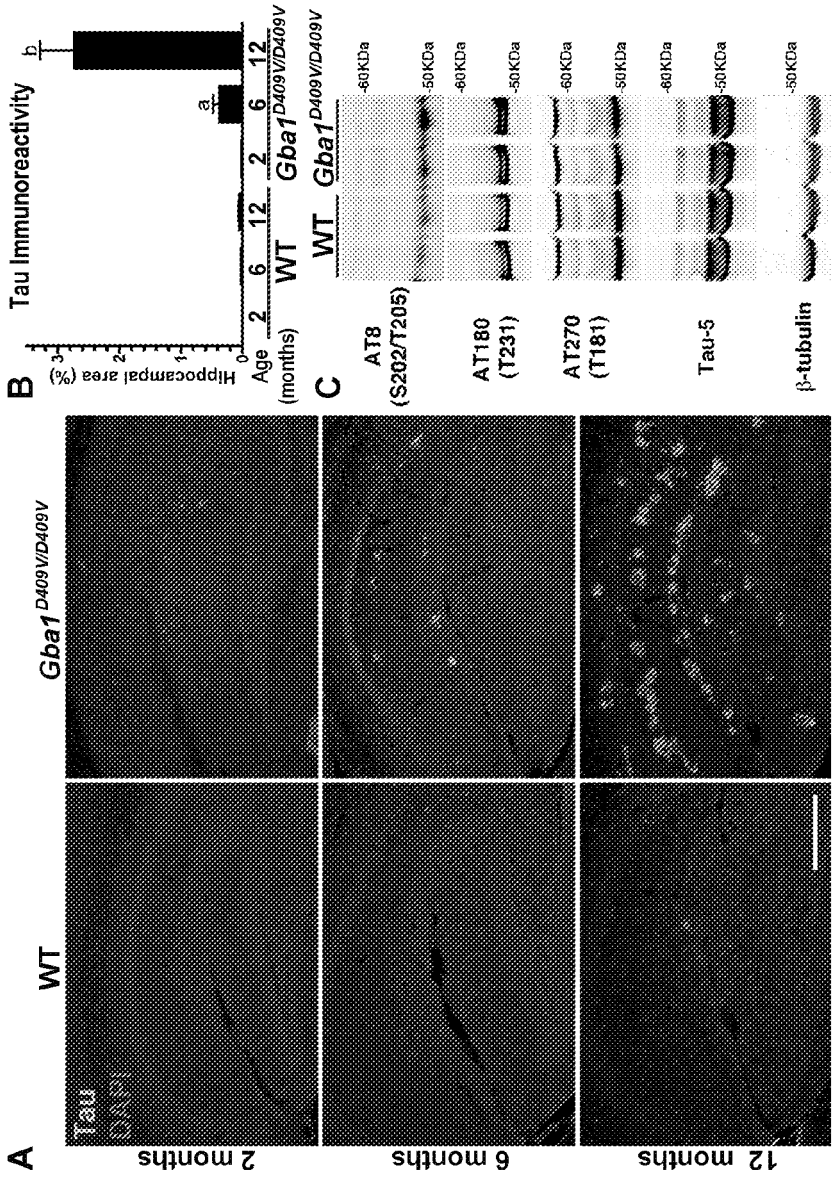

A
WT
Gba1 D409V/D409V
Tau
DAPI
2 months
6 months
12 months
B
Tau Immunoreactivity
Hippocampal area (%)
Age (months)
WT
Gba1 D409V/D409V
C
AT8 (S202/T205)
AT180 (T231)
AT270 (T181)
Tau-5
β-tubulin
60KDa
50KDa

FIG. 1

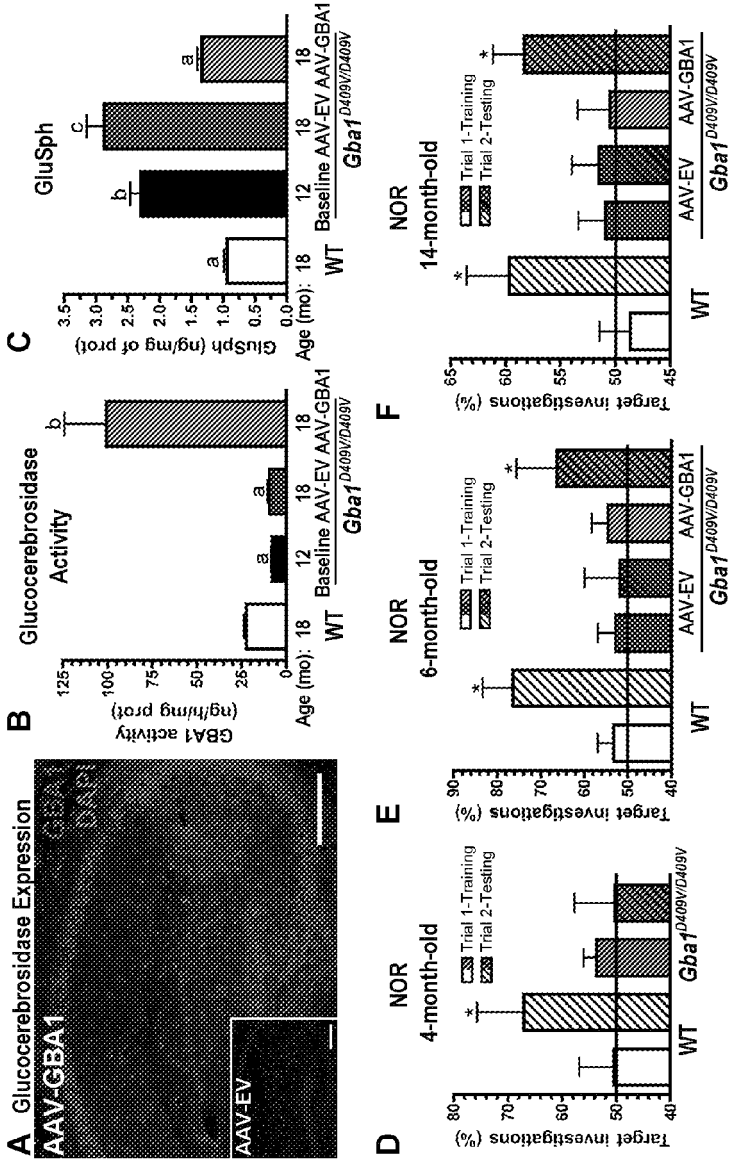

A
Glucocerebrosidase Expression
AAV-GBA1
AAV-EV
B
Glucocerebrosidase Activity
GBA1 activity (ng/h/mg prot)
Age (mo): 18 12 18 18
WT Baseline AAV-EV AAV-GBA1
Gba1D409V/D409V
C
GluSph
GluSph (ng/mg of prot)
Age (mo): 18 12 18 18
WT Baseline AAV-EV AAV-GBA1
Gba1D409V/D409V
D
NOR
4-month-old
Trial 1-Training
Trial 2-Testing
Target investigations (%)
WT
Gba1D409V/D409V
E
NOR
6-month-old
Trial 1-Training
Trial 2-Testing
Target investigations (%)
WT
AAV-EV AAV-GBA1
Gba1D409V/D409V
F
NOR
14-month-old
Trial 1-Training
Trial 2-Testing
Target investigations (%)
WT
AAV-EV AAV-GBA1
Gba1D409V/D409V

FIG. 2

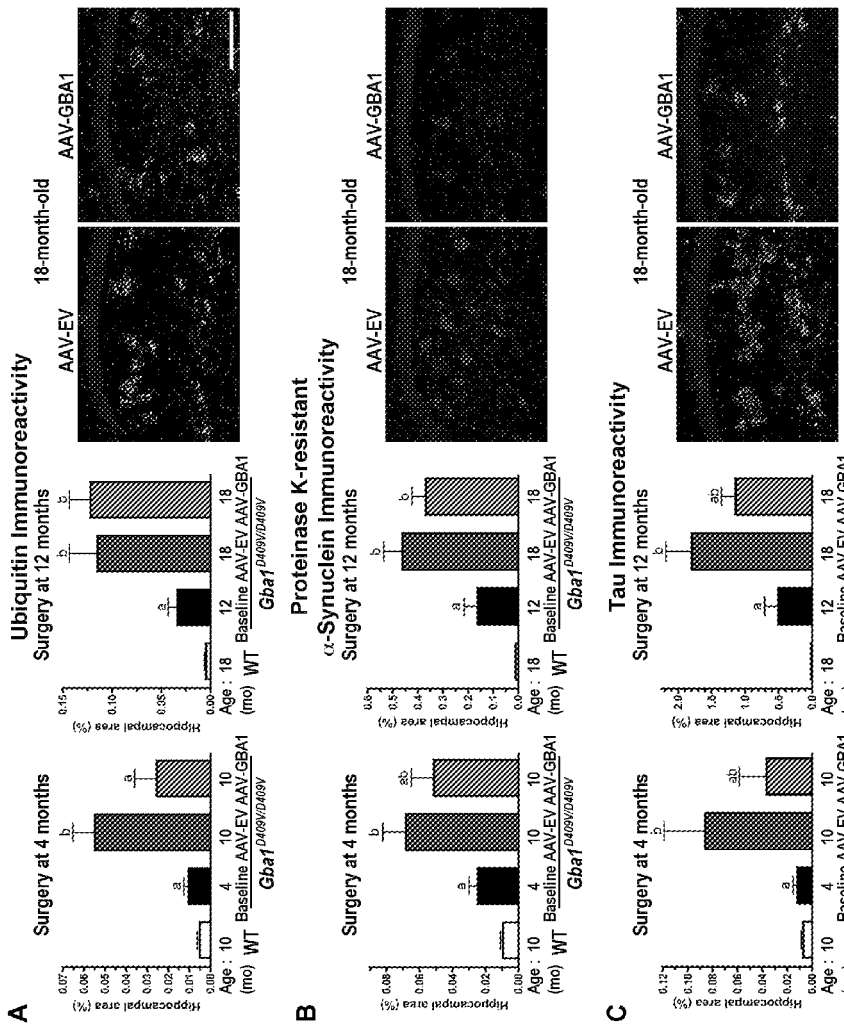

A
Ubiquitin Immunoreactivity
Surgery at 4 months
Surgery at 12 months
AAV-EV
AAV-GBA1
18-month-old
Hippocampal area (%)
Age : 10 4 10 12 18 18
(mo) WT Baseline AAV-EV AAV-GBA1 AAV-EV AAV-GBA1
Gba1D409V/D409V
B
Proteinase K-resistant
α-Synuclein Immunoreactivity
C
Tau Immunoreactivity

FIG. 3

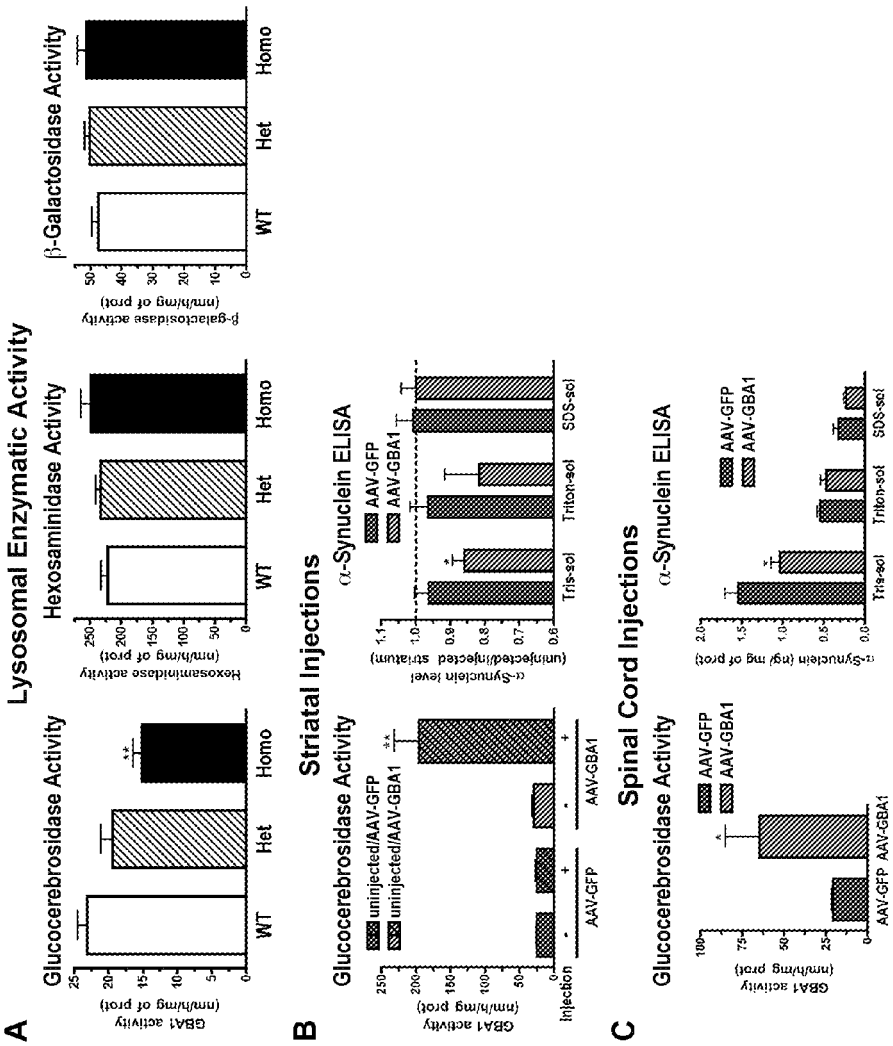

A
Lysosomal Enzymatic Activity
Glucocerebrosidase Activity
GBA1 activity (nmol/h/mg of prot)
WT
Het
Homo
Hexosaminidase Activity
Hexosaminidase activity (nmol/h/mg of prot)
β-Galactosidase Activity
β-galactosidase activity (nmol/h/mg of prot)
B
Striatal Injections
Glucocerebrosidase Activity
uninjected/AAV-GFP
uninjected/AAV-GBA1
GBA1 activity (nmol/h/mg prot)
Injection
AAV-GFP
AAV-GBA1
α-Synuclein ELISA
AAV-GFP
AAV-GBA1
α-Synuclein level (uninjected/injected striatum)
Tris-sol
Triton-sol
SDS-sol
C
Spinal Cord Injections
Glucocerebrosidase Activity
AAV-GFP
AAV-GBA1
GBA1 activity (nmol/h/mg prot)
α-Synuclein ELISA
α-Synuclein (ng/ mg of prot)

FIG. 4

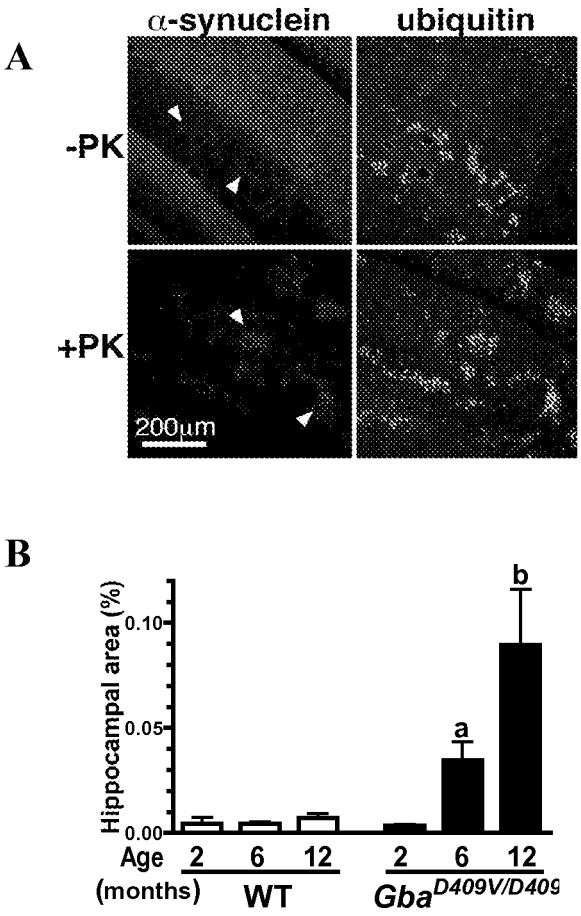

A
α-synuclein
ubiquitin
-PK
+PK
200μm
B
Hippocampal area (%)
0.10
0.05
0.00
a
b
Age
2
6
12
2
6
12
(months)
WT
Gba D409V/D409

FIG. 5

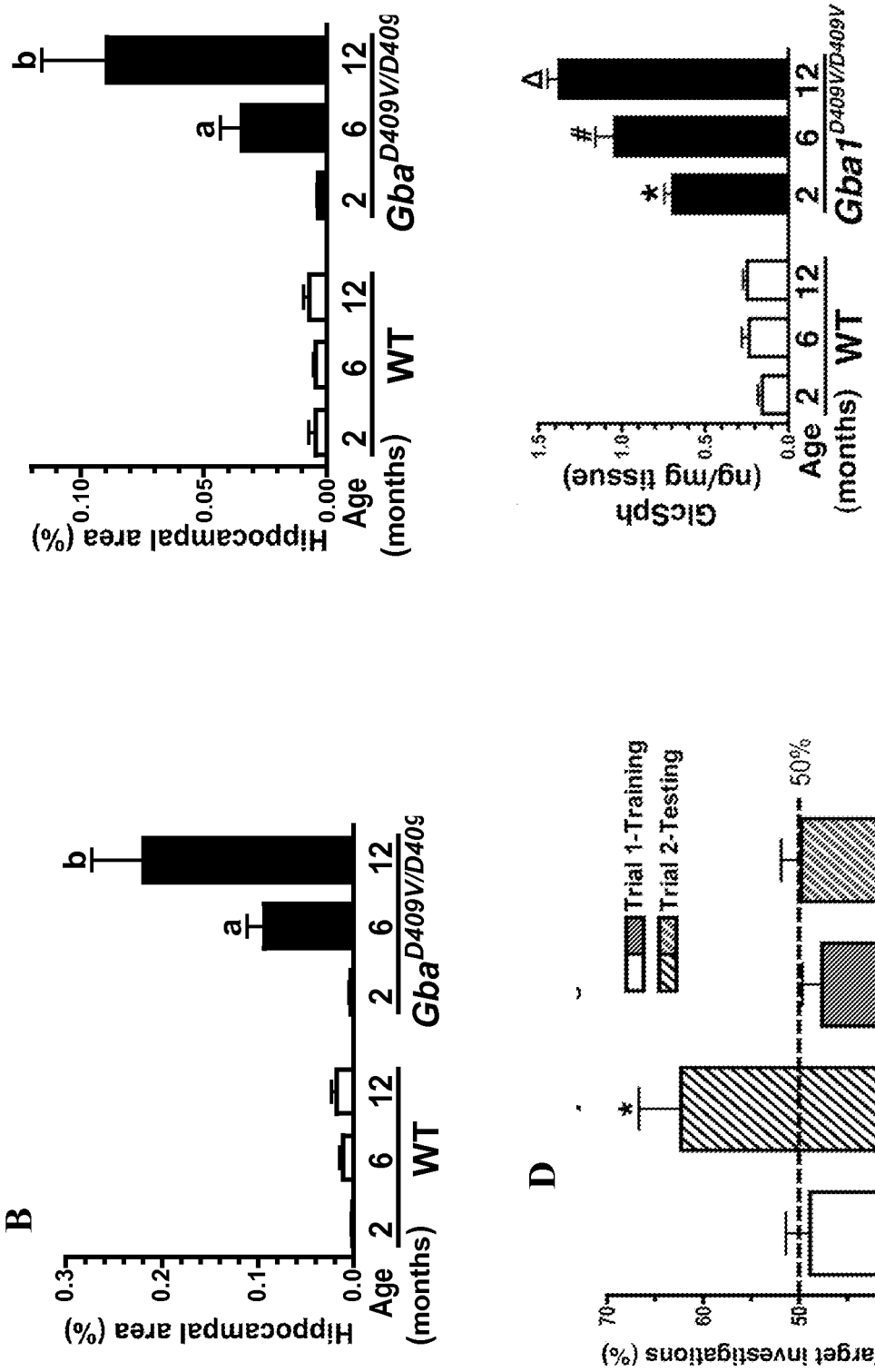

B
Hippocampal area (%)
0.3
0.2
0.1
0.0
a
b
Age 2 6 12 2 6 12
(months) WT Gba D409V/D409
Hippocampal area (%)
0.10
0.05
0.00
a
b
Age 2 6 12 2 6 12
(months) WT Gba D409V/D409
GlcSph (ng/mg tissue)
1.5
1.0
0.5
0.0
*
#
Δ
Age 2 6 12 2 6 12
(months) WT Gba1 D409V/D409V
D
Trial 1-Training
Trial 2-Testing
Target investigations (%)
70
60
50
40
*
50%
WT
Gba1 D409V/D409V

FIG. 6

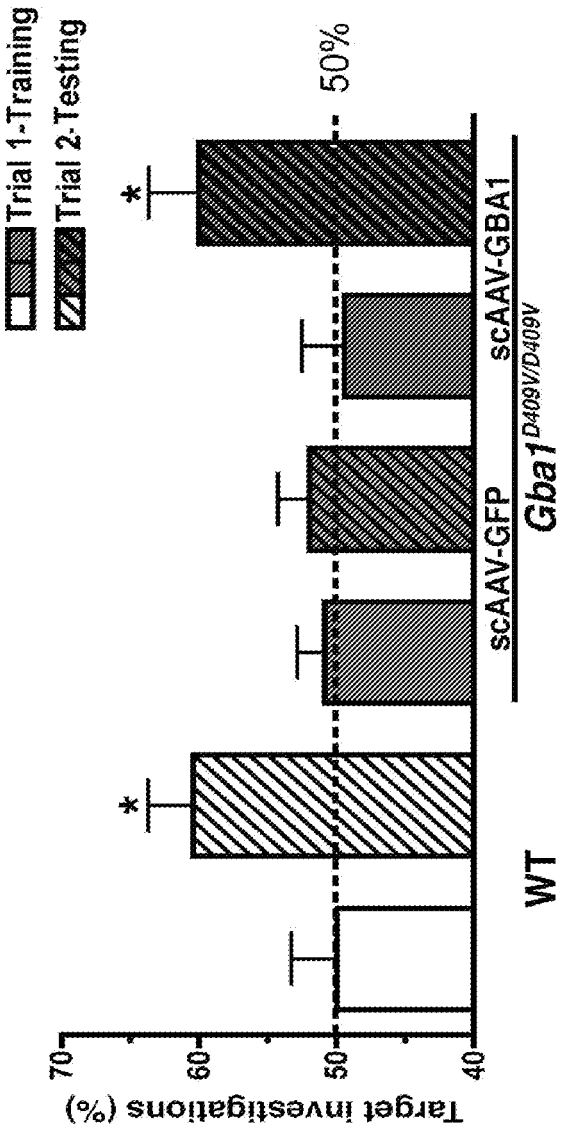

Trial 1-Training
Trial 2-Testing
50%
*
*
Target investigations (%)
70
60
50
40
WT
scAAV-GFP
scAAV-GBA1
Gba1D409V/D409V

FIG. 7

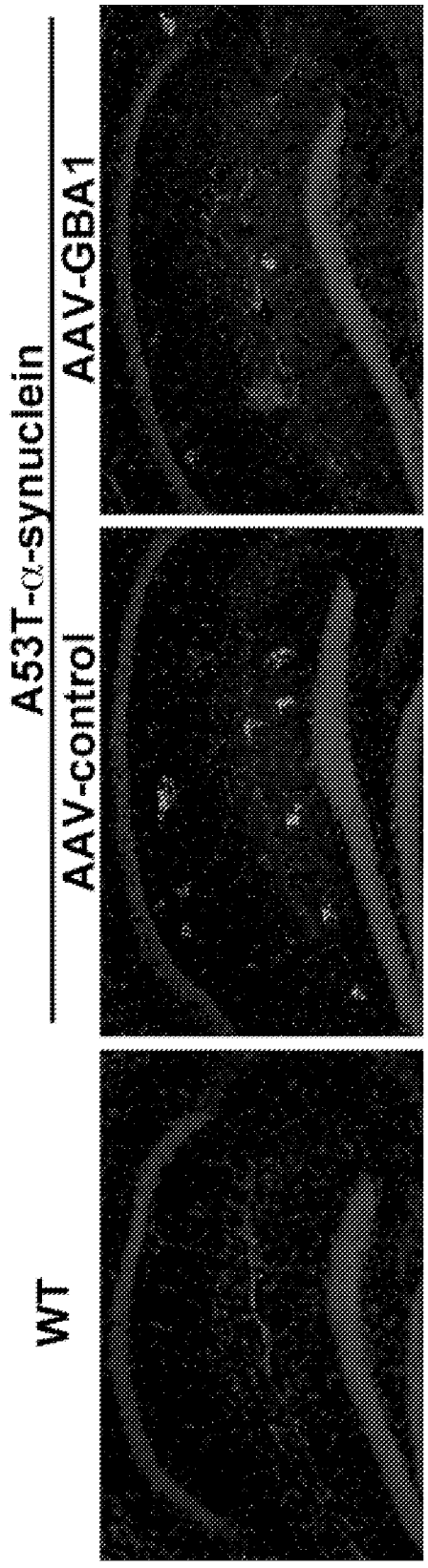
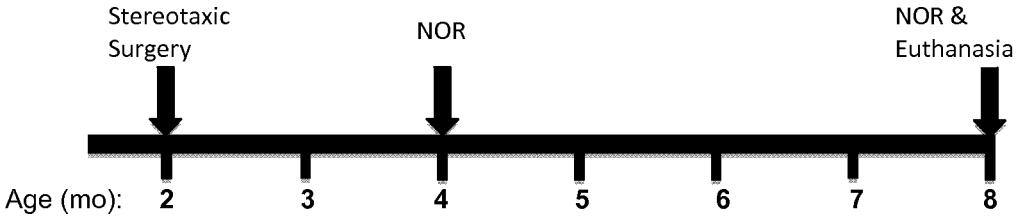


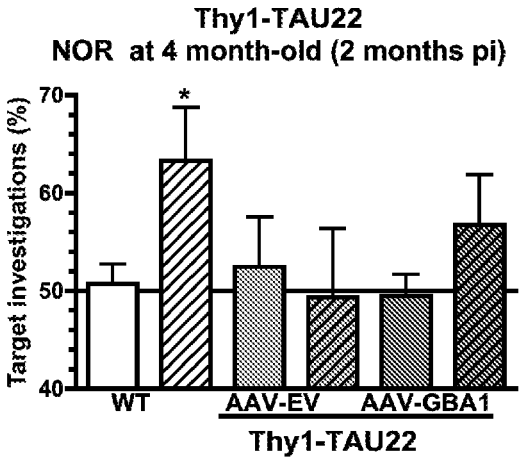
FIG. 8

A

Groups		(n)
WT uninjected	control	8
Thy1-TAU22	AAV1-control	9
Thy1-TAU22	AAV1-GBA1	13



B



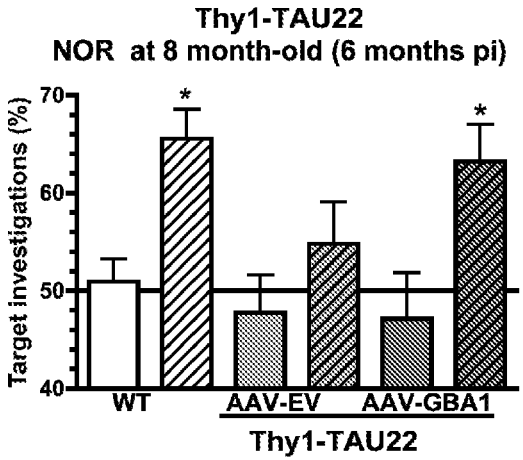


FIG. 9