

FIG. 1A

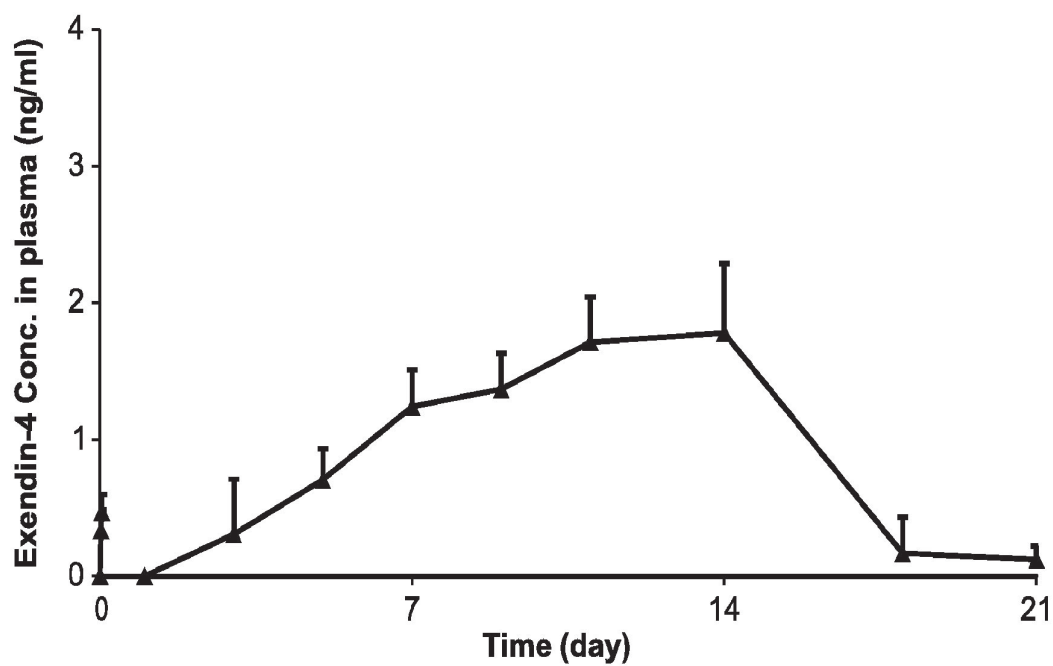


FIG. 1B

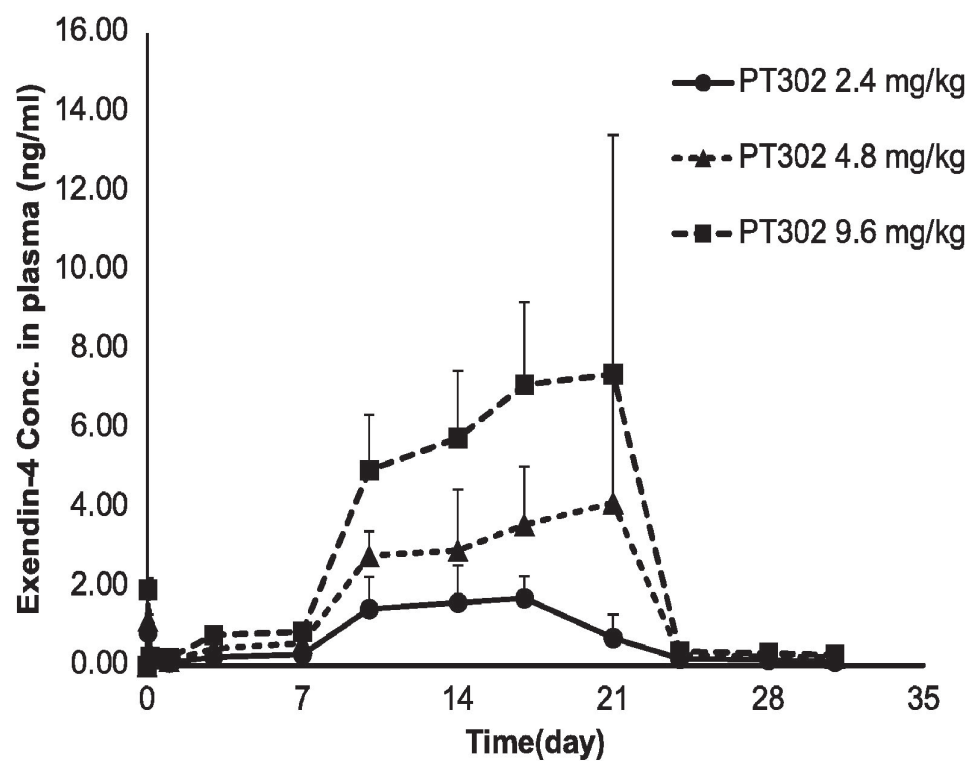


FIG. 2

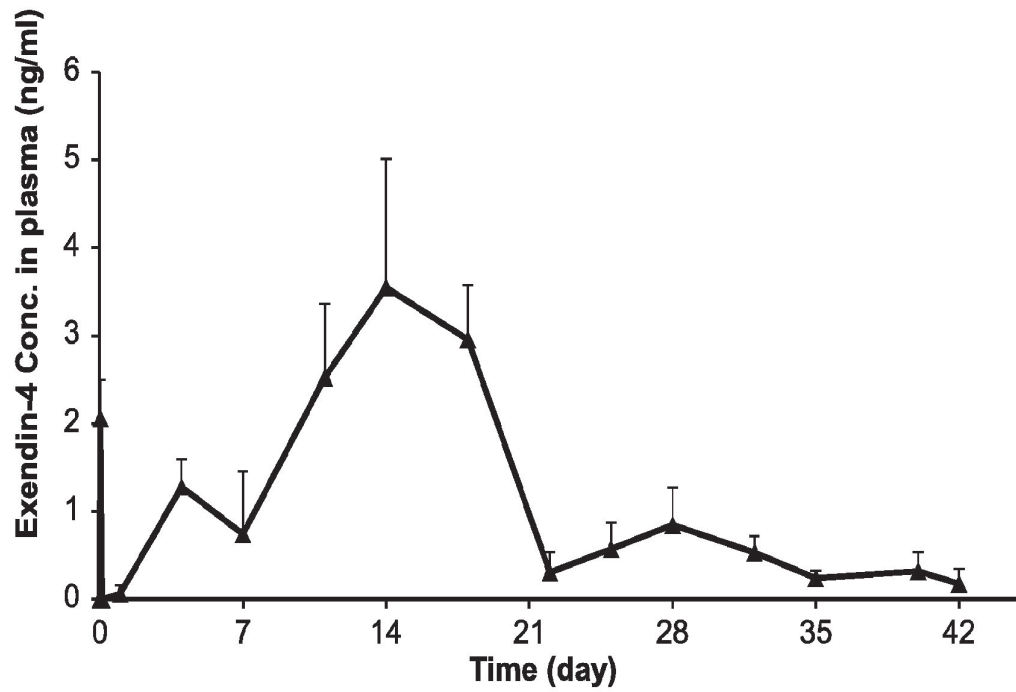


FIG. 3

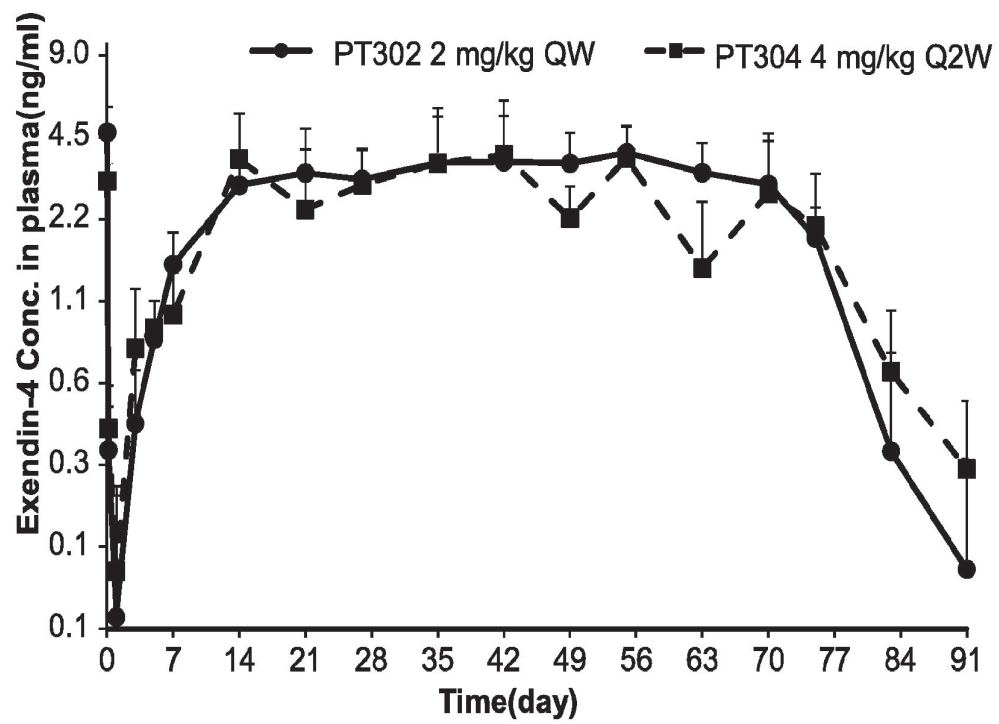


FIG. 4A

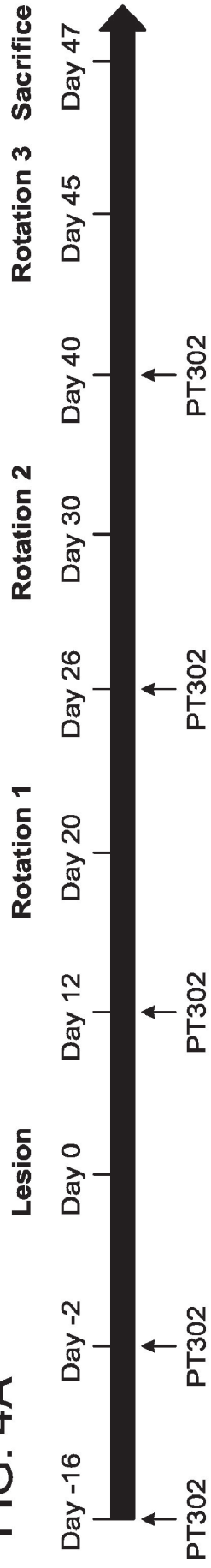


FIG. 4B

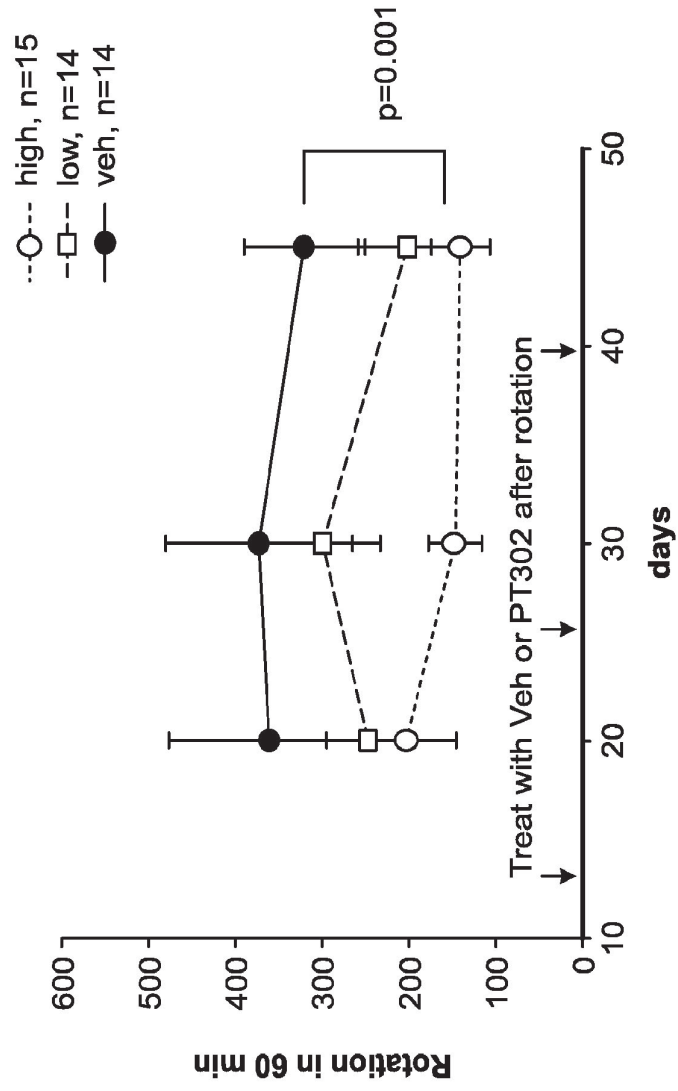


FIG. 4C

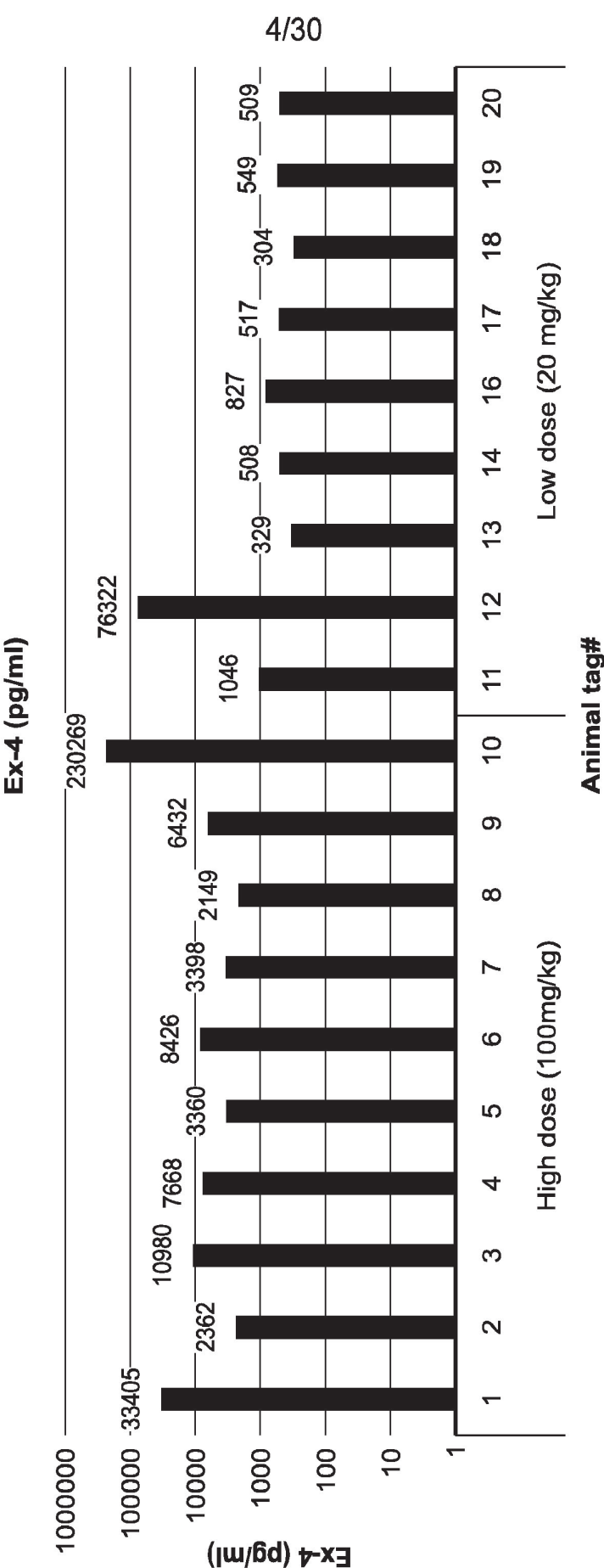


FIG. 5A

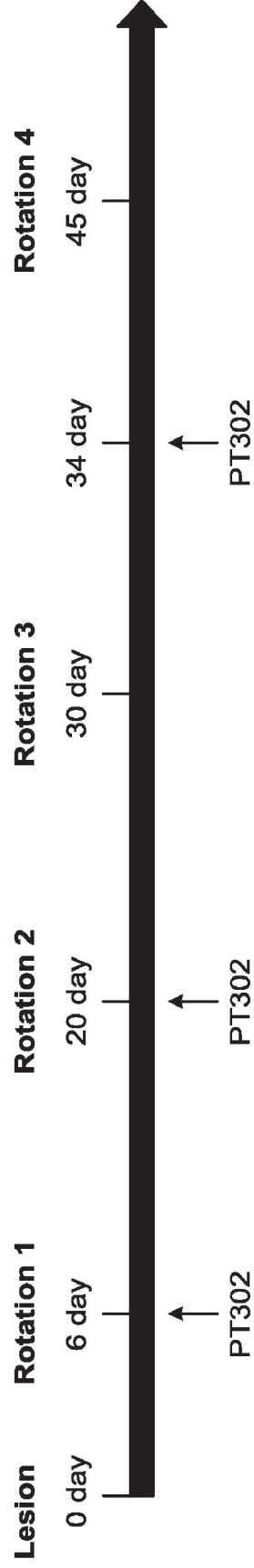


FIG. 5B

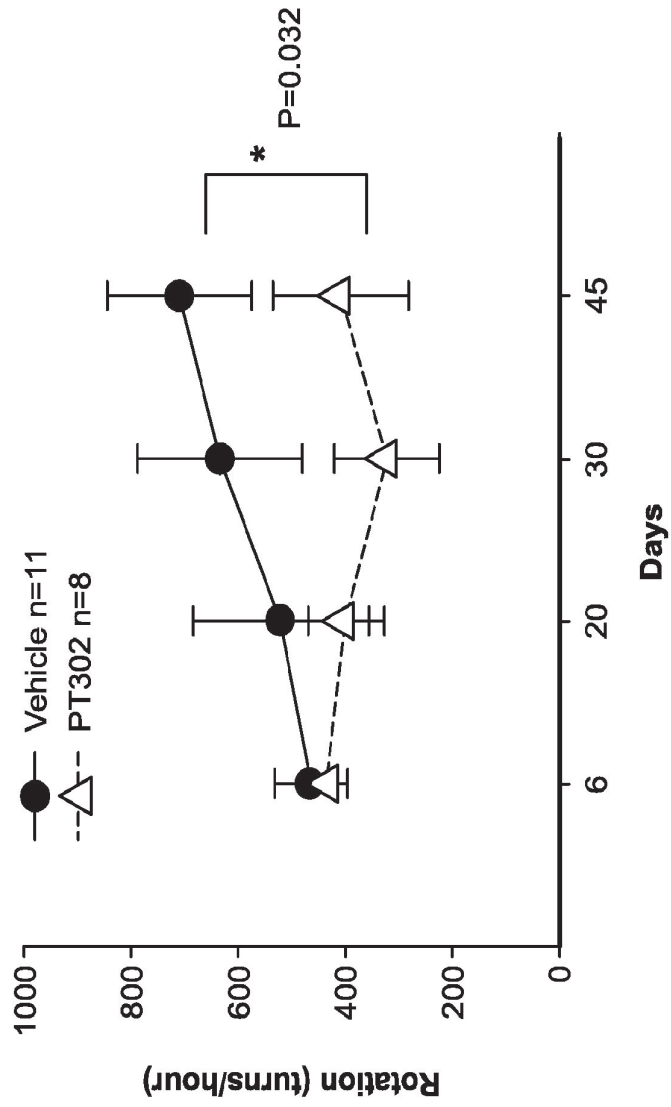


FIG. 5C

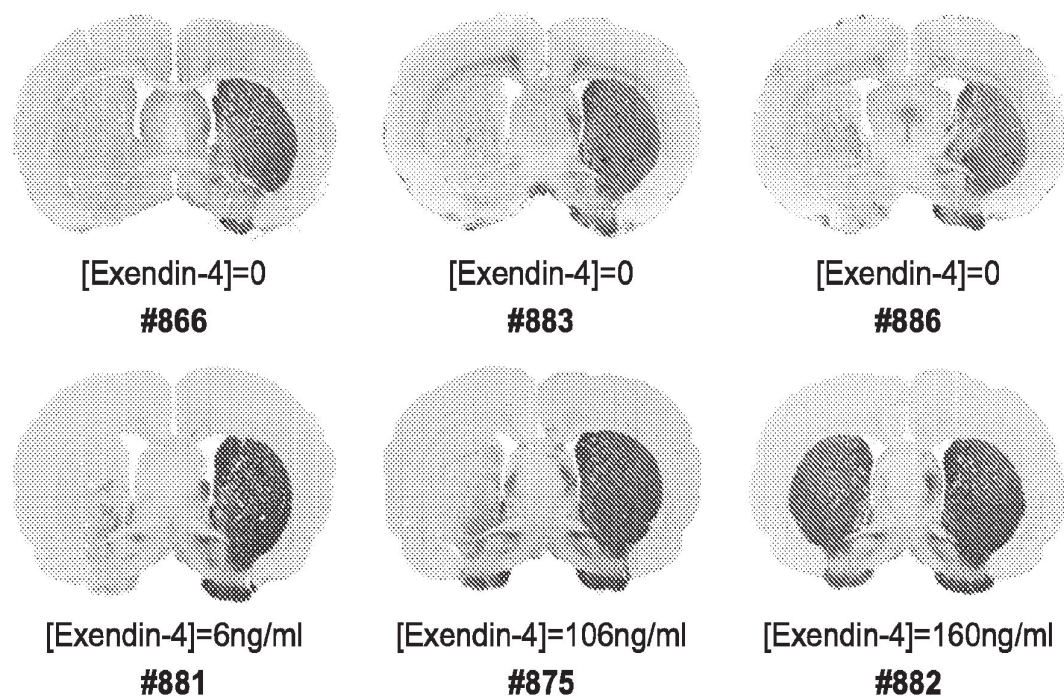


FIG. 5D

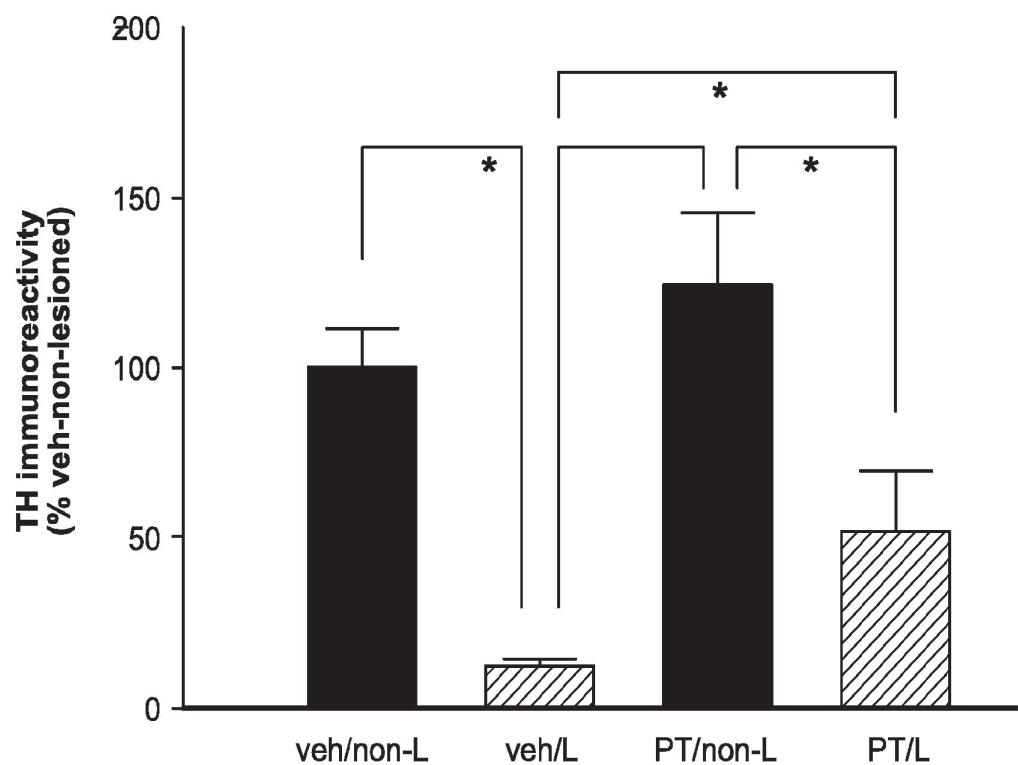


FIG. 5E

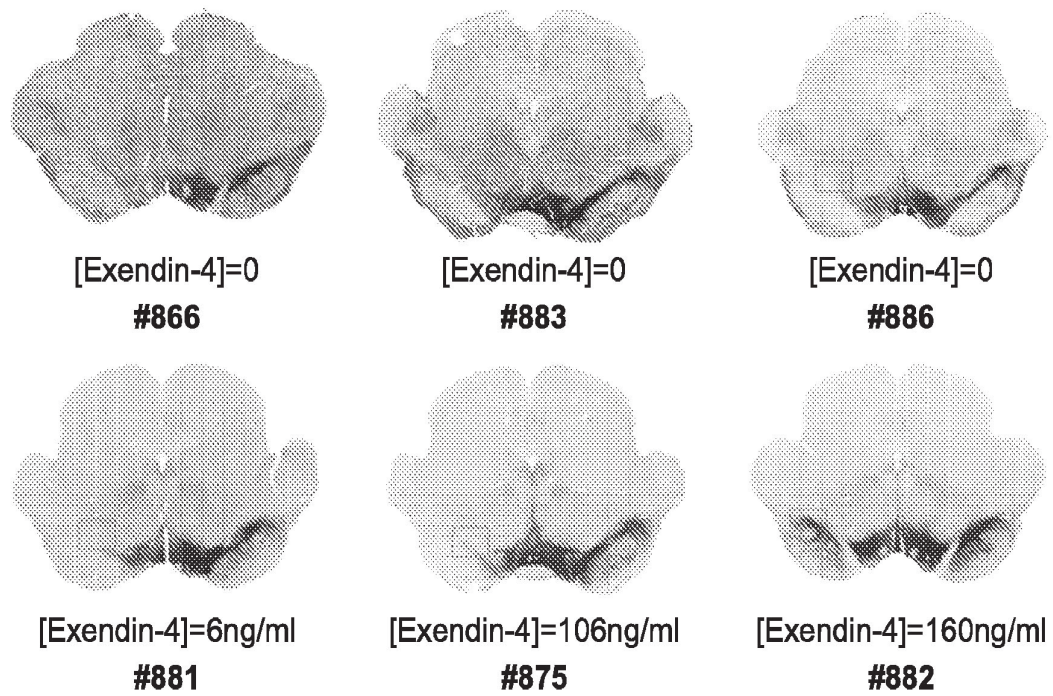


FIG. 5F

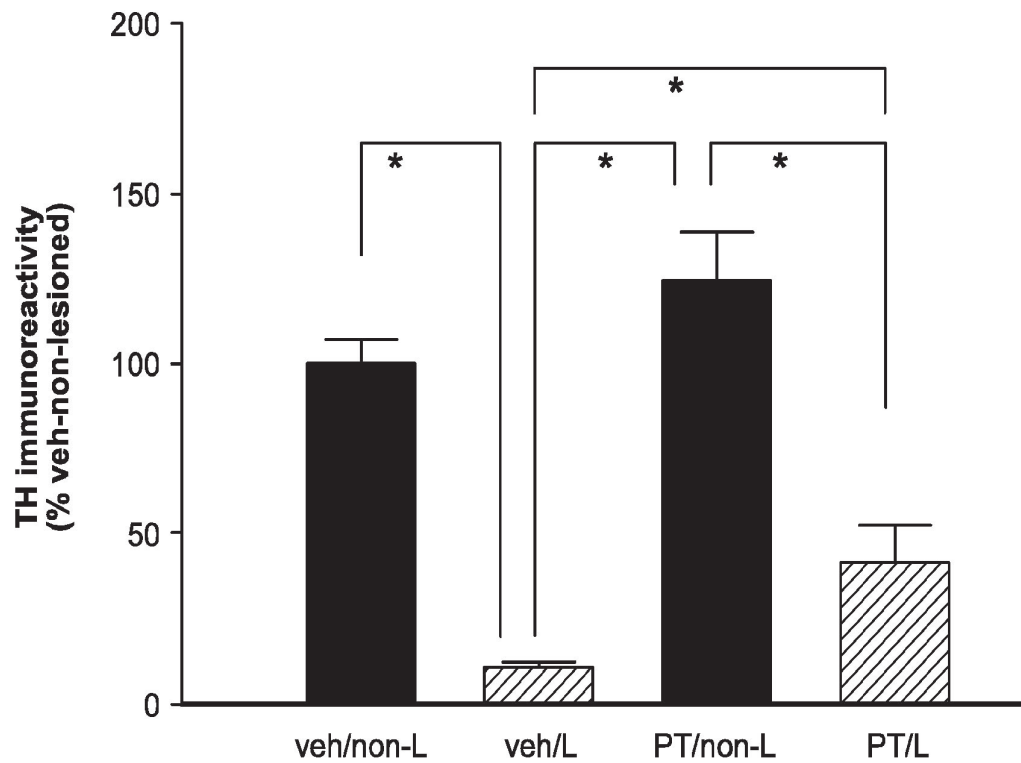
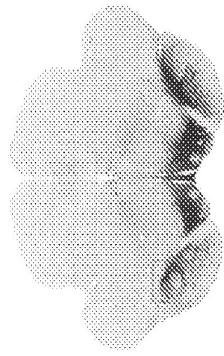


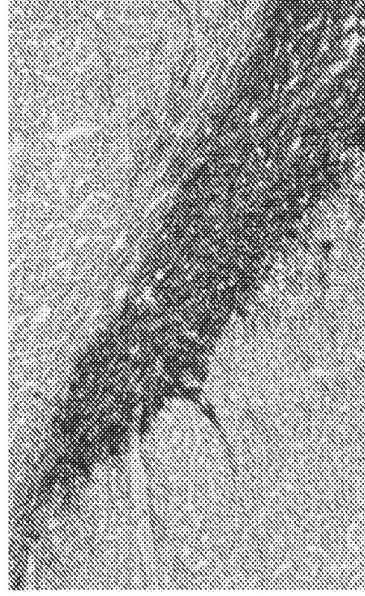
FIG. 5G



PT302(#882)

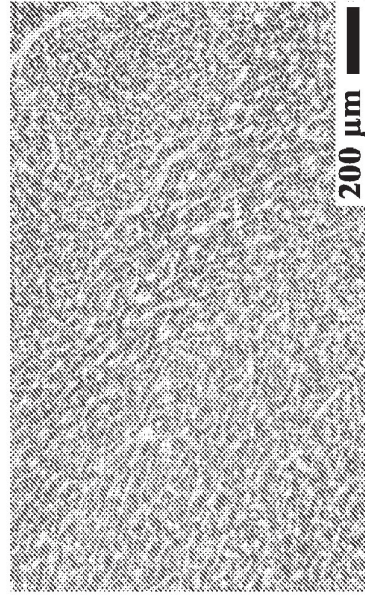
200 μ m

FIG. 5H



Non-lesioned
side nigra

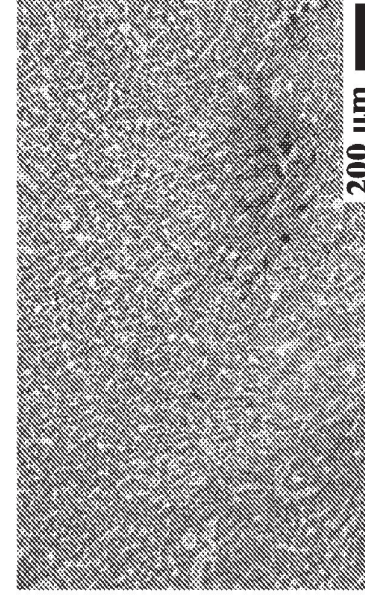
FIG. 5I



veh(#886)

200 μ m

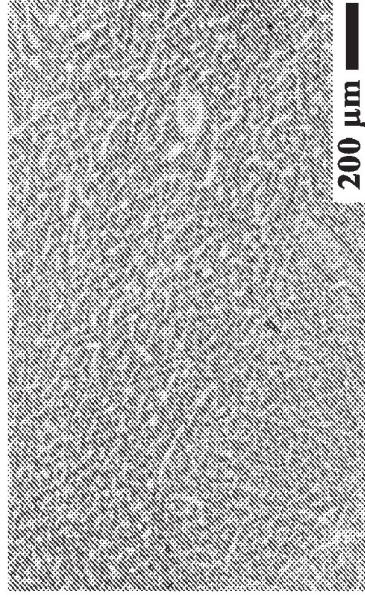
FIG. 5J



PT302(#875)

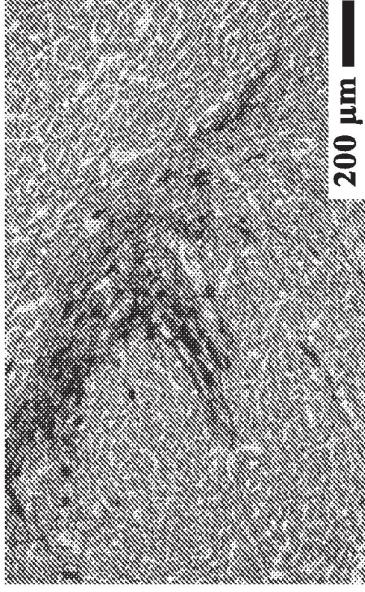
200 μ m

FIG. 5K



PT302(#881)

FIG. 5L



PT302(#882)

FIG. 5M

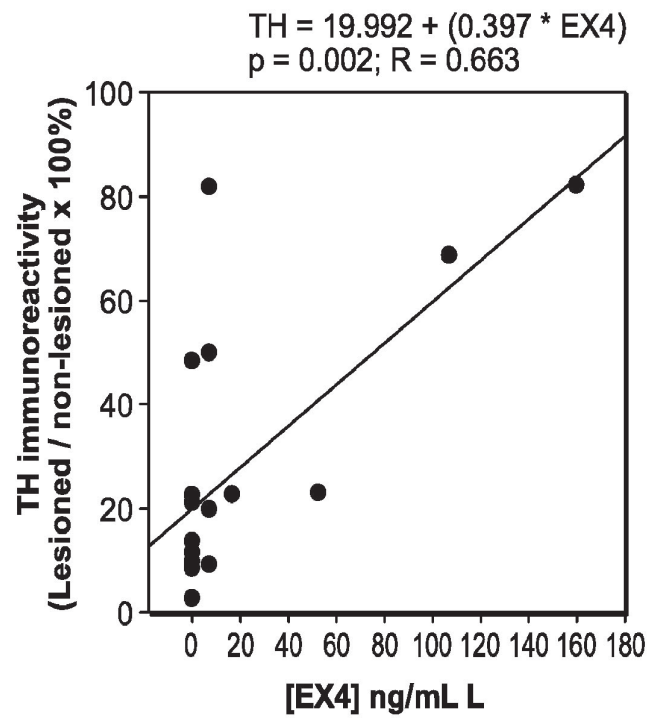


FIG. 5N

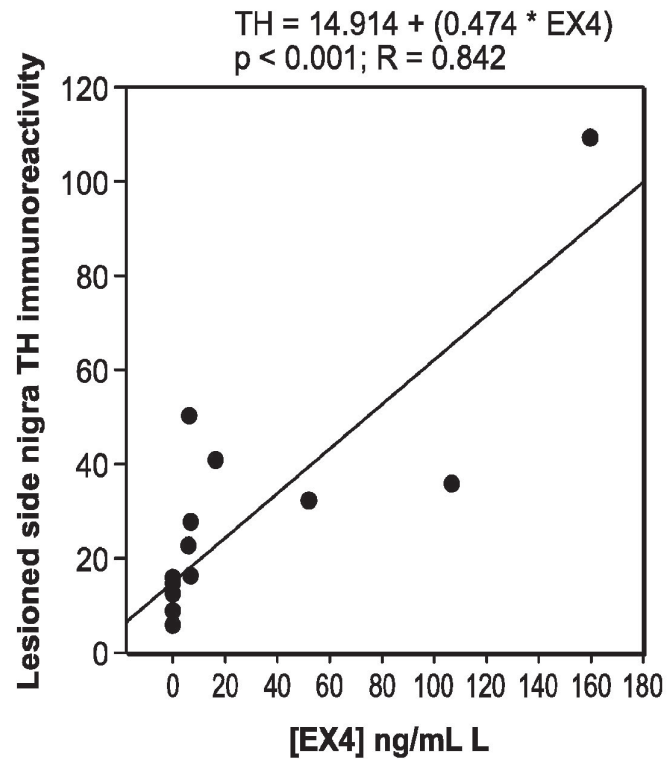


FIG. 6A

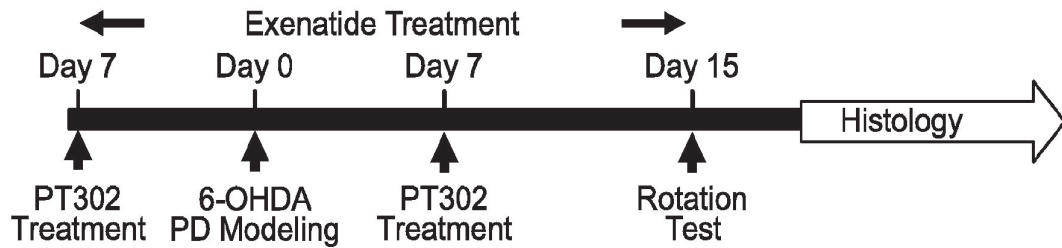


FIG. 6B



Dunnett's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Significant?	Summary	Adjusted P Value
Control vs. Ex-4	152	54.96 to 249	Yes	**	0.005
Control vs. PT302 0.4mg/kg	173	75.96 to 270	Yes	**	0.0022

FIG. 6C

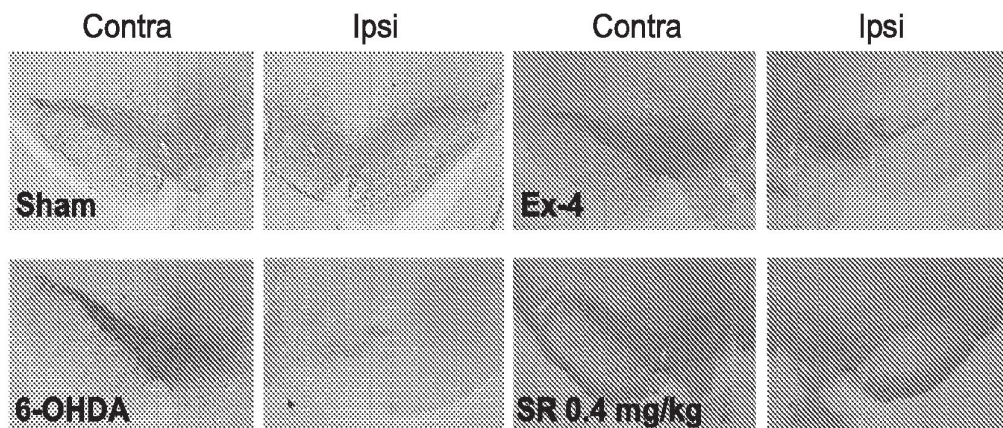


FIG. 6D

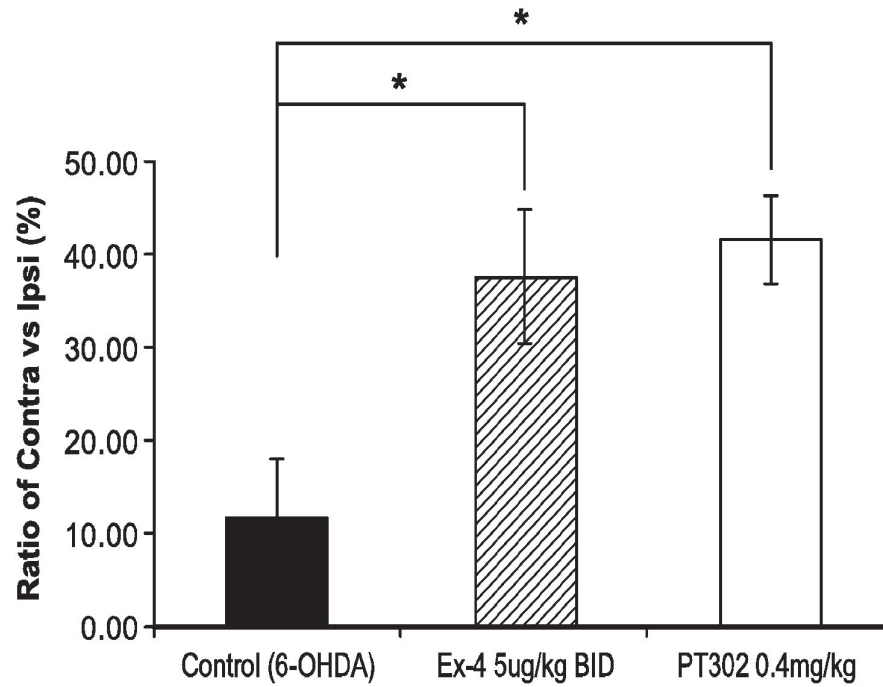


FIG. 7A

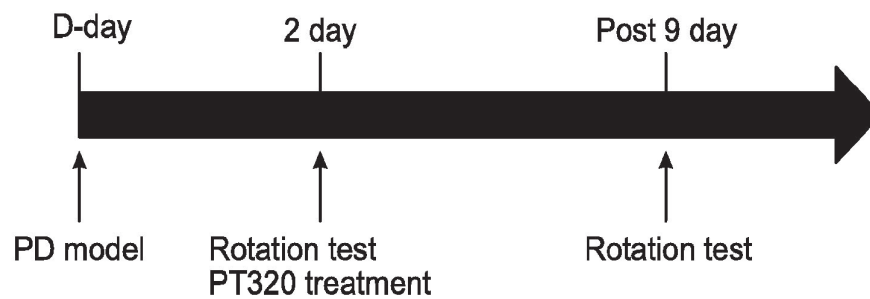
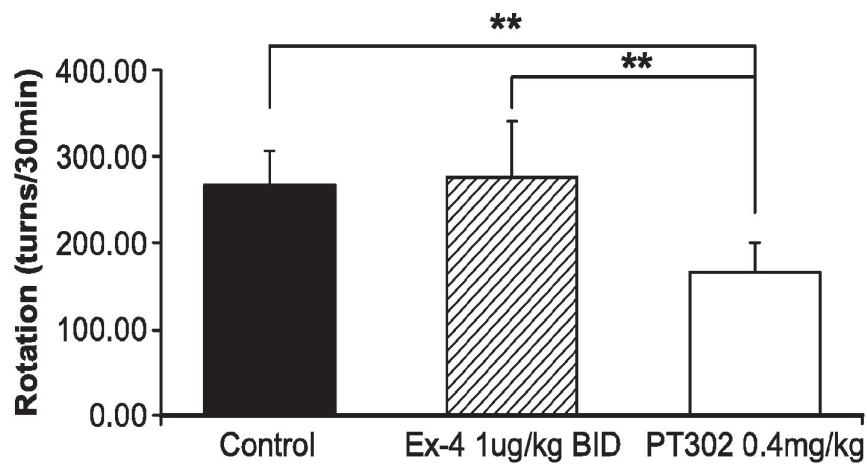
Study design

FIG. 7B



Dunnett's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Significant?	Summary	Adjusted P Value
Control vs. Ex-4 1ug BID	-8,8	-86.23 to 68.63	No	ns	0.9518
Control vs. PT302 0.4m g/kg	102.9	28.8 to 177.1	Yes	**	0.0075
Ex-4 1ug BID vs. PT302 0.4m g/kg	111.7	37.6 to 185.9	Yes	**	0.0042

FIG. 8A

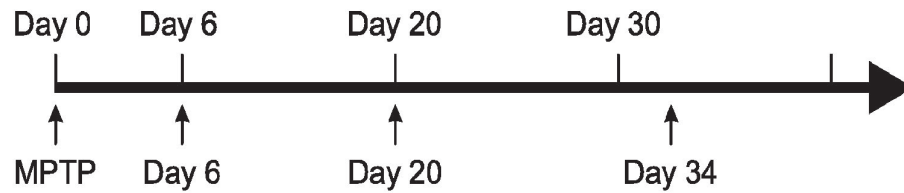


FIG. 8B

PT302 treatment of mice with MPTP-induced Parkinsonism mitigates behavioral deficits, as assessed by the Grip Test, whereas equivalent dosing of immediate release Exendin-4 dose not

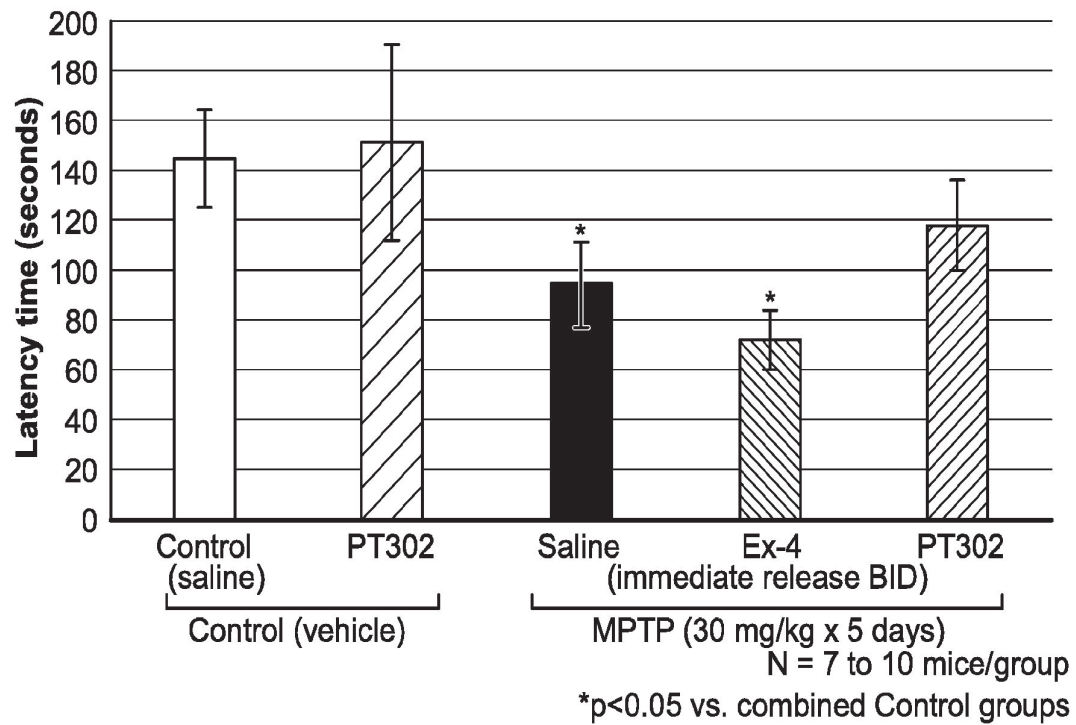


FIG. 9A

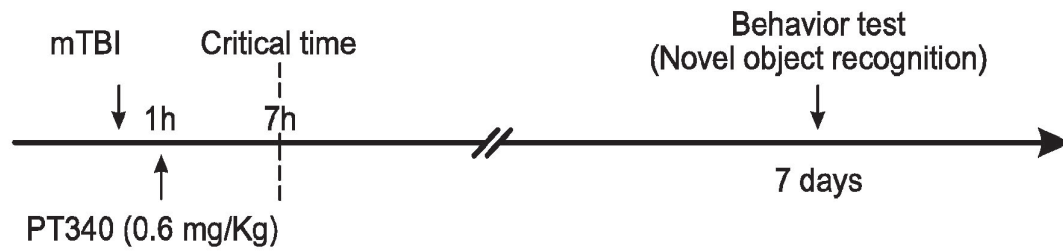


FIG. 9B

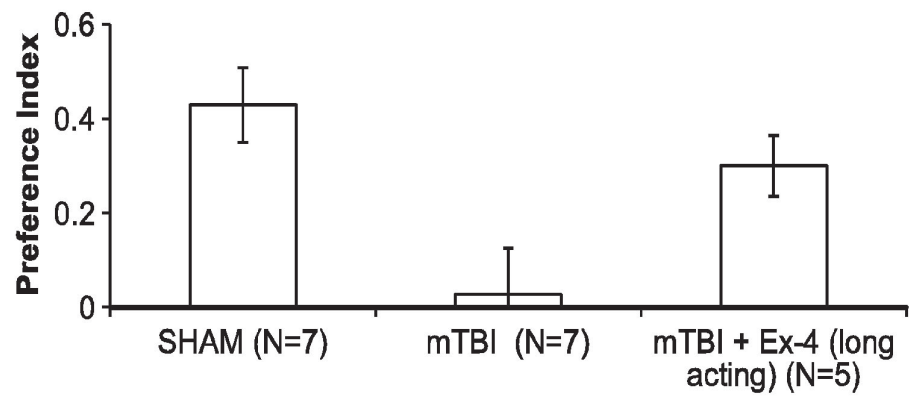


FIG. 10A

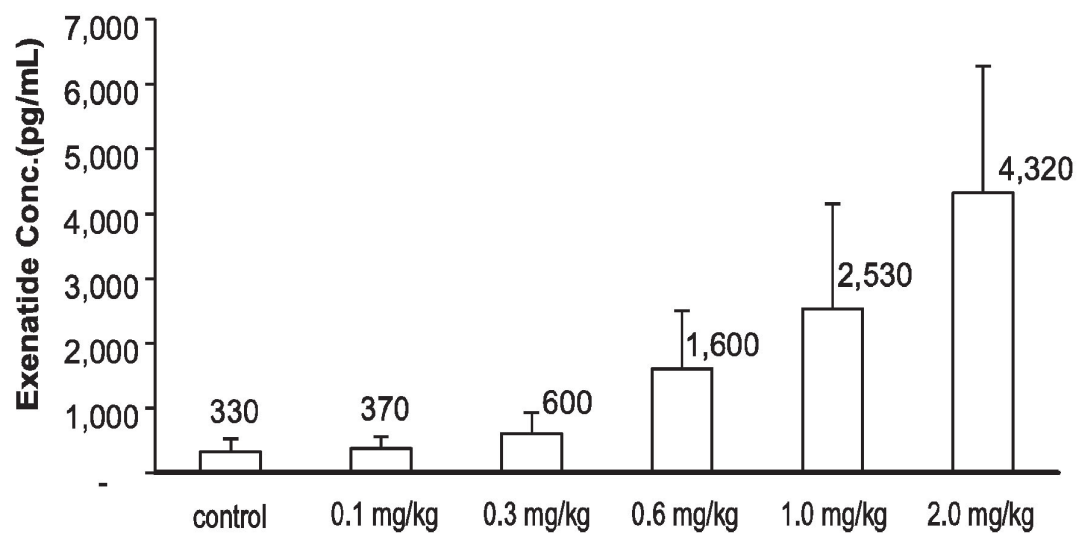


FIG. 10B

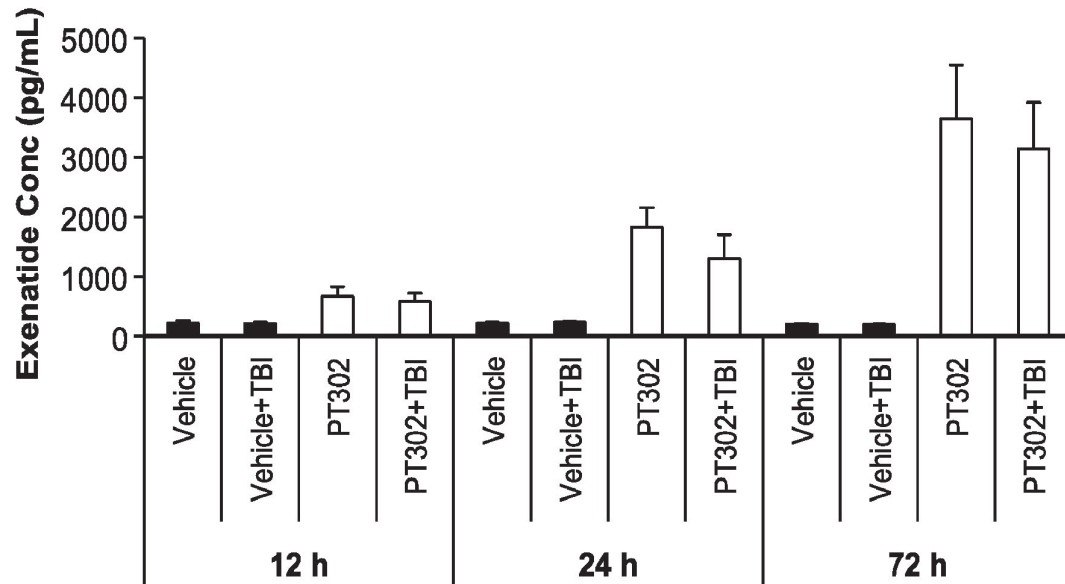


FIG. 10C

Semi-Log plot of plasma Exendin-4 levels in male ICR mice after a single subcutaneous injection of PT302 (0.024 mg/kg, 0.12 mg/kg, 0.6 mg/kg)

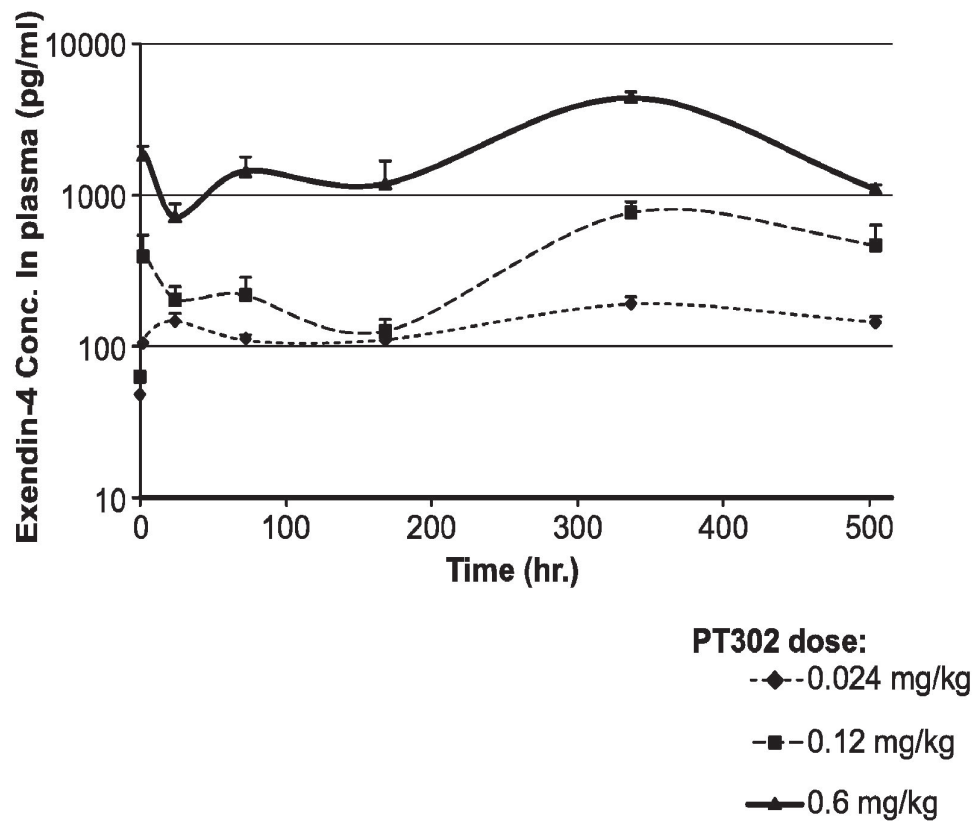


FIG. 11A

Novel object recognition at 7 days following mild traumatic brain injury (mTBI)
Mice were subjected to a 30g weight drop and treated with PT302 (0, 0.024, 0.12 or 0.6 kg/kg s.c.) after mTBI. Control animals were handled similarly but received no mTBI

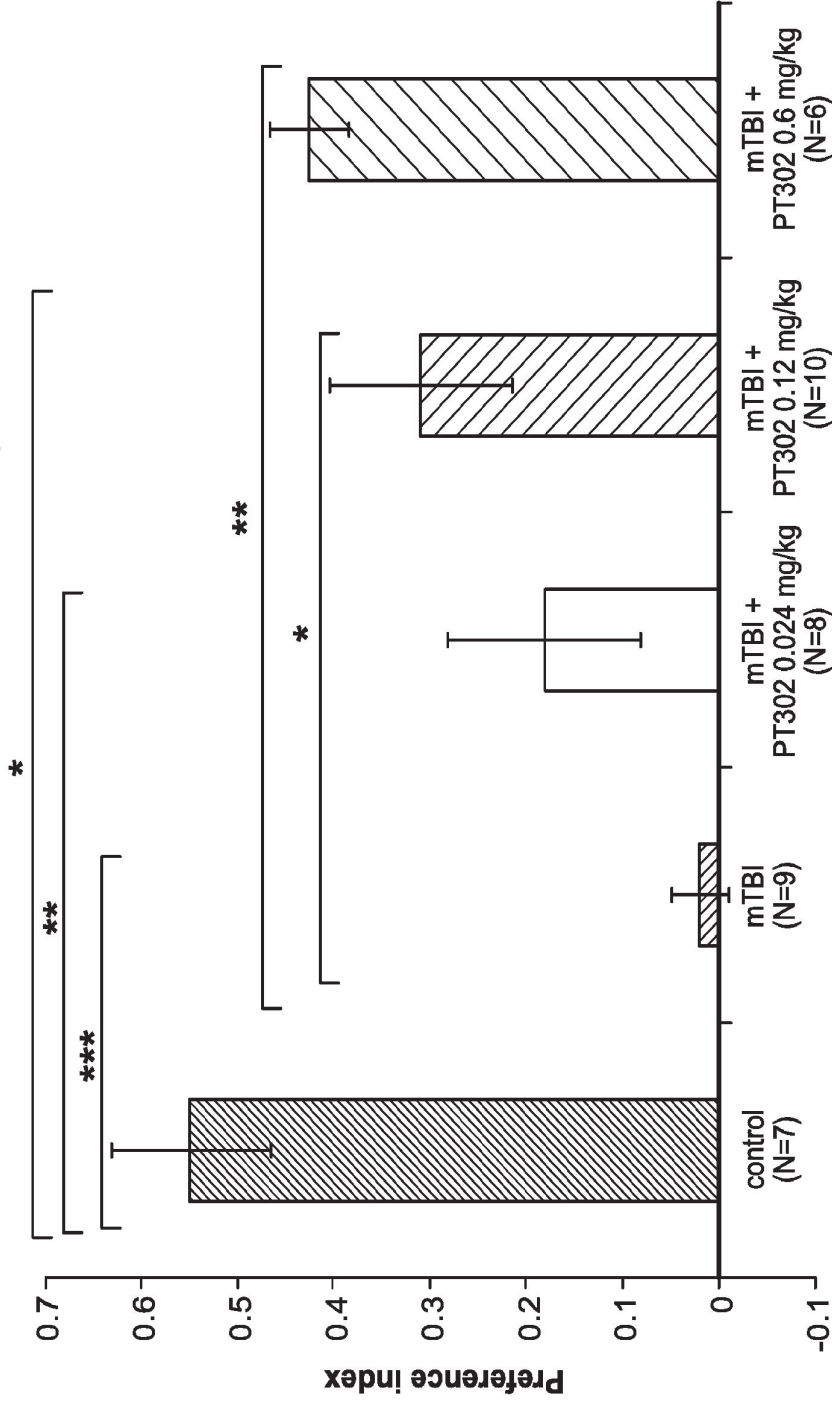


FIG. 11B

Y-maze evaluation at 7 days following mild traumatic brain injury (mTBI)
Mice were subjected to a 30g weight drop and treated with PT302 (0, 0.024, 0.12 or 0.6 kg/kg s.c.) after mTBI. Control animals were handled similarly but received no mTBI

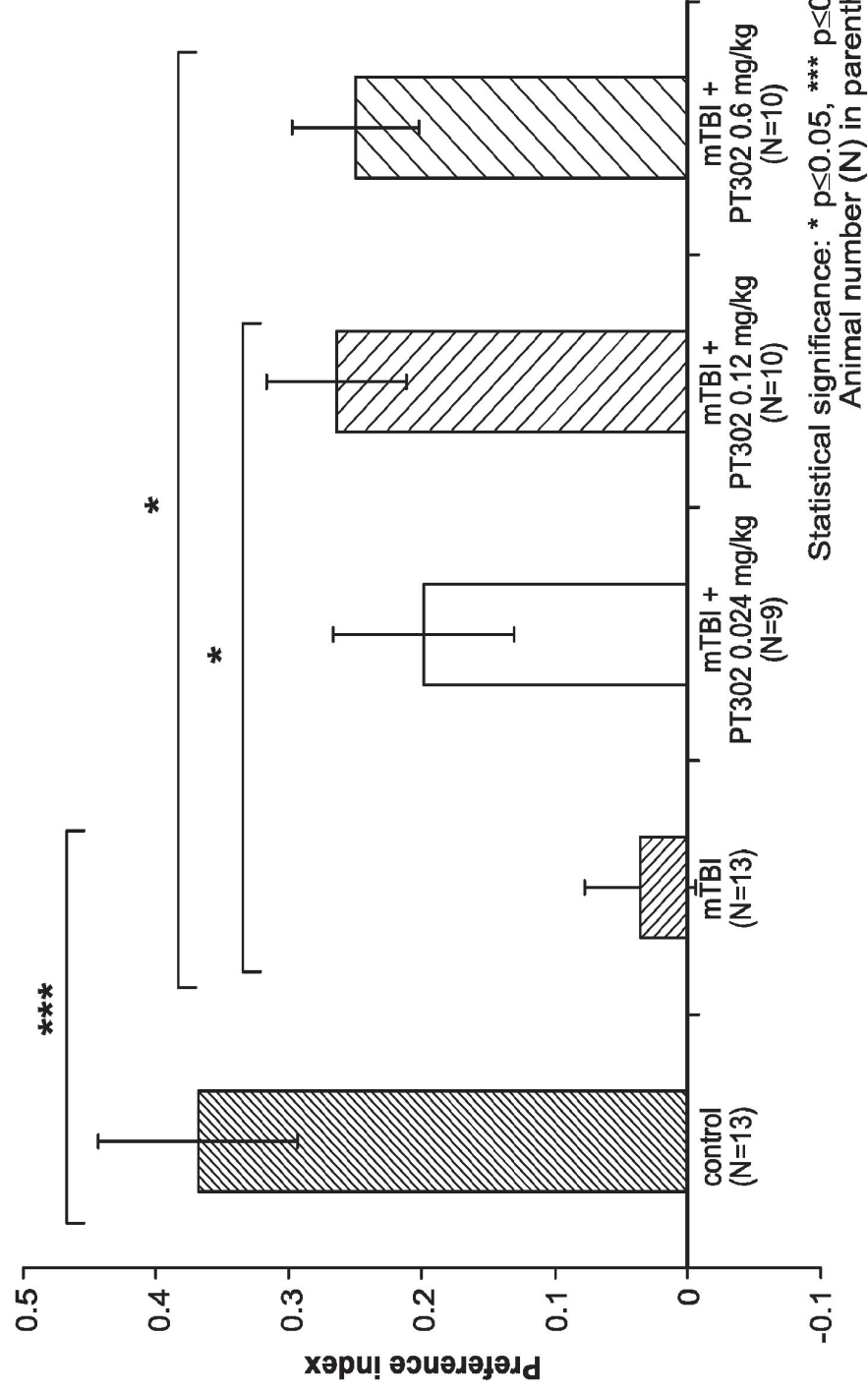
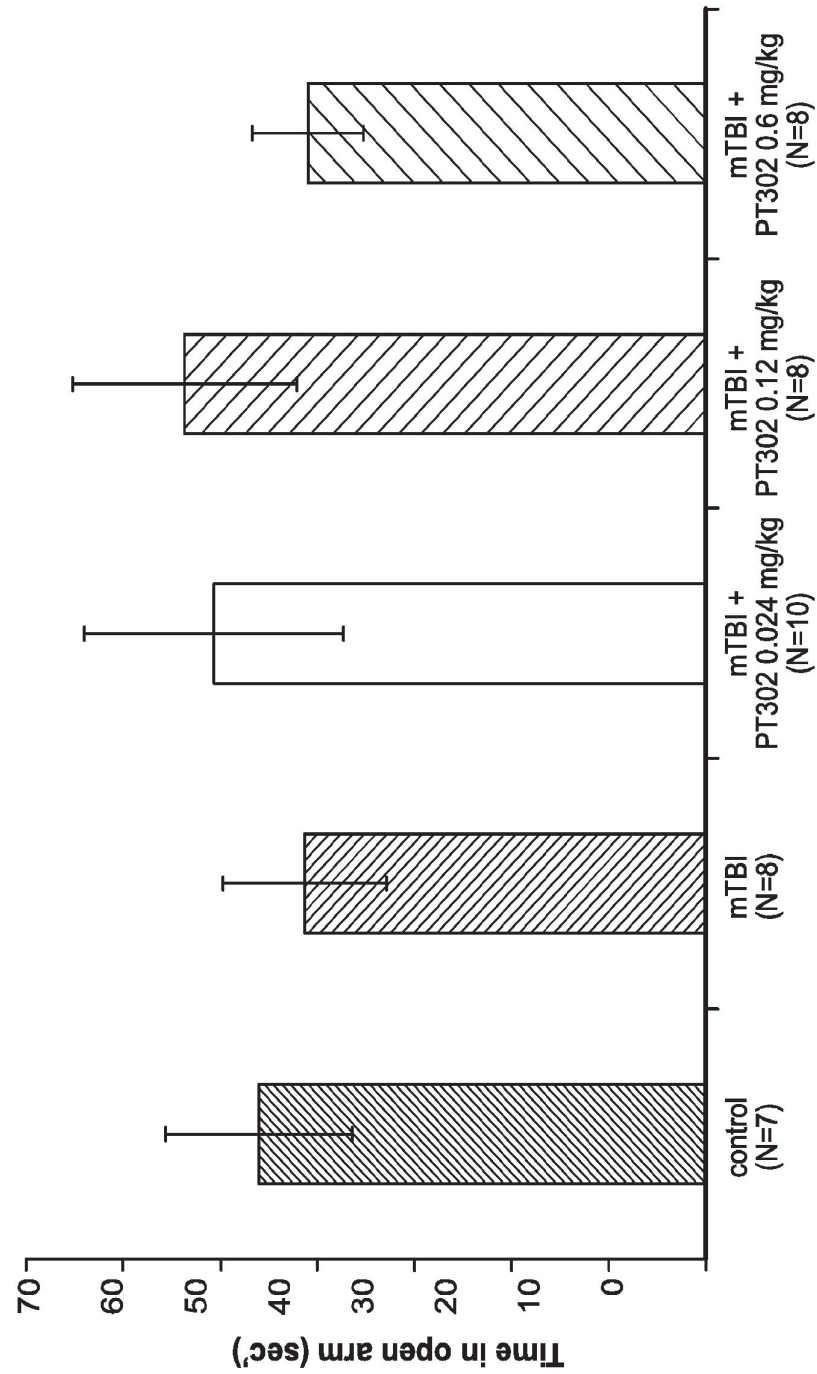


FIG. 11C **Elevated plus maze evaluation at 7 days following mild traumatic brain injury (mTBI)**
Mice were subjected to a 30g weight drop and treated with PT302 (0, 0.024, 0.12 or 0.6 kg/kg s.c.)
after mTBI. Control animals were handled similarly but received no mTBI



N.B. The elevated plus maze provides an evaluation of 'anxiety' - a lack of effect indicates that mTBI was not anxiogenic - and hence not a confound when assessing Novel Object Recognition and Y-maze paradigms

Animal number (N) in parenthesis

FIG. 12A **Novel object recognition at 30 days following mild traumatic brain injury (mTBI)**
Mice were subjected to a 30g weight drop and treated with PT302 (0, 0.024, 0.12 or 0.6 kg/kg s.c.)
after mTBI. Control animals were handled similarly but received no mTBI

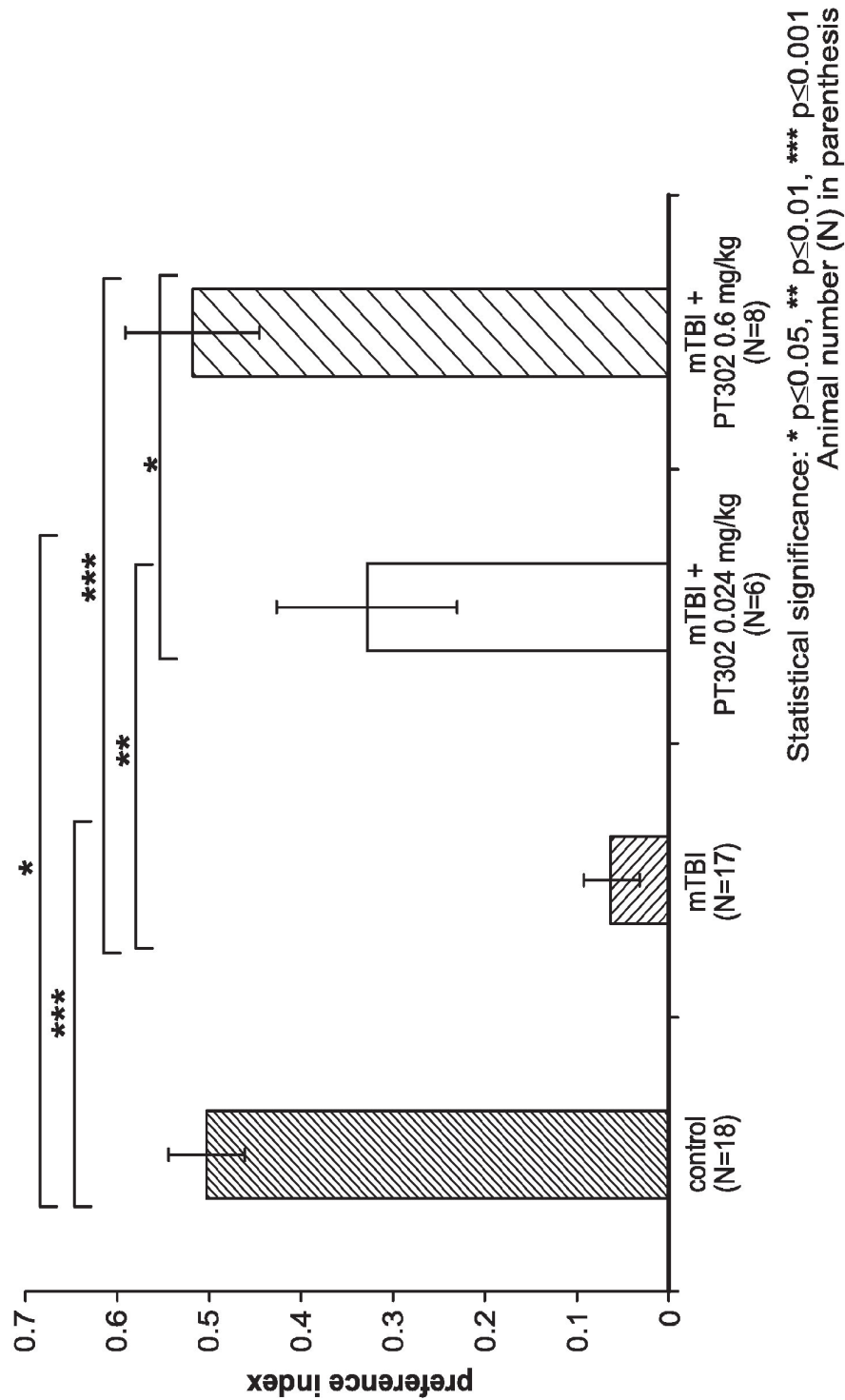
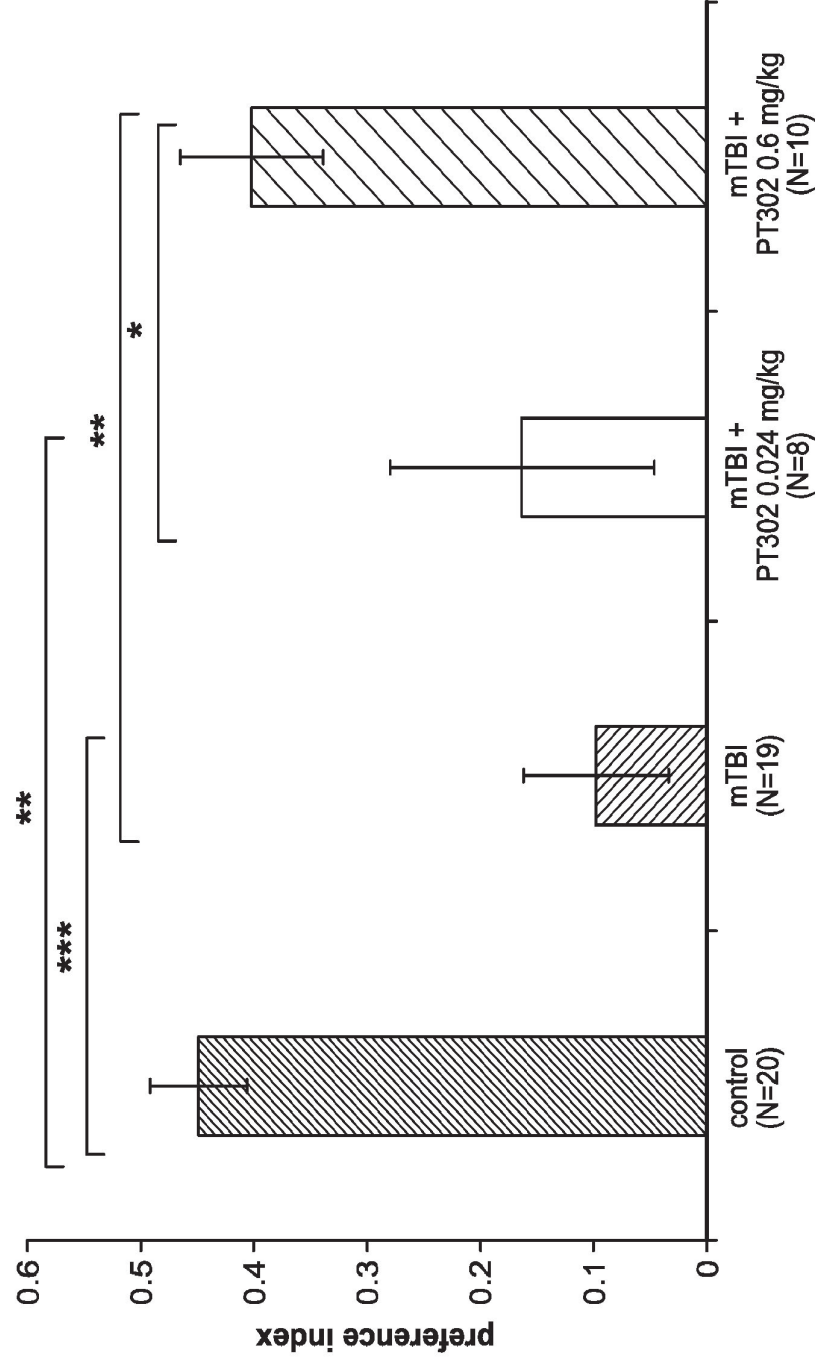


FIG. 12B

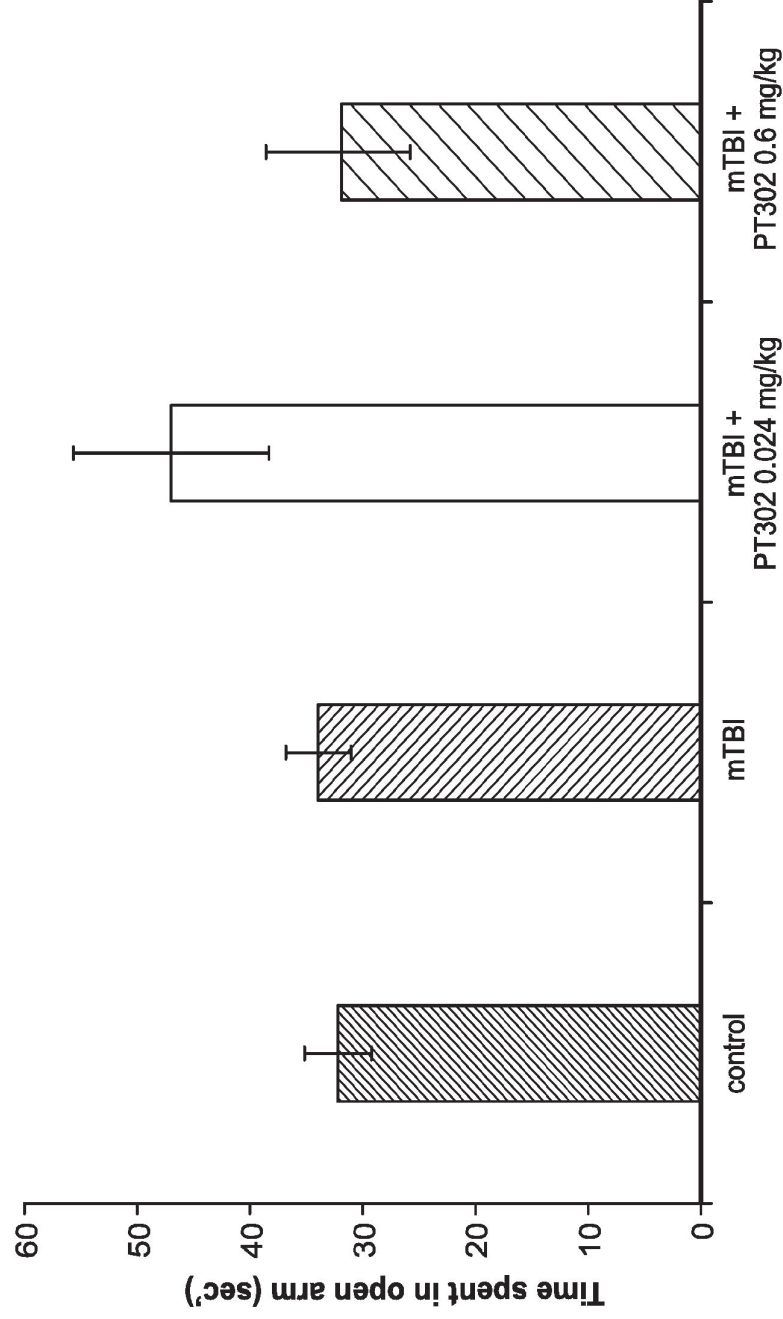
Y-maze evaluation at 30 days following mild traumatic brain injury (mTBI)
Mice were subjected to a 30g weight drop and treated with PT302 (0, 0.024, 0.12 or 0.6 kg/kg s.c.) after mTBI. Control animals were handled similarly but received no mTBI



Statistical significance: * $p \leq 0.05$, *** $p \leq 0.001$
Animal number (N) in parenthesis

FIG. 12C

Elevated plus maze evaluation at 30 days following mild traumatic brain injury (mTBI)
Mice were subjected to a 30g weight drop and treated with PT302 (0, 0.024, 0.12 or 0.6 kg/kg s.c.) after mTBI. Control animals were handled similarly but received no mTBI



N.B. The elevated plus maze provides an evaluation of 'anxiety' - a lack of effect indicates that mTBI was not anxiogenic - and hence not a confound when assessing Novel Object Recognition and Y-maze paradigms

Animal number (N = 8 to 9 mice per group)

FIG. 13A

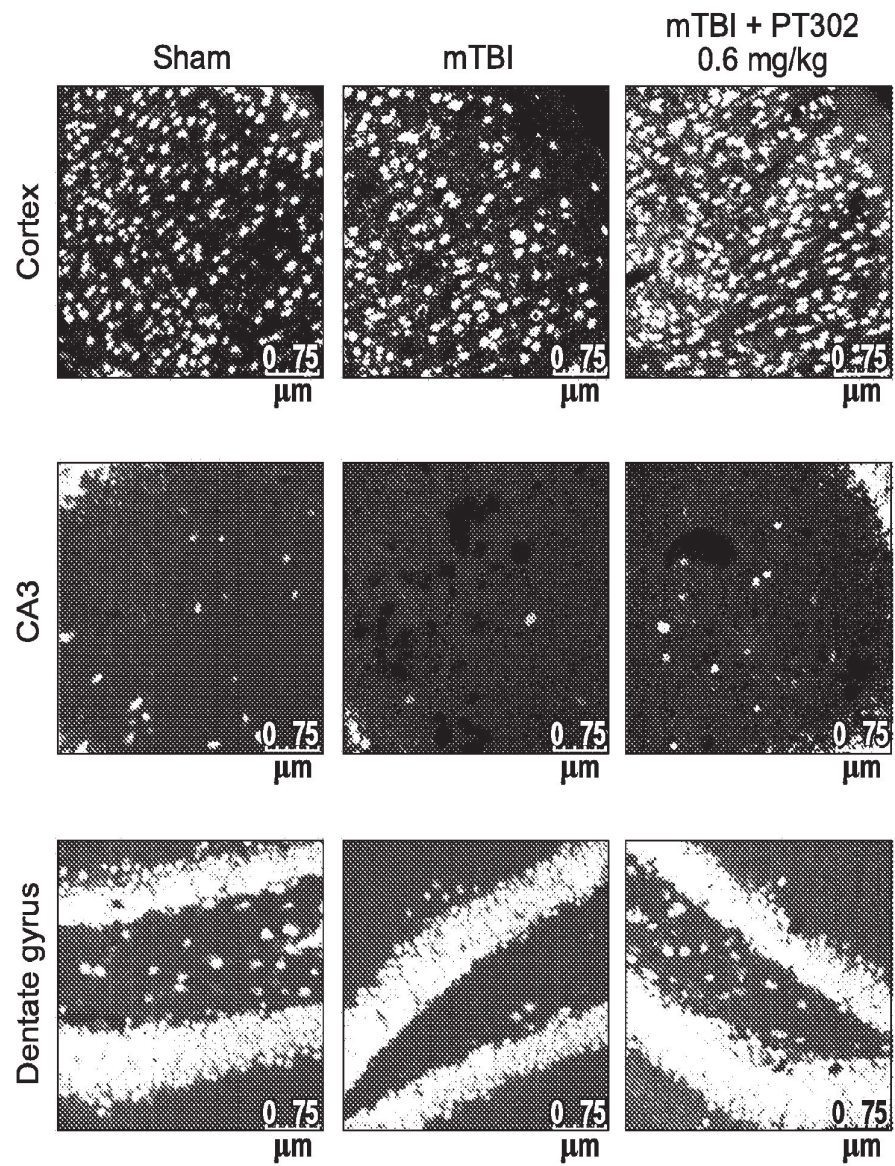


FIG. 13B

PT302 mitigates neuronal loss (NeuN positive staining cell loss) within the cerebral cortex of mice challenged with mTBI, evaluated on day 30

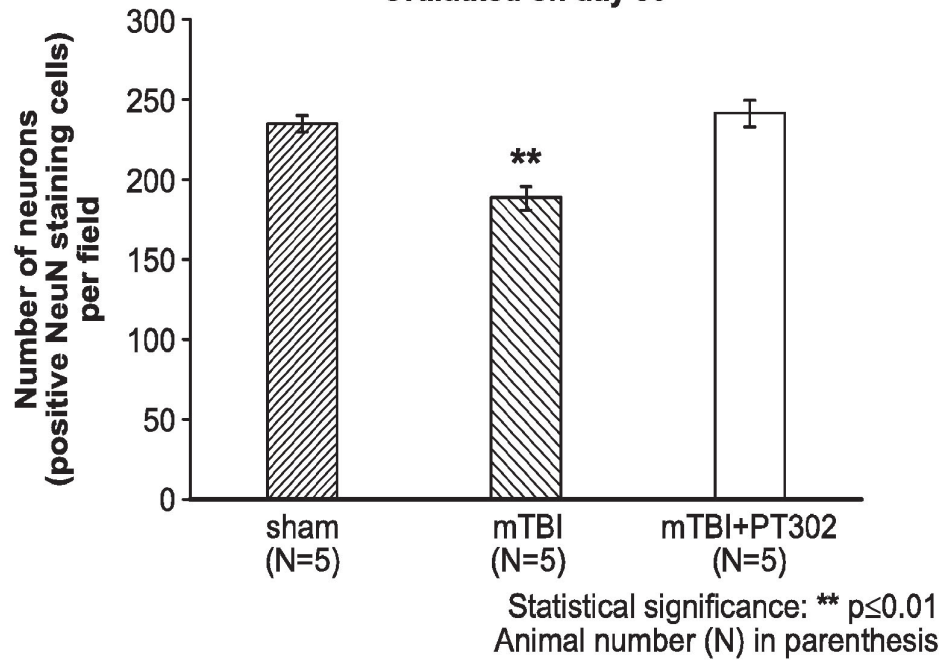


FIG. 13C

PT302 mitigates neuronal loss (NeuN positive staining cell loss) within the CA3 hippocampal region of mice challenged with mTBI, evaluated on day 30

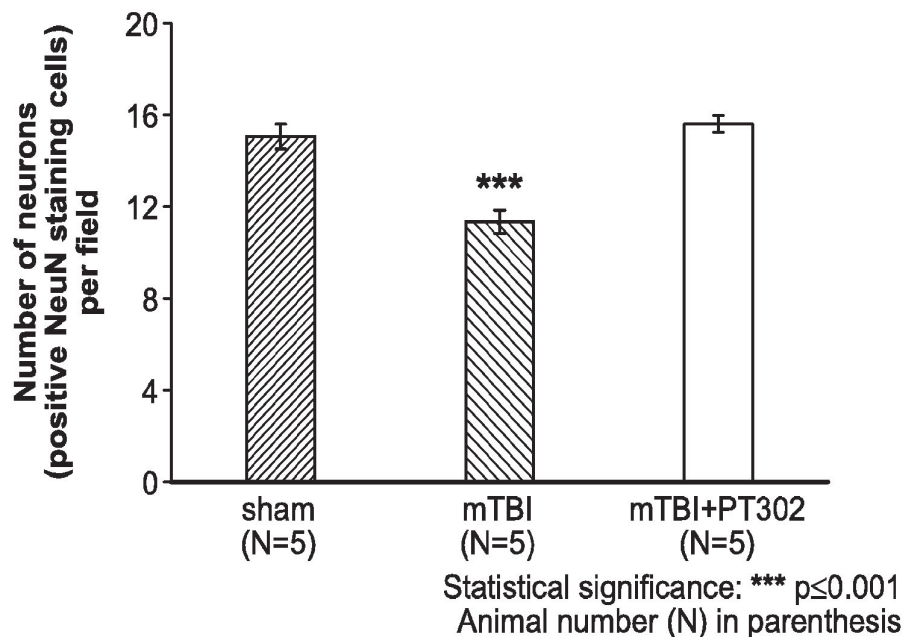


FIG. 13D

PT302 mitigates neuronal loss (NeuN positive staining cell loss) within the dentate gyrus brain region of mice challenged with mTBI, evaluated on day 30

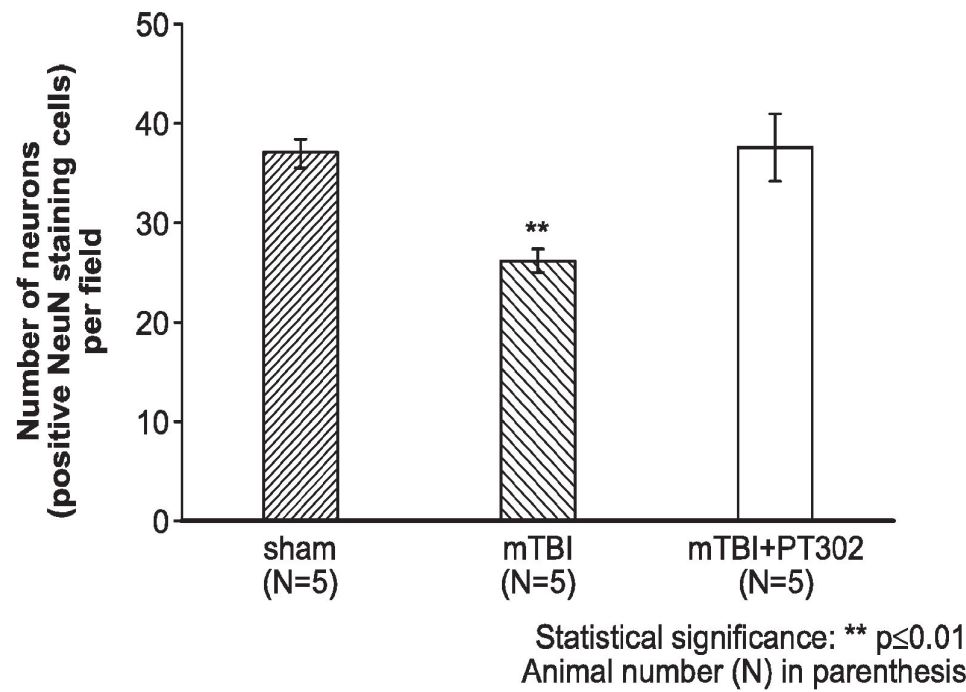


FIG. 14

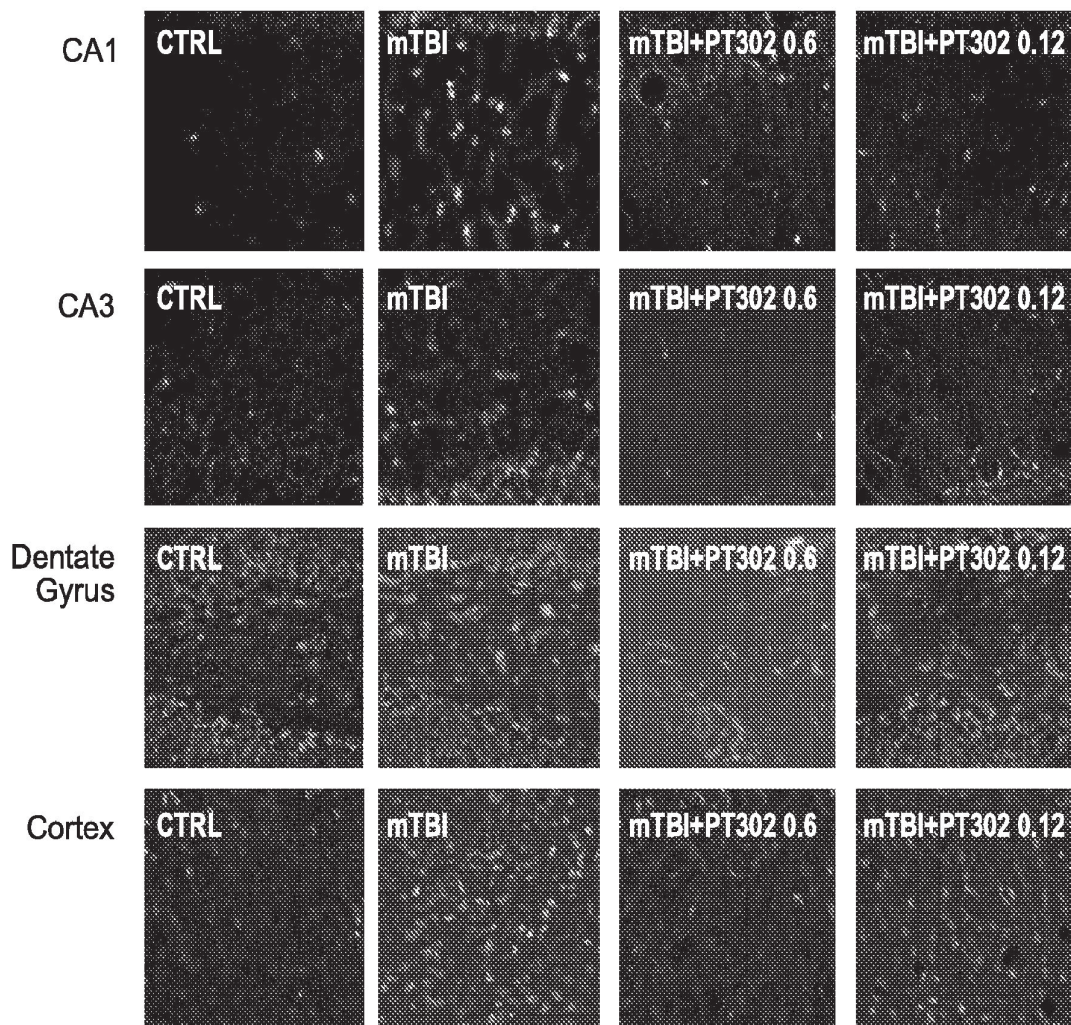


FIG. 14B

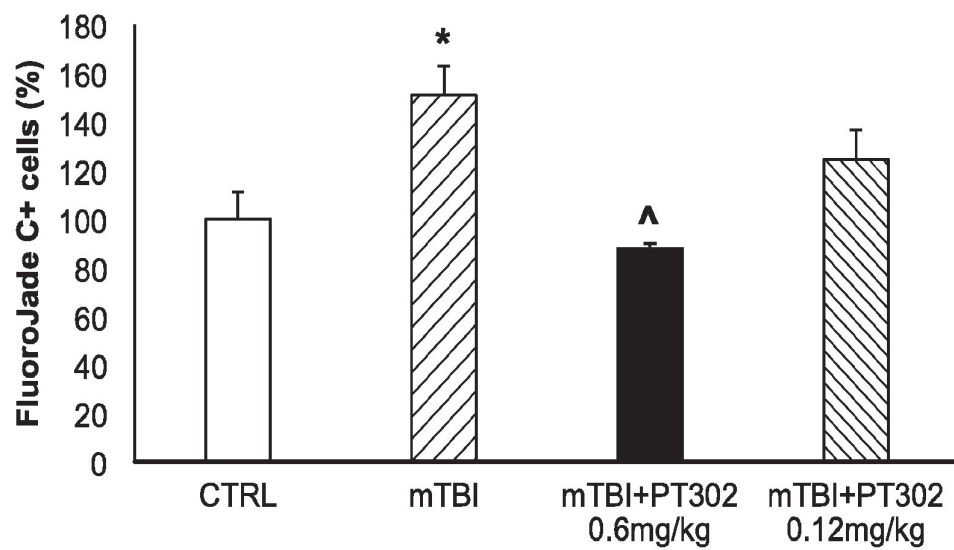


FIG. 14C

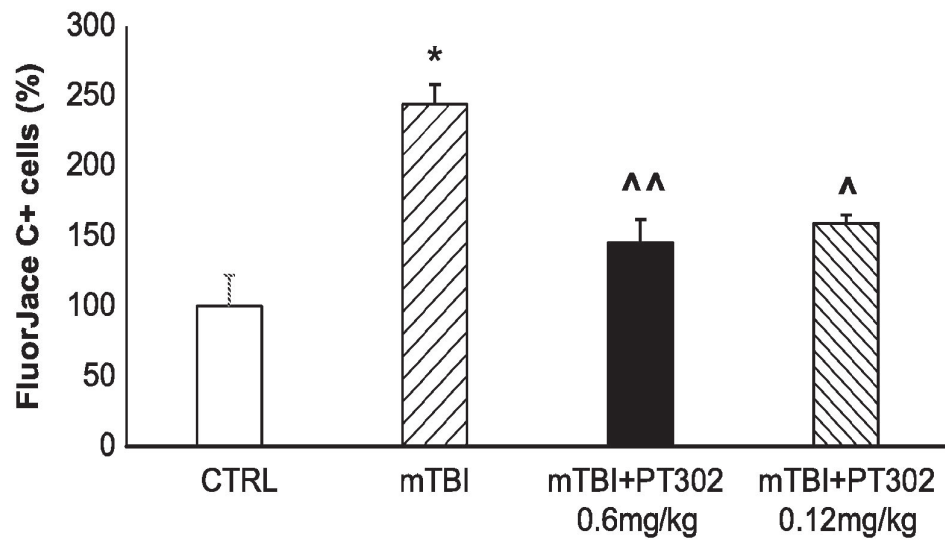


FIG. 14D

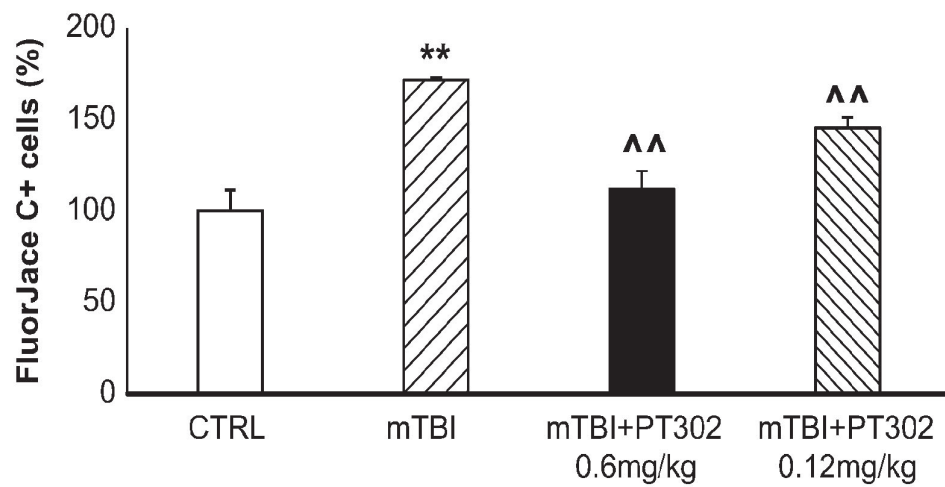


FIG. 14E

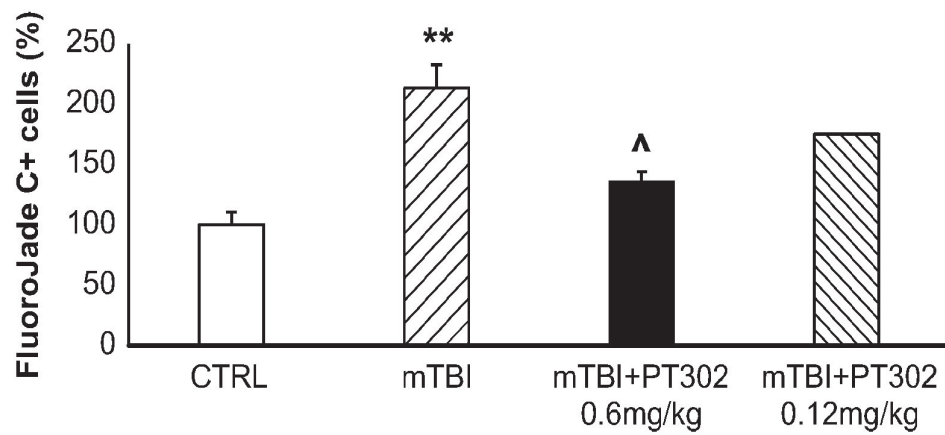


FIG. 15A

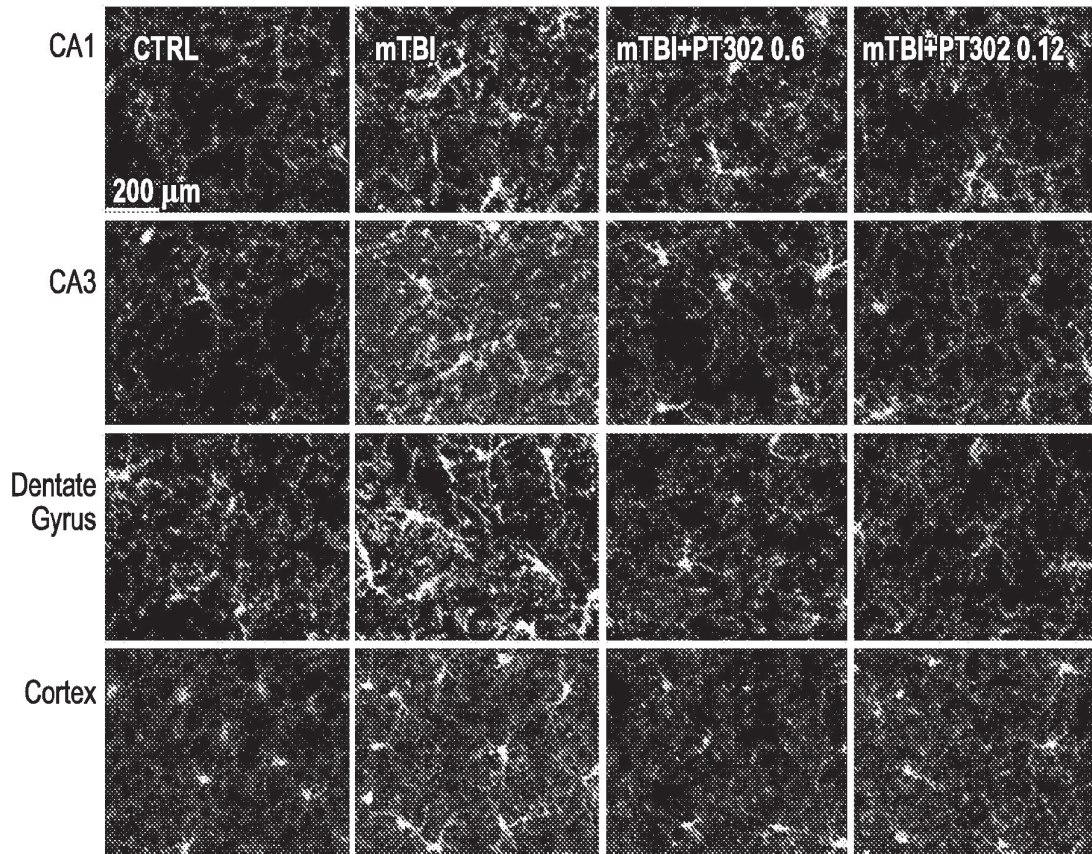


FIG. 15B

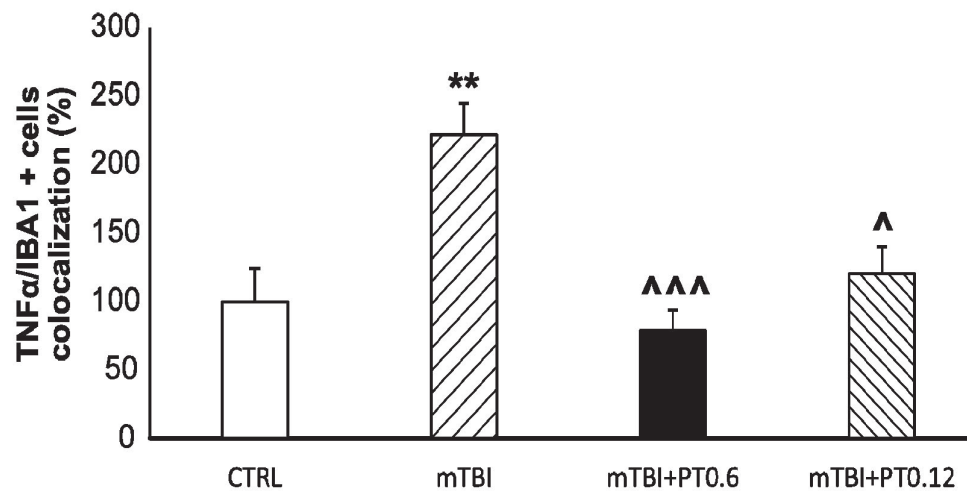


FIG. 15C

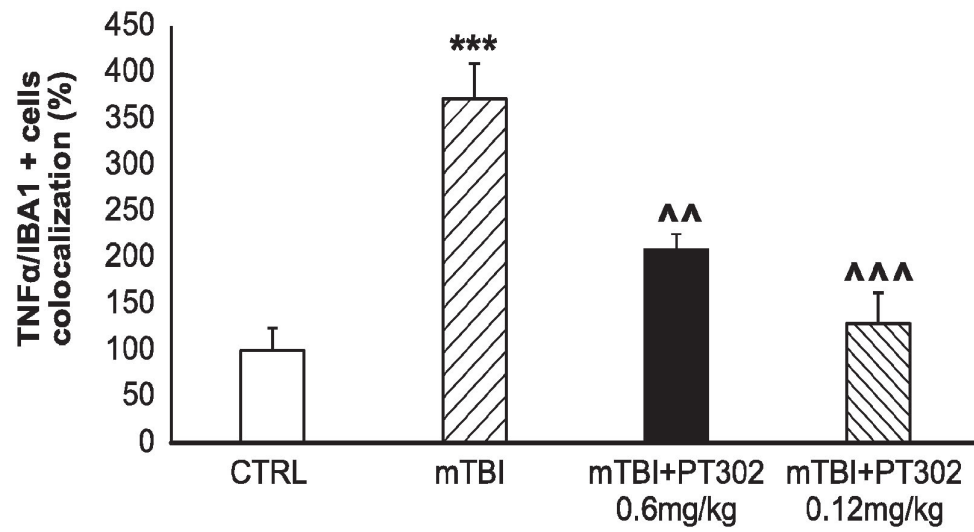


FIG. 15D

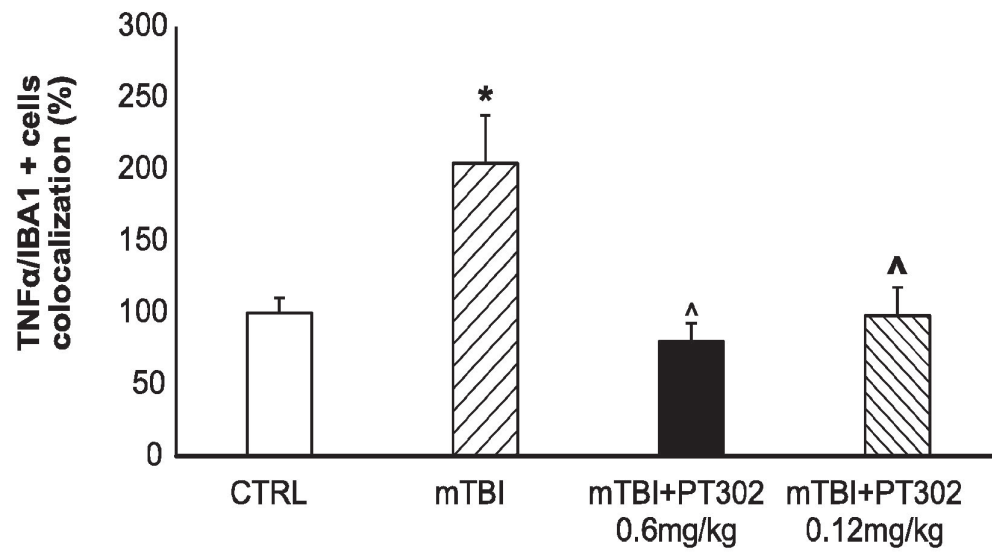


FIG. 15E

