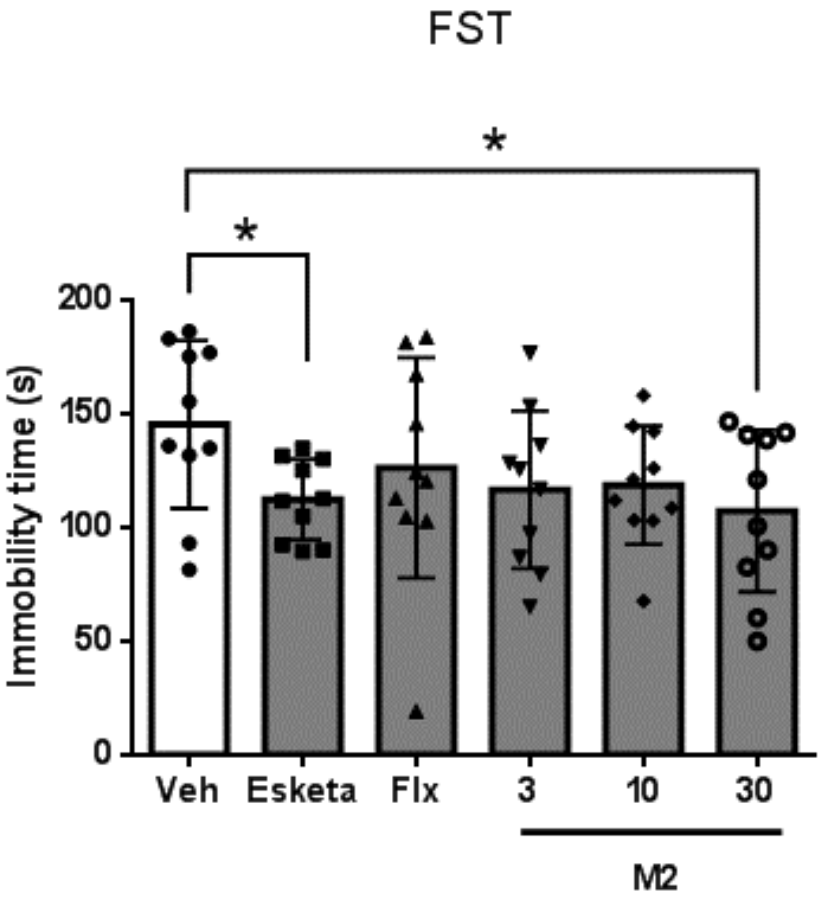


FIG. 1

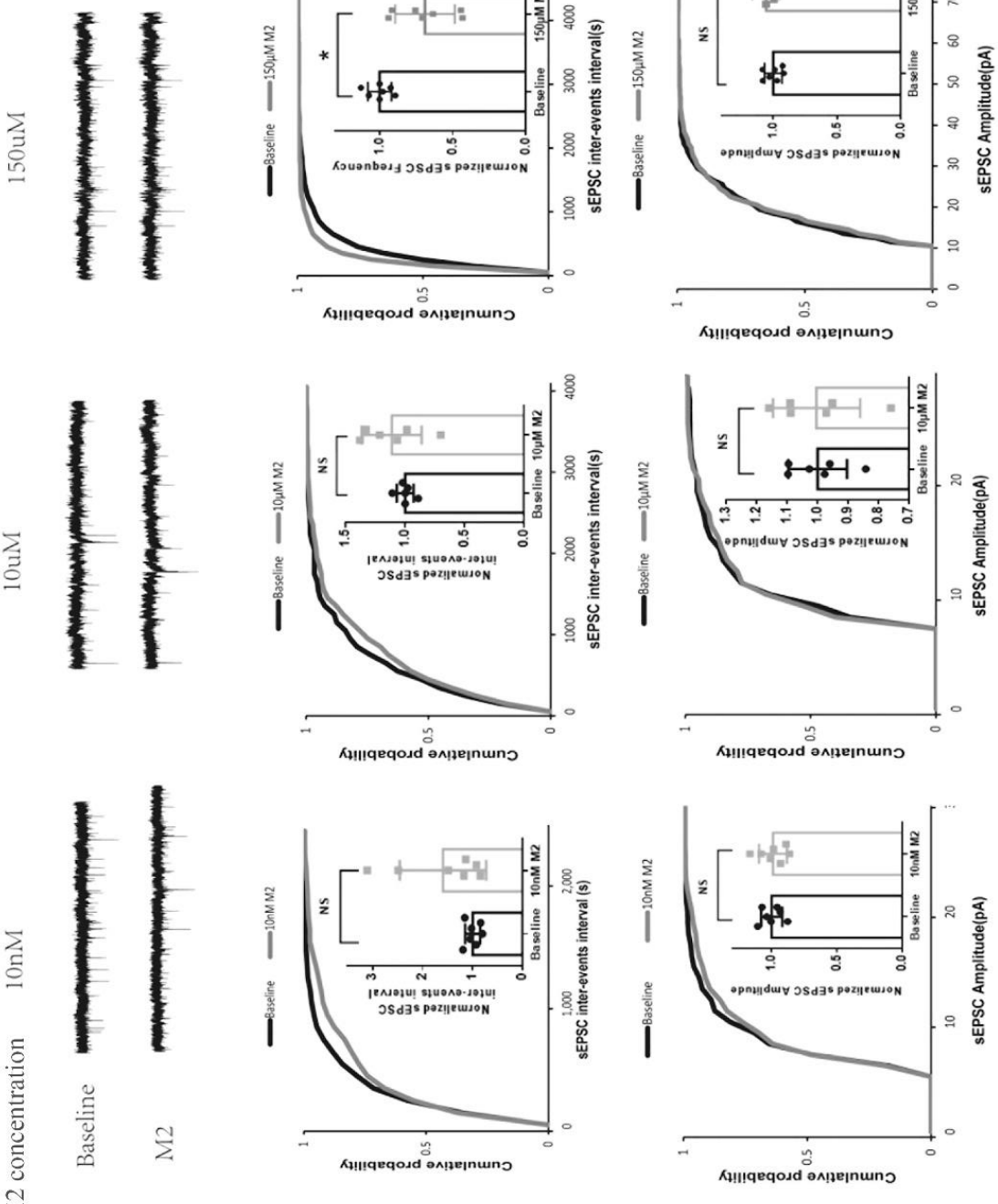

M2 concentration
10nM
10uM
150uM
Baseline
M2
Baseline
10nM M2
10μM M2
150μM M2
Cumulative probability
sEPSC inter-events interval(s)
sEPSC Amplitude(pA)
Normalized sEPSC inter-events interval
Normalized sEPSC Frequency
Normalized sEPSC Amplitude
NS
*
Baseline
10nM M2
10μM M2
150uM M2

FIG. 2

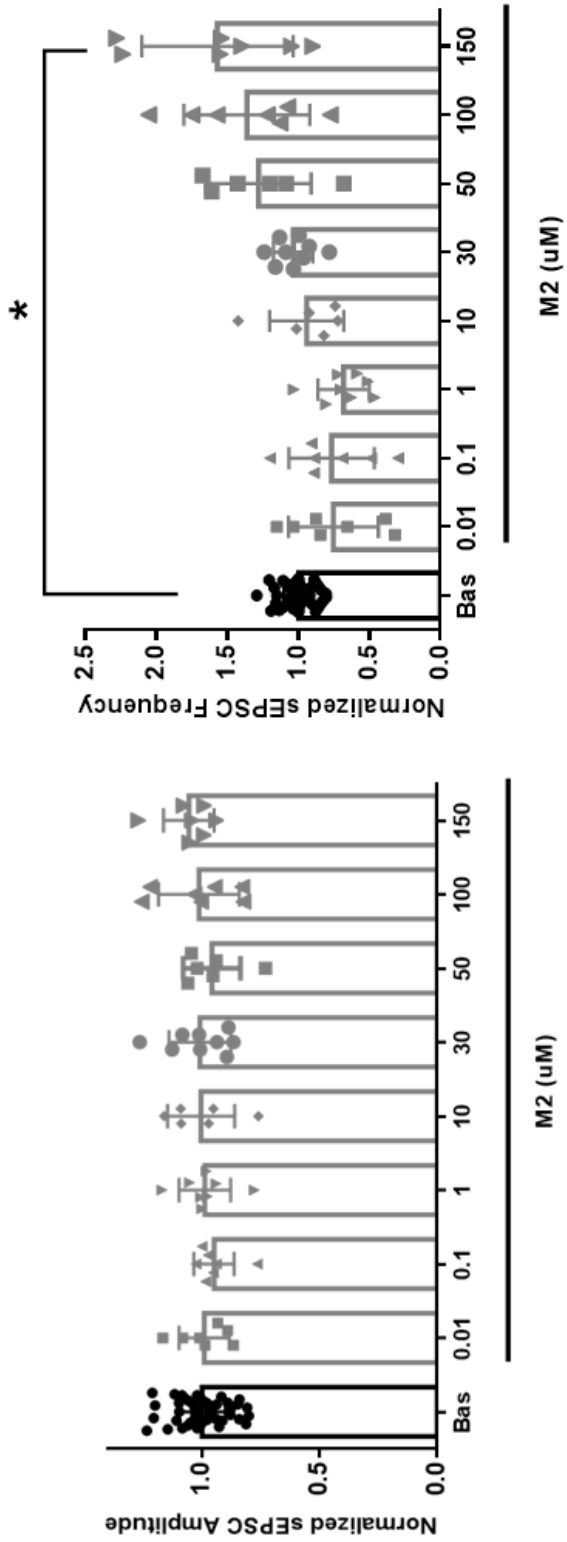

Normalized sEPSC Frequency
2.5
2.0
1.5
1.0
0.5
0.0
*
Bas
0.01
0.1
1
10
30
50
100
150
M2 (uM)
Normalized sEPSC Amplitude
1.0
0.5
0.0
Bas
0.01
0.1
1
10
30
50
100
150
M2 (uM)

FIG. 3

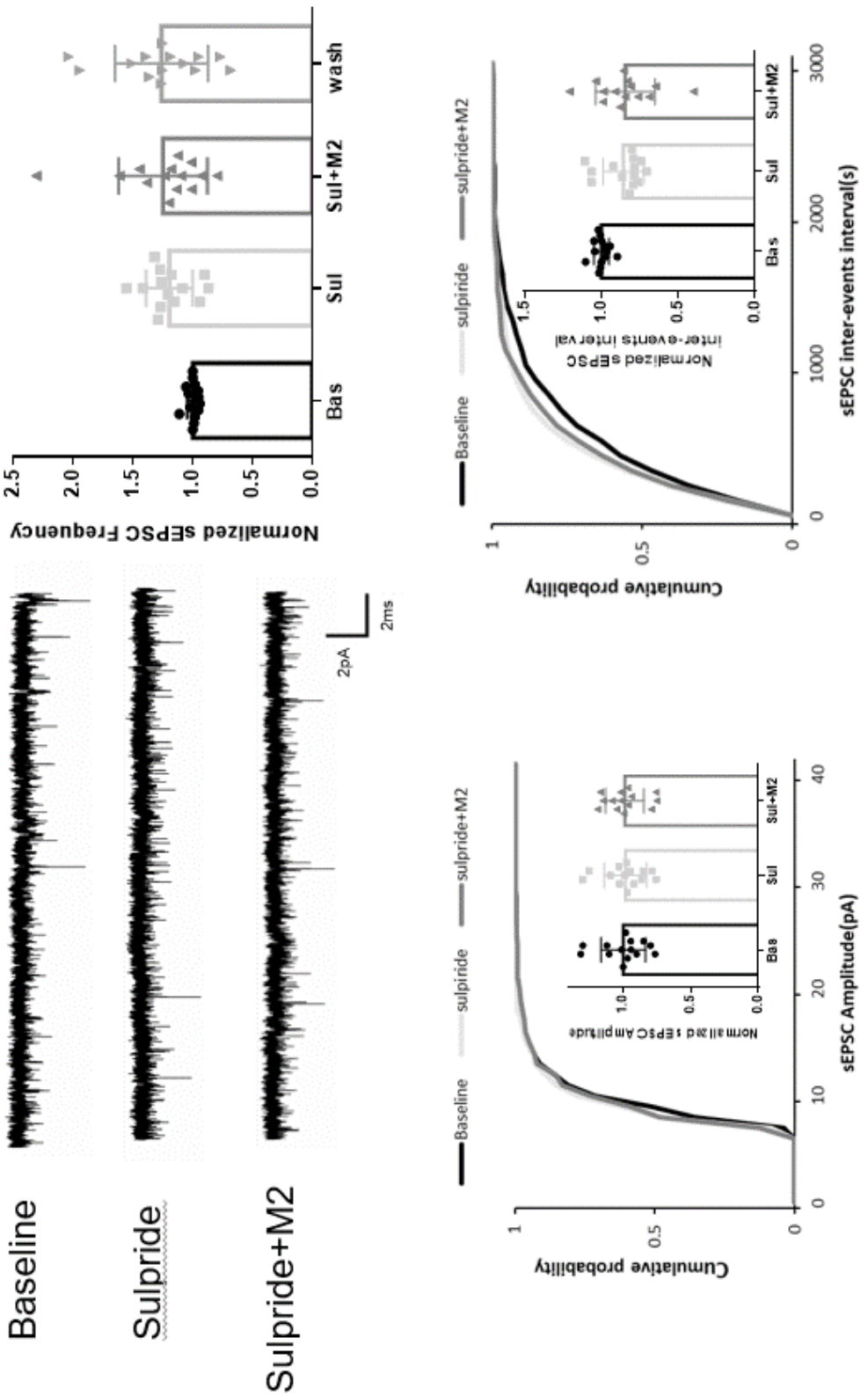

Baseline
Sulpride
Sulpride+M2
2pA
2ms
Normalized sEPSC Frequency
2.5
2.0
1.5
1.0
0.5
0.0
Bas
Sul
Sul+M2
wash
Baseline
sulpiride
sulpride+M2
Cumulative probability
1
0.5
0
0
1000
2000
3000
sEPSC inter-events interval(s)
Normalized sEPSC inter-events interval
1.5
1.0
0.5
0.0
Bas
Sul
Sul+M2
Baseline
sulpiride
sulpride+M2
Cumulative probability
1
0.5
0
0
10
20
30
40
sEPSC Amplitude(pA)
Normalized sEPSC Amplitude
1.0
0.5
0.0
Bas
Sul
Sul+M2

FIG. 4

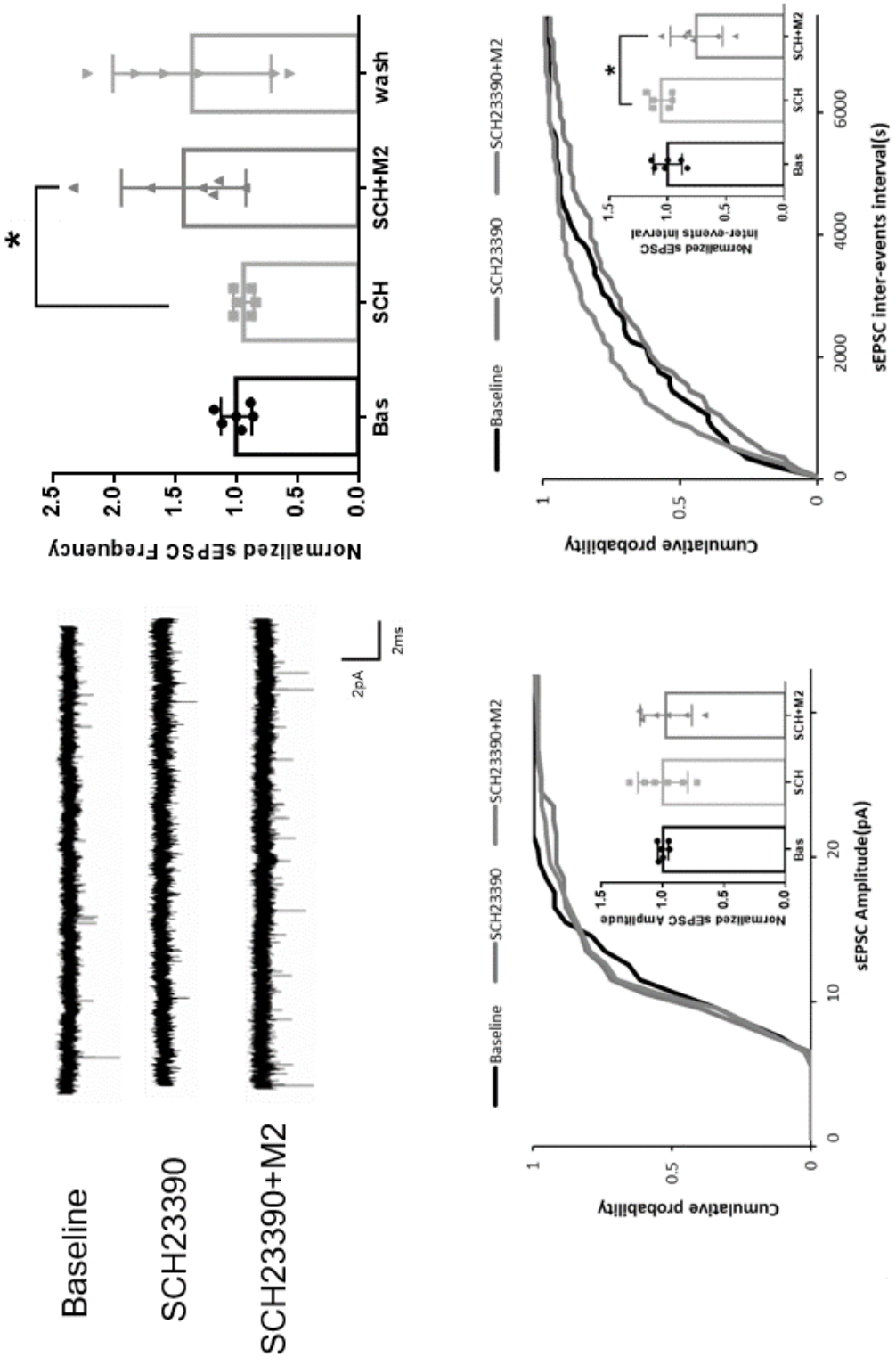

Baseline
SCH23390
SCH23390+M2
2pA
2ms
Normalized sEPSC Frequency
2.5
2.0
1.5
1.0
0.5
0.0
*
Bas
SCH
SCH+M2
wash
Cumulative probability
Baseline
SCH23390
SCH23390+M2
sEPSC inter-events interval(s)
Normalized sEPSC inter-events interval
sEPSC Amplitude(pA)
Normalized sEPSC Amplitude

FIG. 5

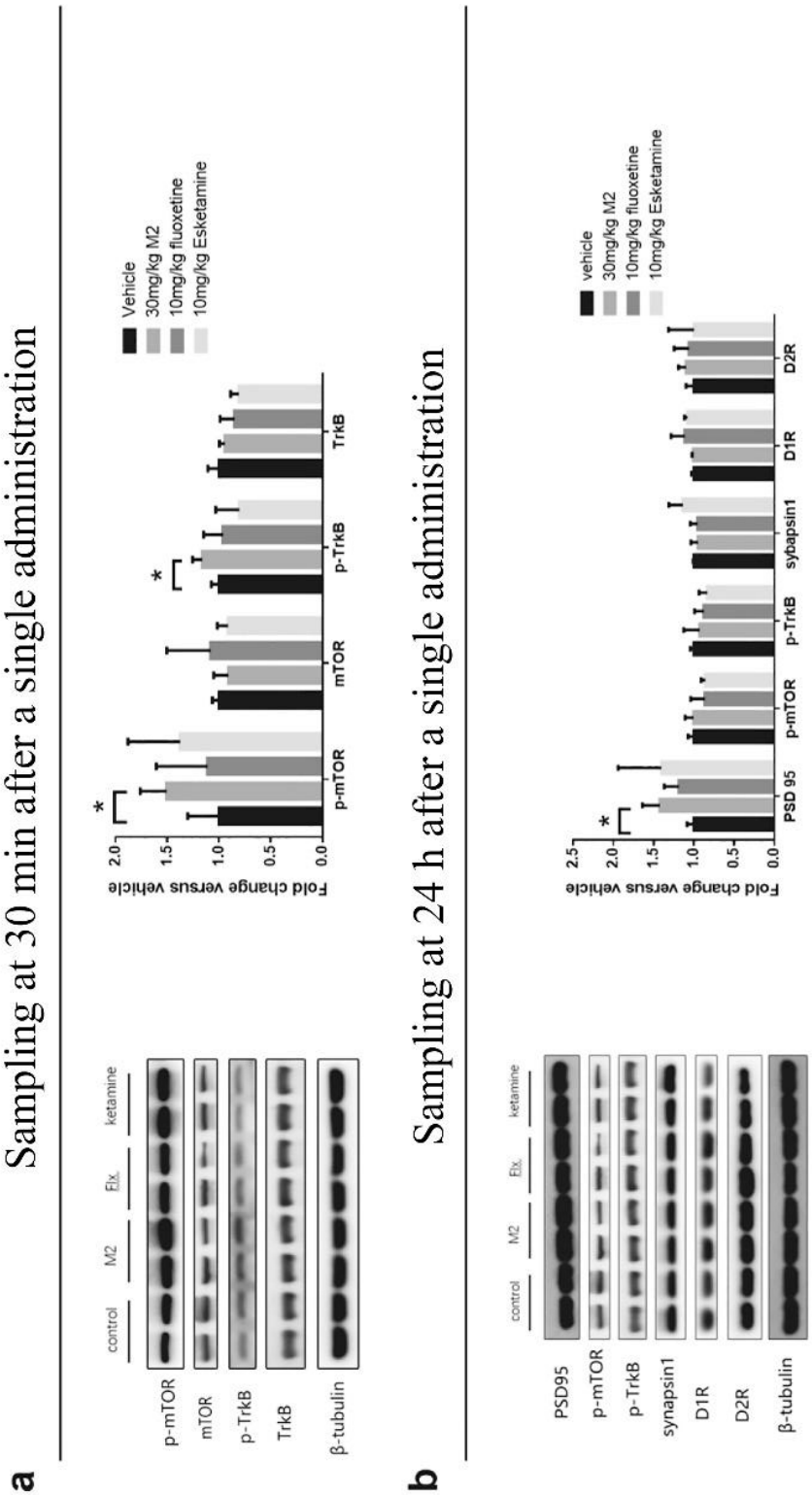

a
Sampling at 30 min after a single administration
control
M2
Fix.
ketamine
p-mTOR
mTOR
p-TrkB
TrkB
β-tubulin
Vehicle
30mg/kg M2
10mg/kg fluoxetine
10mg/kg Esketamine
Fold change versus vehicle
2.0
1.5
1.0
0.5
0.0
*
*
p-mTOR
mTOR
p-TrkB
TrkB
b
Sampling at 24 h after a single administration
control
M2
Fix.
ketamine
PSD95
p-mTOR
p-TrkB
synapsin1
D1R
D2R
β-tubulin
vehicle
30mg/kg M2
10mg/kg fluoxetine
10mg/kg Esketamine
Fold change versus vehicle
2.5
2.0
1.5
1.0
0.5
0.0
*
PSD 95
p-mTOR
p-TrkB
sybapsin1
D1R
D2R

FIG. 6

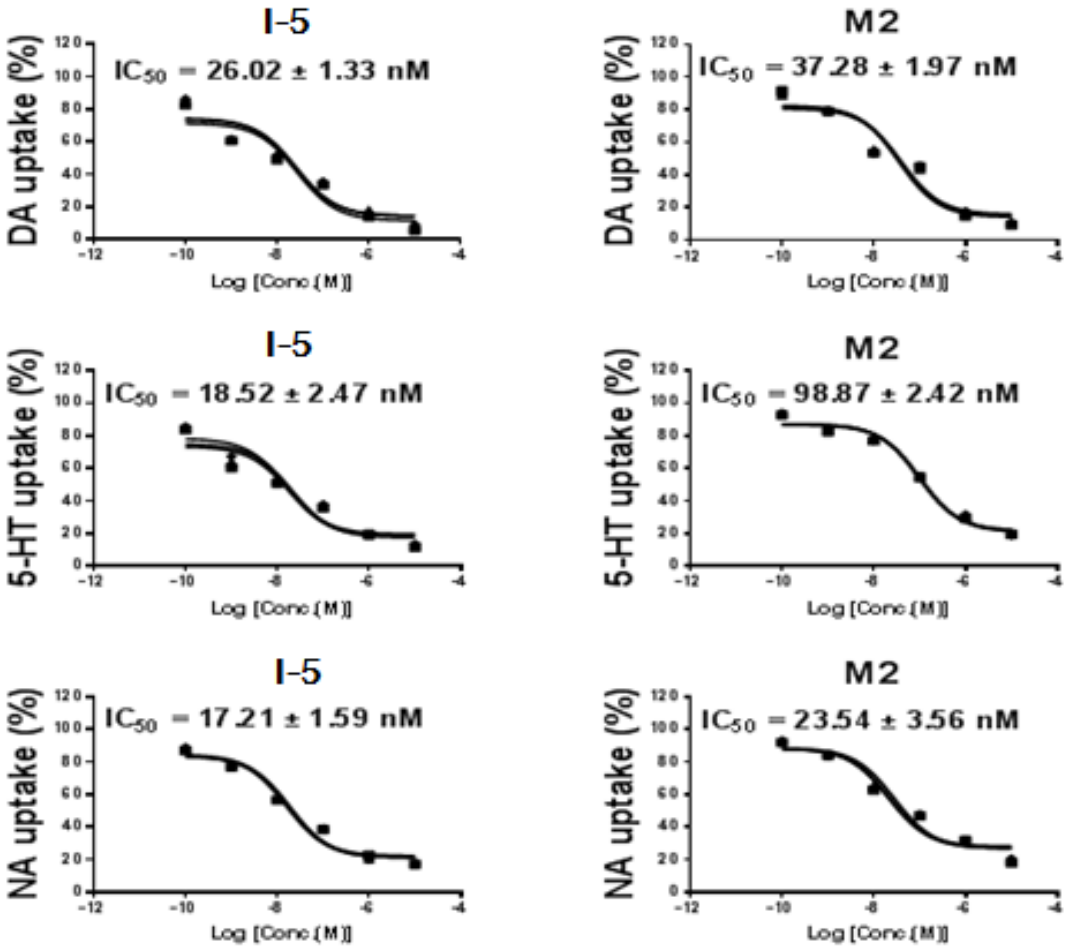

I-5
IC50 = 26.02 ± 1.33 nM
DA uptake (%)
Log [Conc (M)]
M2
IC50 = 37.28 ± 1.97 nM
DA uptake (%)
Log [Conc (M)]
I-5
IC50 = 18.52 ± 2.47 nM
5-HT uptake (%)
Log [Conc (M)]
M2
IC50 = 98.87 ± 2.42 nM
5-HT uptake (%)
Log [Conc (M)]
I-5
IC50 = 17.21 ± 1.59 nM
NA uptake (%)
Log [Conc (M)]
M2
IC50 = 23.54 ± 3.56 nM
NA uptake (%)
Log [Conc (M)]

FIG. 7

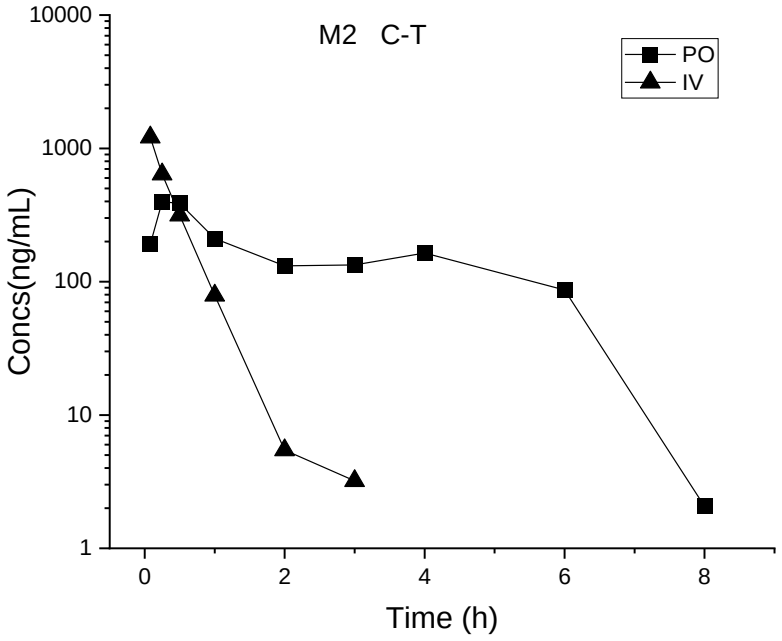

M2 C-T
PO
IV
Concs(ng/mL)
Time (h)
10000
1000
100
10
1
0
2
4
6
8

FIG. 8

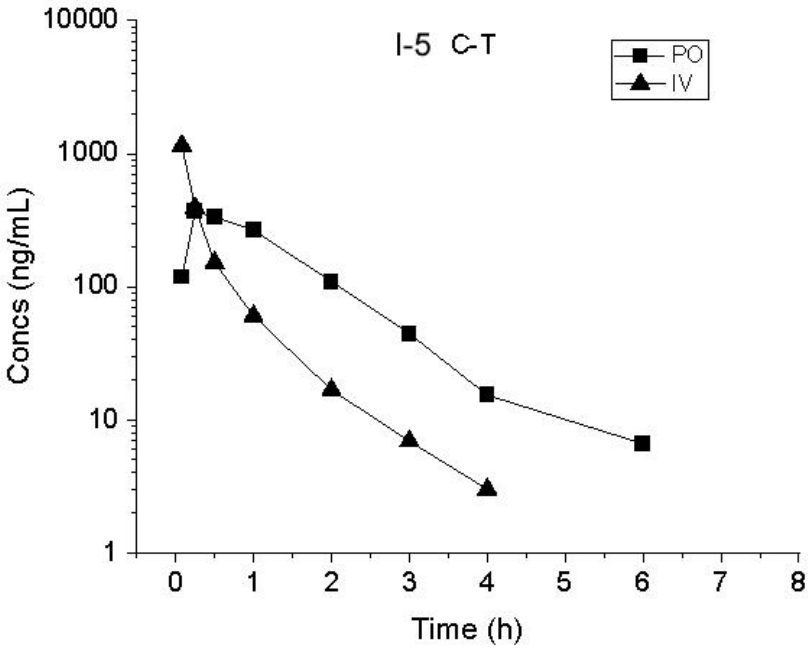

I-5 C-T
PO
IV
Concs (ng/mL)
Time (h)
10000
1000
100
10
1
0
1
2
3
4
5
6
7
8

FIG. 9