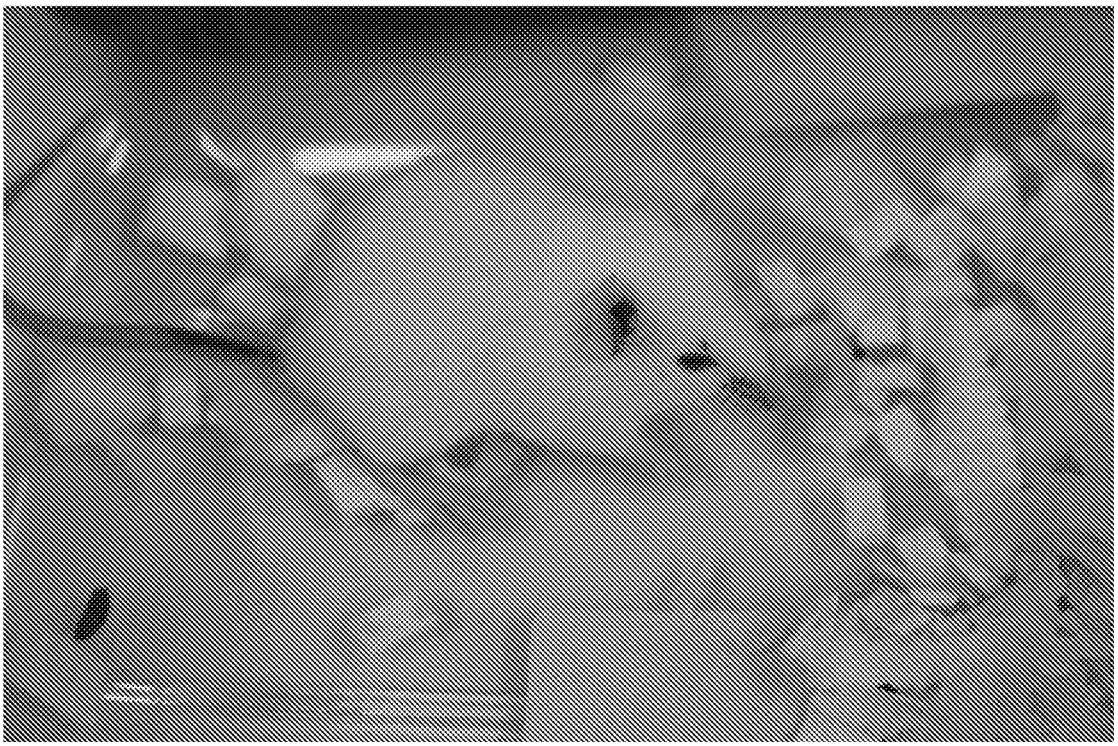


FIG. 1A



FIG. 1B

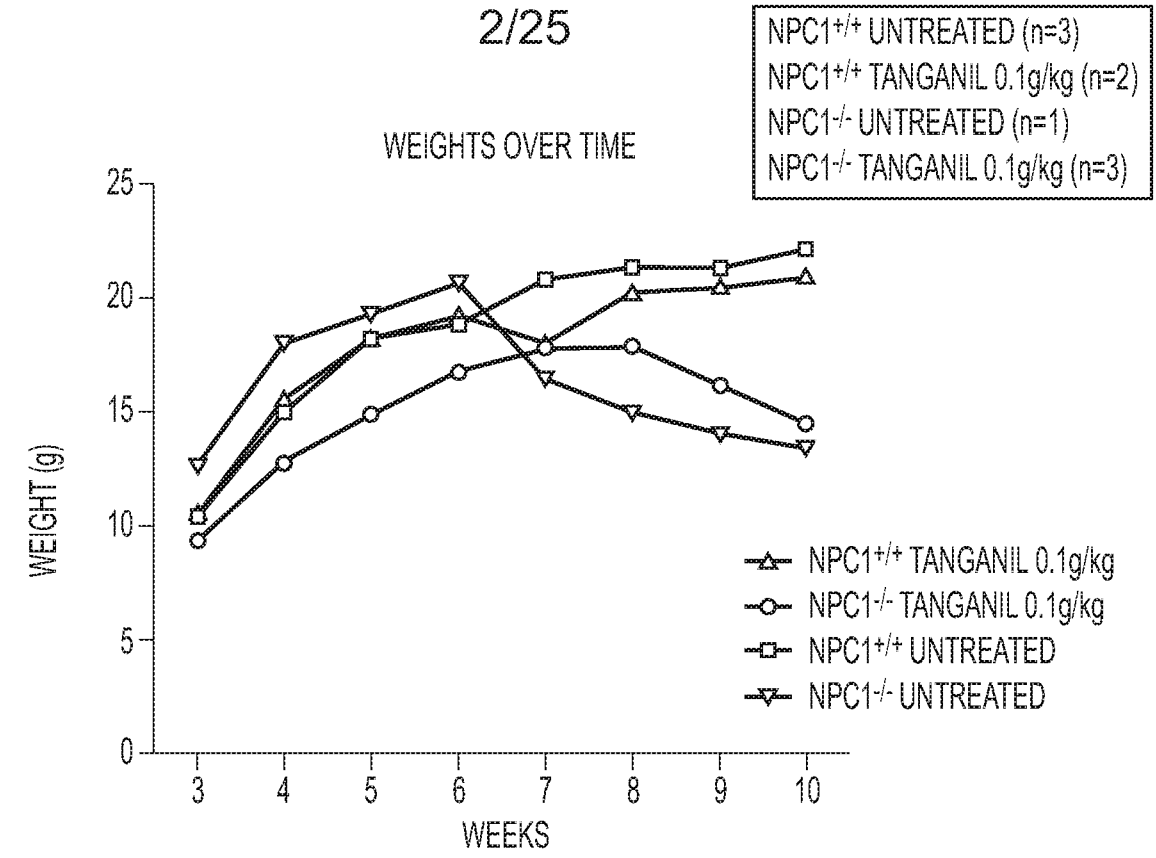
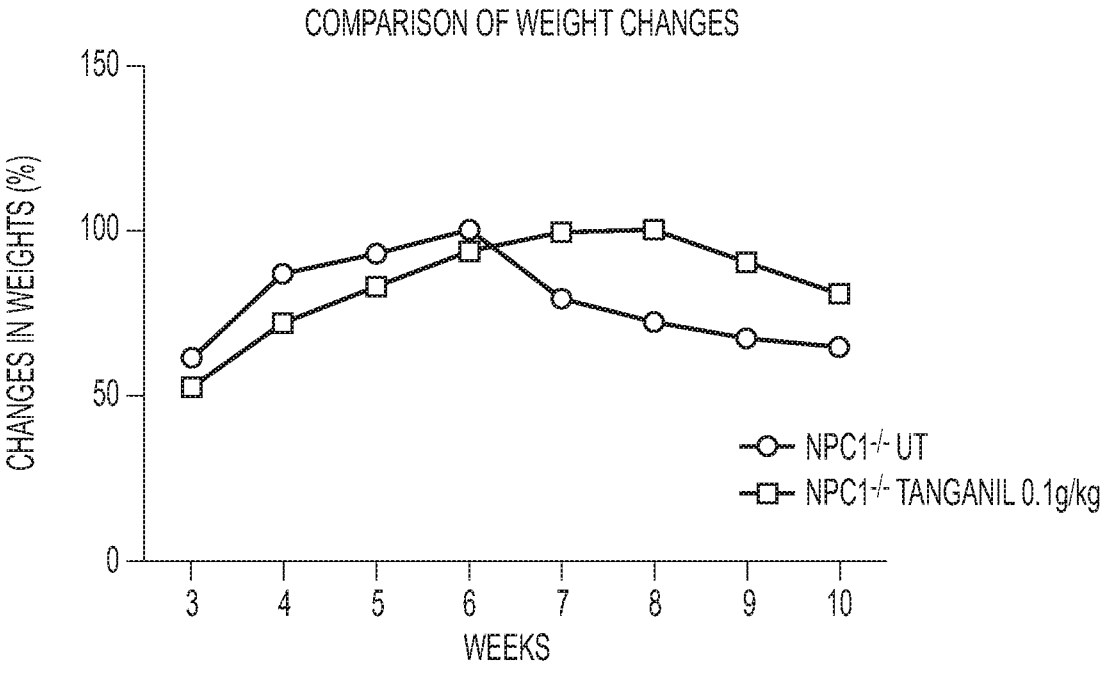


FIG. 2A



NPC1+/+ UNTREATED (n=3)
NPC1+/+ TANGANIL 0.1g/kg (n=2)
NPC1-/- UNTREATED (n=1)
NPC1-/- TANGANIL 0.1g/kg (n=3)

FIG. 2B

NPC1$^{+/+}$ UNTREATED (n=3)
NPC1$^{+/+}$ TANGANIL 0.1g/kg (n=2)
NPC1$^{-/-}$ UNTREATED (n=1)
NPC1$^{-/-}$ TANGANIL 0.1g/kg (n=3)
NO STATISTICAL ANALYSIS PERFORMED DUE TO LOW POWER - ONLY 1 UNTREATED NPC1 ANIMAL.

NPC1$^{+/+}$ UNTREATED
NPC1$^{+/+}$ TANGANIL 0.1g/kg
NPC1$^{-/-}$ UNTREATED
NPC1$^{-/-}$ TANGANIL 0.1g/kg

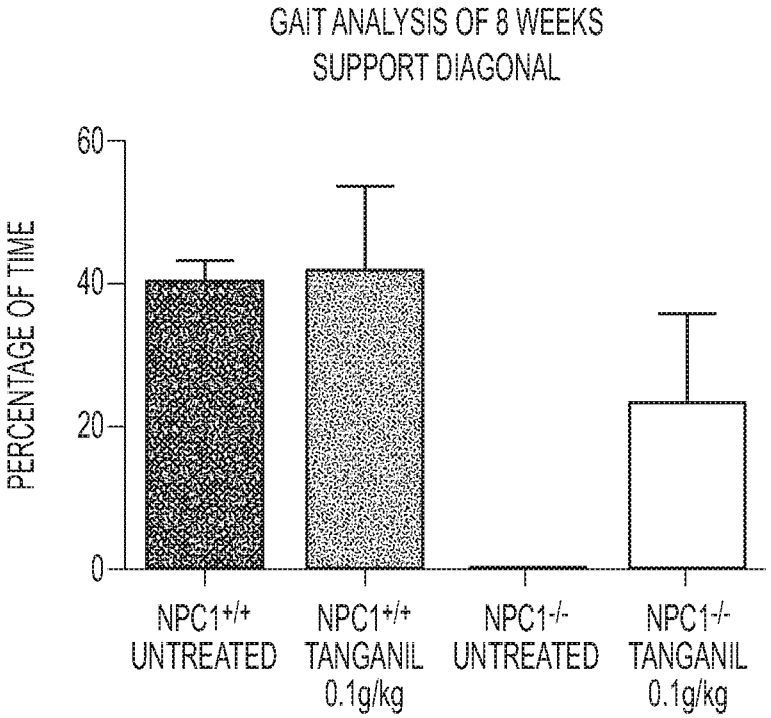


FIG. 3A

NPC1$^{+/+}$ UNTREATED (n=3)
NPC1$^{+/+}$ TANGANIL 0.1g/kg (n=2)
NPC1$^{-/-}$ UNTREATED (n=1)
NPC1$^{-/-}$ TANGANIL 0.1g/kg (n=3)
NO STATISTICAL ANALYSIS PERFORMED DUE TO LOW POWER - ONLY 1 UNTREATED NPC1 ANIMAL.

NPC1$^{+/+}$ UNTREATED
NPC1$^{+/+}$ TANGANIL 0.1g/kg
NPC1$^{-/-}$ UNTREATED
NPC1$^{-/-}$ TANGANIL 0.1g/kg

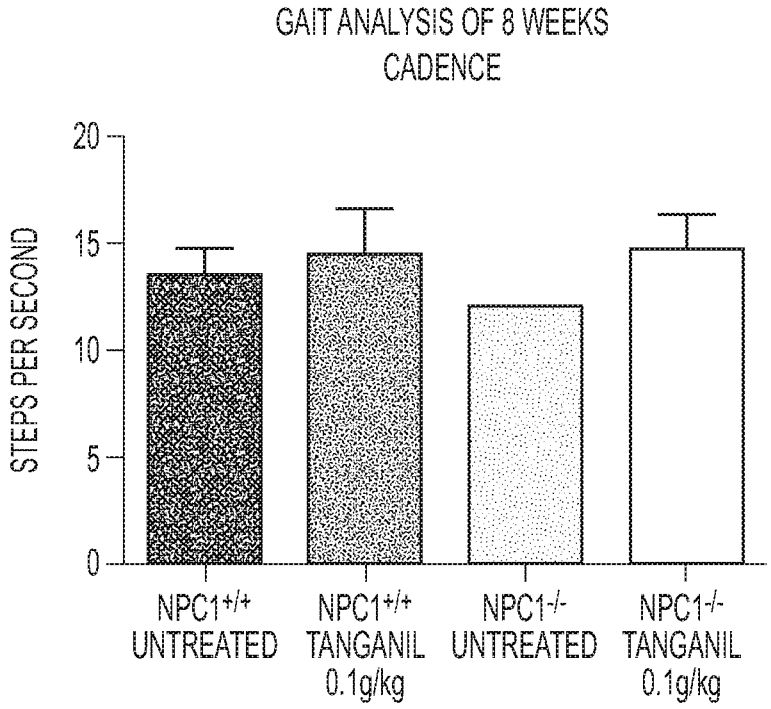


FIG. 3B

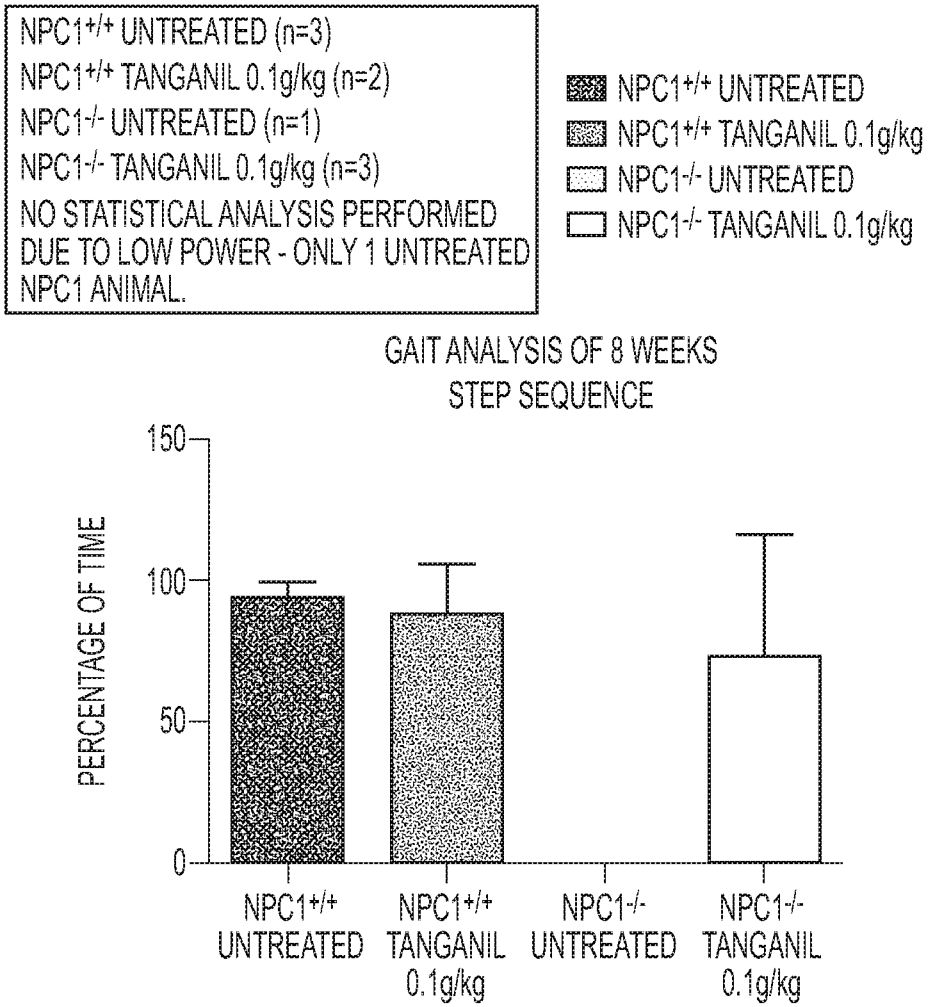

NPC1+/+ UNTREATED (n=3)
NPC1+/+ TANGANIL 0.1g/kg (n=2)
NPC1-/- UNTREATED (n=1)
NPC1-/- TANGANIL 0.1g/kg (n=3)
NO STATISTICAL ANALYSIS PERFORMED DUE TO LOW POWER - ONLY 1 UNTREATED NPC1 ANIMAL.
NPC1+/+ UNTREATED
NPC1+/+ TANGANIL 0.1g/kg
NPC1-/- UNTREATED
NPC1-/- TANGANIL 0.1g/kg
GAIT ANALYSIS OF 8 WEEKS
STEP SEQUENCE
PERCENTAGE OF TIME
150
100
50
0
NPC1+/+ UNTREATED
NPC1+/+ TANGANIL 0.1g/kg
NPC1-/- UNTREATED
NPC1-/- TANGANIL 0.1g/kg

FIG. 3C

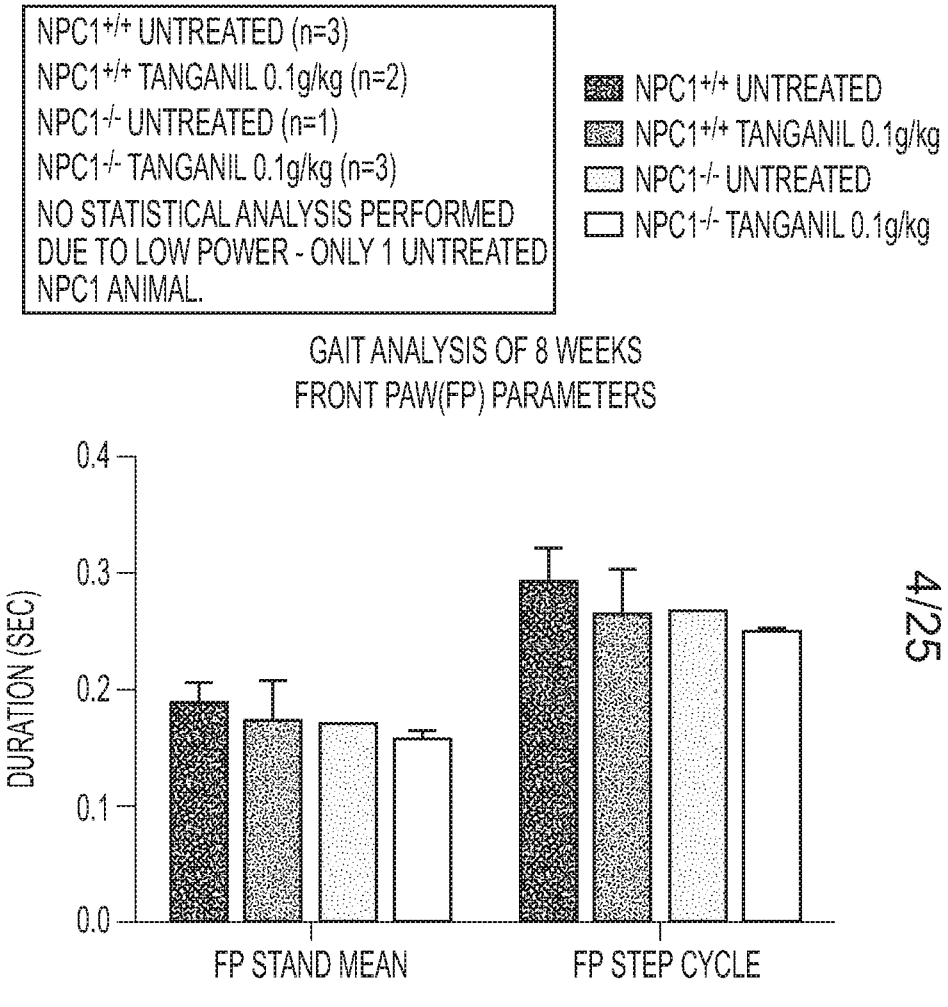

NPC1+/+ UNTREATED (n=3)
NPC1+/+ TANGANIL 0.1g/kg (n=2)
NPC1-/- UNTREATED (n=1)
NPC1-/- TANGANIL 0.1g/kg (n=3)
NO STATISTICAL ANALYSIS PERFORMED DUE TO LOW POWER - ONLY 1 UNTREATED NPC1 ANIMAL.
NPC1+/+ UNTREATED
NPC1+/+ TANGANIL 0.1g/kg
NPC1-/- UNTREATED
NPC1-/- TANGANIL 0.1g/kg
GAIT ANALYSIS OF 8 WEEKS
FRONT PAW(FP) PARAMETERS
DURATION (SEC)
0.4
0.3
0.2
0.1
0.0
FP STAND MEAN
FP STEP CYCLE

FIG. 3D

NPC1$^{+/+}$ UNTREATED (n=3)
NPC1$^{+/+}$ TANGANIL 0.1g/kg (n=2)
NPC1$^{-/-}$ UNTREATED (n=1)
NPC1$^{-/-}$ TANGANIL 0.1g/kg (n=3)
NO STATISTICAL ANALYSIS PERFORMED DUE TO LOW POWER - ONLY 1 UNTREATED NPC1 ANIMAL.

NPC1$^{+/+}$ UNTREATED
NPC1$^{+/+}$ TANGANIL 0.1g/kg
NPC1$^{-/-}$ UNTREATED
NPC1$^{-/-}$ TANGANIL 0.1g/kg

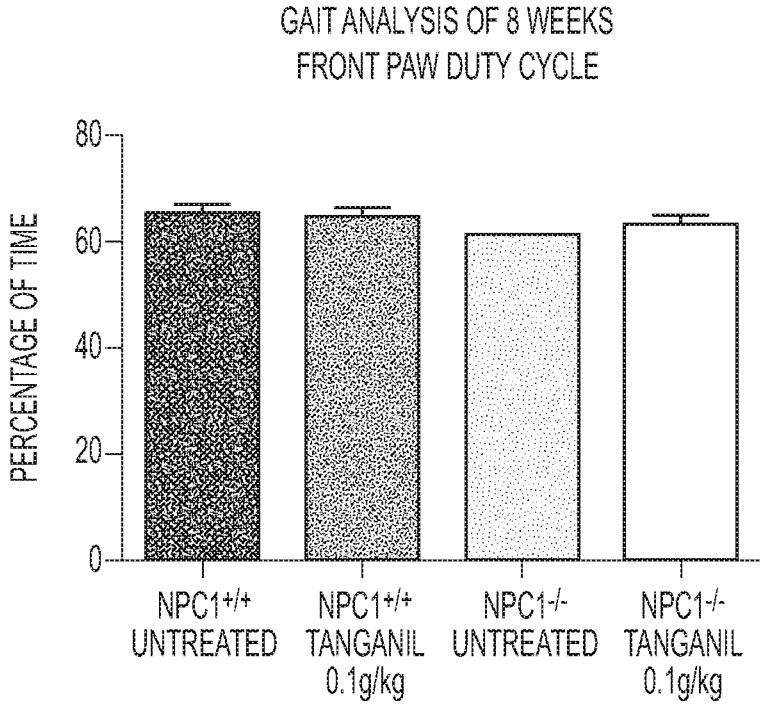


FIG. 3E

NPC1$^{+/+}$ UNTREATED (n=3)
NPC1$^{+/+}$ TANGANIL 0.1g/kg (n=2)
NPC1$^{-/-}$ UNTREATED (n=1)
NPC1$^{-/-}$ TANGANIL 0.1g/kg (n=3)
NO STATISTICAL ANALYSIS PERFORMED DUE TO LOW POWER - ONLY 1 UNTREATED NPC1 ANIMAL.

NPC1$^{+/+}$ UNTREATED
NPC1$^{+/+}$ TANGANIL 0.1g/kg
NPC1$^{-/-}$ UNTREATED
NPC1$^{-/-}$ TANGANIL 0.1g/kg

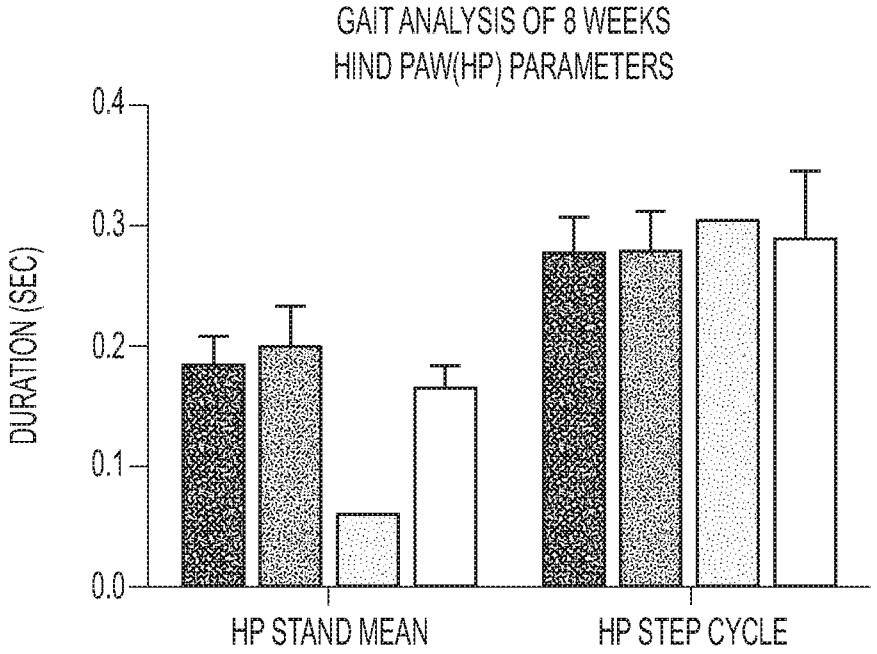


FIG. 3F

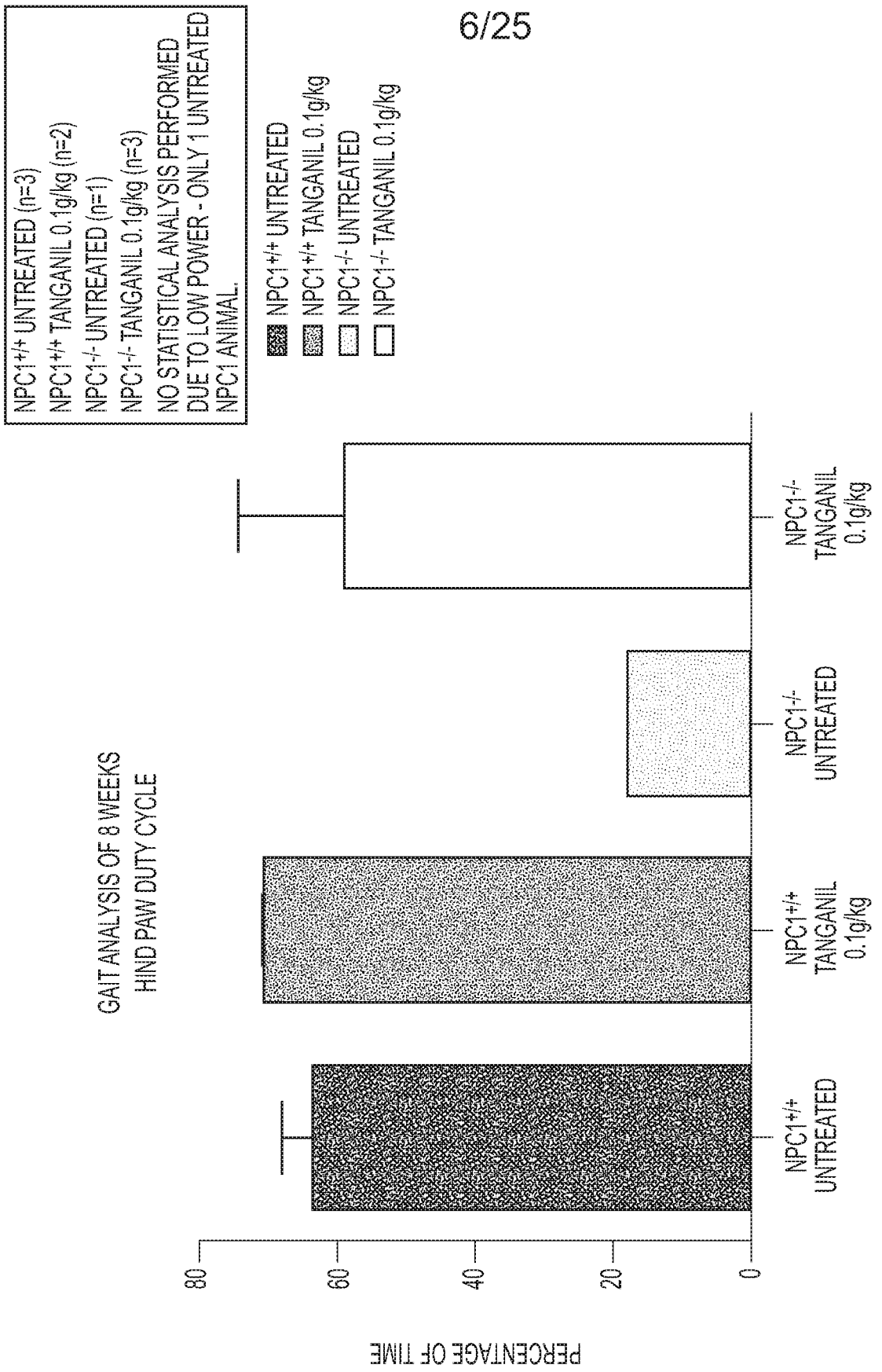

NPC1+/+ UNTREATED (n=3)
NPC1+/+ TANGANIL 0.1g/kg (n=2)
NPC1-/- UNTREATED (n=1)
NPC1-/- TANGANIL 0.1g/kg (n=3)
NO STATISTICAL ANALYSIS PERFORMED DUE TO LOW POWER - ONLY 1 UNTREATED NPC1 ANIMAL.
NPC1+/+ UNTREATED
NPC1+/+ TANGANIL 0.1g/kg
NPC1-/- UNTREATED
NPC1-/- TANGANIL 0.1g/kg
GAIT ANALYSIS OF 8 WEEKS
HIND PAW DUTY CYCLE
PERCENTAGE OF TIME
0
20
40
60
80
NPC1+/+ UNTREATED
NPC1+/+ TANGANIL 0.1g/kg
NPC1-/- UNTREATED
NPC1-/- TANGANIL 0.1g/kg

FIG. 3G

NPC1$^{+/+}$ UNTREATED (n=3)
NPC1$^{+/+}$ TANGANIL 0.1g/kg (n=2)
NPC1$^{-/-}$ UNTREATED (n=1)
NPC1$^{-/-}$ TANGANIL 0.1g/kg (n=3)
NO STATISTICAL ANALYSIS PERFORMED DUE TO LOW POWER - ONLY 1 UNTREATED NPC1 ANIMAL.

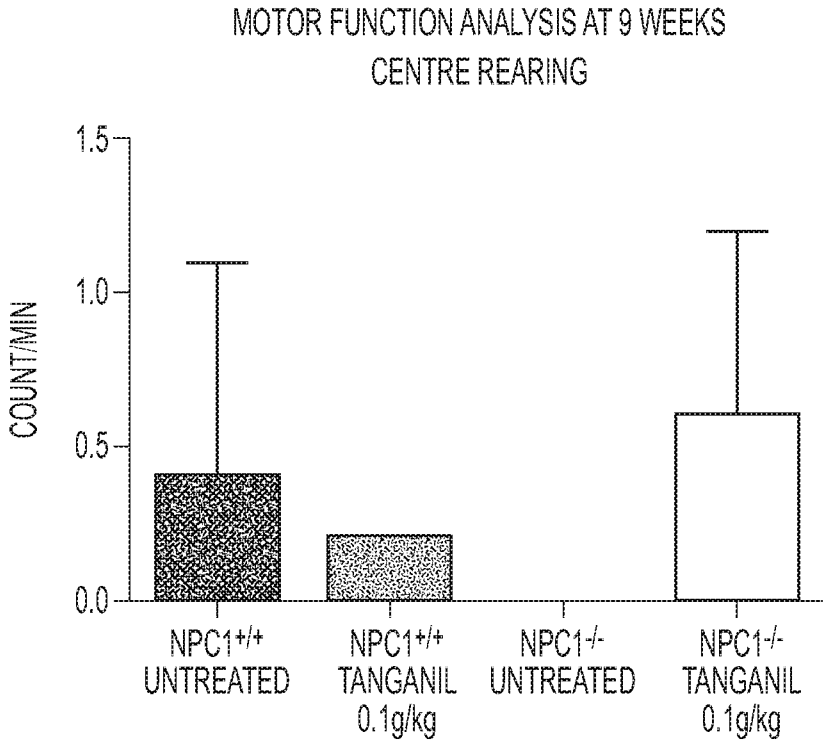


FIG. 4A

NPC1$^{+/+}$ UNTREATED (n=3)
NPC1$^{+/+}$ TANGANIL 0.1g/kg (n=2)
NPC1$^{-/-}$ UNTREATED (n=1)
NPC1$^{-/-}$ TANGANIL 0.1g/kg (n=3)
NO STATISTICAL ANALYSIS PERFORMED DUE TO LOW POWER - ONLY 1 UNTREATED NPC1 ANIMAL.

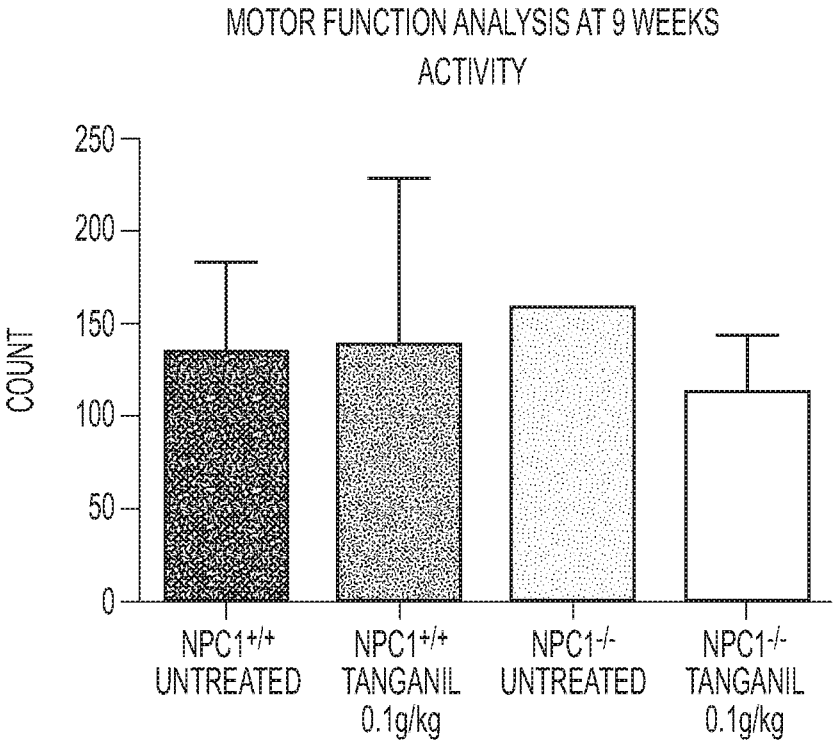


FIG. 4B


NPC1+/+ UNTREATED (n=3)
NPC1+/+ TANGANIL 0.1g/kg (n=2)
NPC1-/- UNTREATED (n=1)
NPC1-/- TANGANIL 0.1g/kg (n=3)
NO STATISTICAL ANALYSIS PERFORMED
DUE TO LOW POWER - ONLY 1 UNTREATED
NPC1 ANIMAL.

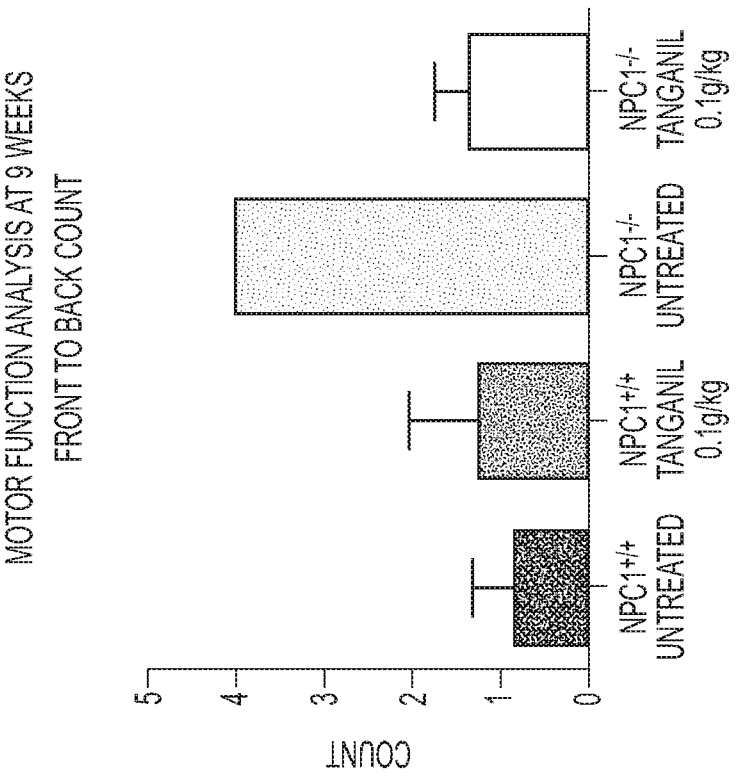
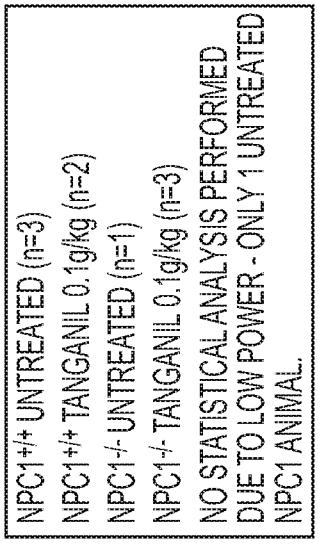

MOTOR FUNCTION ANALYSIS AT 9 WEEKS
FRONT TO BACK COUNT
COUNT
0
1
2
3
4
5
NPC1+/+ UNTREATED
NPC1+/+ TANGANIL 0.1g/kg
NPC1-/- UNTREATED
NPC1-/- TANGANIL 0.1g/kg

FIG. 4D


NPC1+/+ UNTREATED (n=3)
NPC1+/+ TANGANIL 0.1g/kg (n=2)
NPC1-/- UNTREATED (n=1)
NPC1-/- TANGANIL 0.1g/kg (n=3)
NO STATISTICAL ANALYSIS PERFORMED
DUE TO LOW POWER - ONLY 1 UNTREATED
NPC1 ANIMAL.

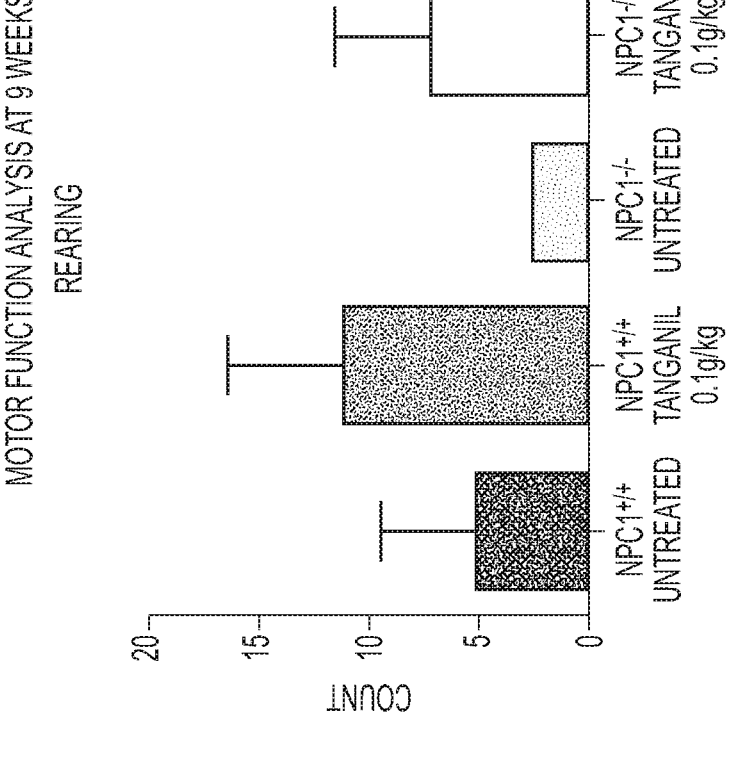

MOTOR FUNCTION ANALYSIS AT 9 WEEKS
REARING
COUNT
0
5
10
15
20
NPC1+/+ UNTREATED
NPC1+/+ TANGANIL 0.1g/kg
NPC1-/- UNTREATED
NPC1-/- TANGANIL 0.1g/kg

FIG. 4C

NPC1$^{+/+}$ UNTREATED (n=3)
NPC1$^{+/+}$ TANGANIL 0.1g/kg (n=2)
NPC1$^{-/-}$ UNTREATED (n=1)
NPC1$^{-/-}$ TANGANIL 0.1g/kg (n=3)
NO STATISTICAL ANALYSIS PERFORMED DUE TO LOW POWER - ONLY 1 UNTREATED NPC1 ANIMAL.

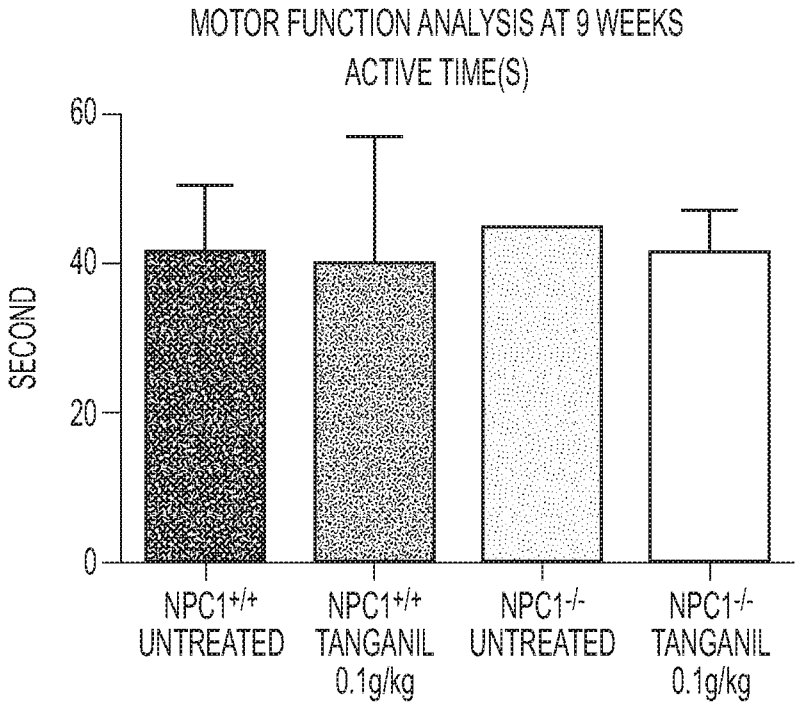


FIG. 4E

NPC1$^{+/+}$ UNTREATED (n=3)
NPC1$^{+/+}$ TANGANIL 0.1g/kg (n=2)
NPC1$^{-/-}$ UNTREATED (n=1)
NPC1$^{-/-}$ TANGANIL 0.1g/kg (n=3)
NO STATISTICAL ANALYSIS PERFORMED DUE TO LOW POWER - ONLY 1 UNTREATED NPC1 ANIMAL.

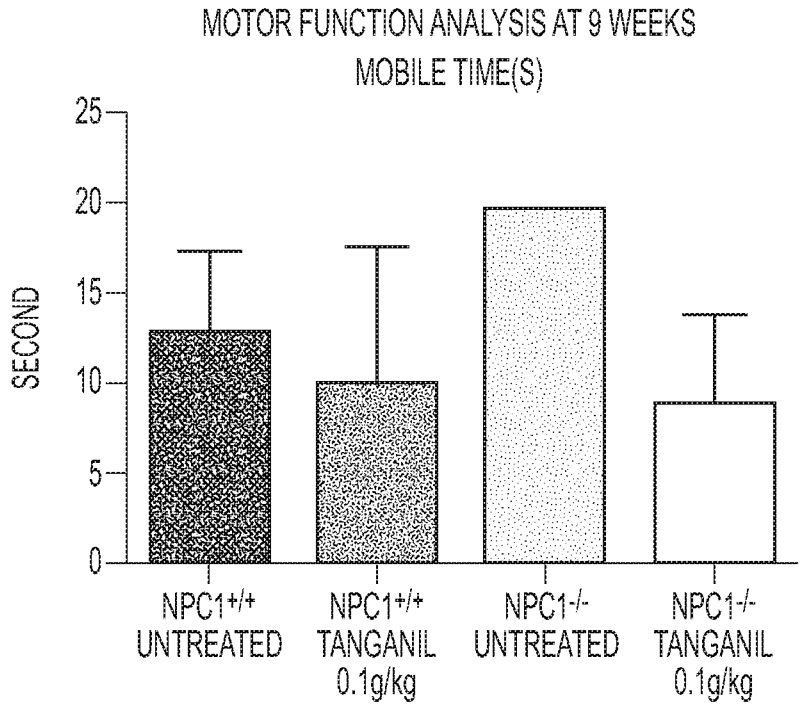
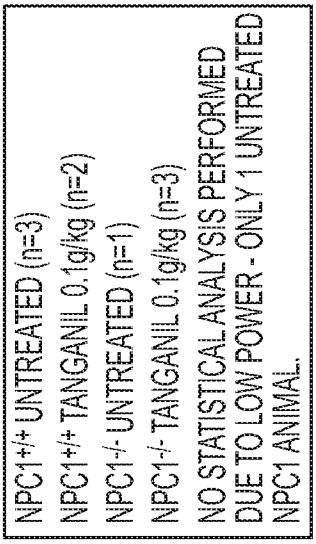


FIG. 4F


NPC1+/+ UNTREATED (n=3)
NPC1+/+ TANGANIL 0.1g/kg (n=2)
NPC1-/- UNTREATED (n=1)
NPC1-/- TANGANIL 0.1g/kg (n=3)
NO STATISTICAL ANALYSIS PERFORMED
DUE TO LOW POWER - ONLY 1 UNTREATED
NPC1 ANIMAL.

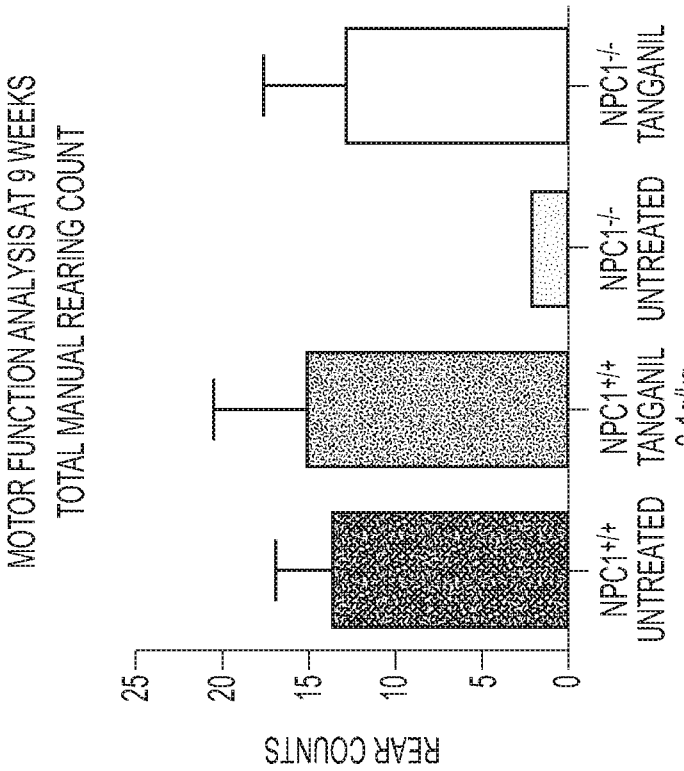

MOTOR FUNCTION ANALYSIS AT 9 WEEKS
TOTAL MANUAL REARING COUNT
REAR COUNTS
25
20
15
10
5
0
NPC1+/+ UNTREATED
NPC1+/+ TANGANIL 0.1g/kg
NPC1-/- UNTREATED
NPC1-/- TANGANIL

FIG. 4H


NPC1+/+ UNTREATED (n=3)
NPC1+/+ TANGANIL 0.1g/kg (n=2)
NPC1-/- UNTREATED (n=1)
NPC1-/- TANGANIL 0.1g/kg (n=3)
NO STATISTICAL ANALYSIS PERFORMED
DUE TO LOW POWER - ONLY 1 UNTREATED
NPC1 ANIMAL.

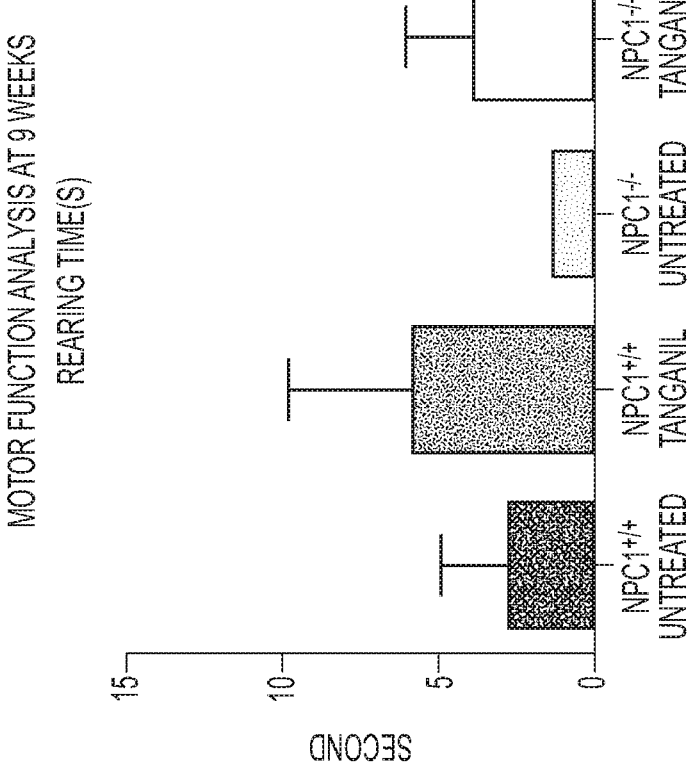

MOTOR FUNCTION ANALYSIS AT 9 WEEKS
REARING TIME(S)
SECOND
15
10
5
0
NPC1+/+ UNTREATED
NPC1+/+ TANGANIL 0.1g/kg
NPC1-/- UNTREATED
NPC1-/- TANGANIL 0.1g/kg

FIG. 4G

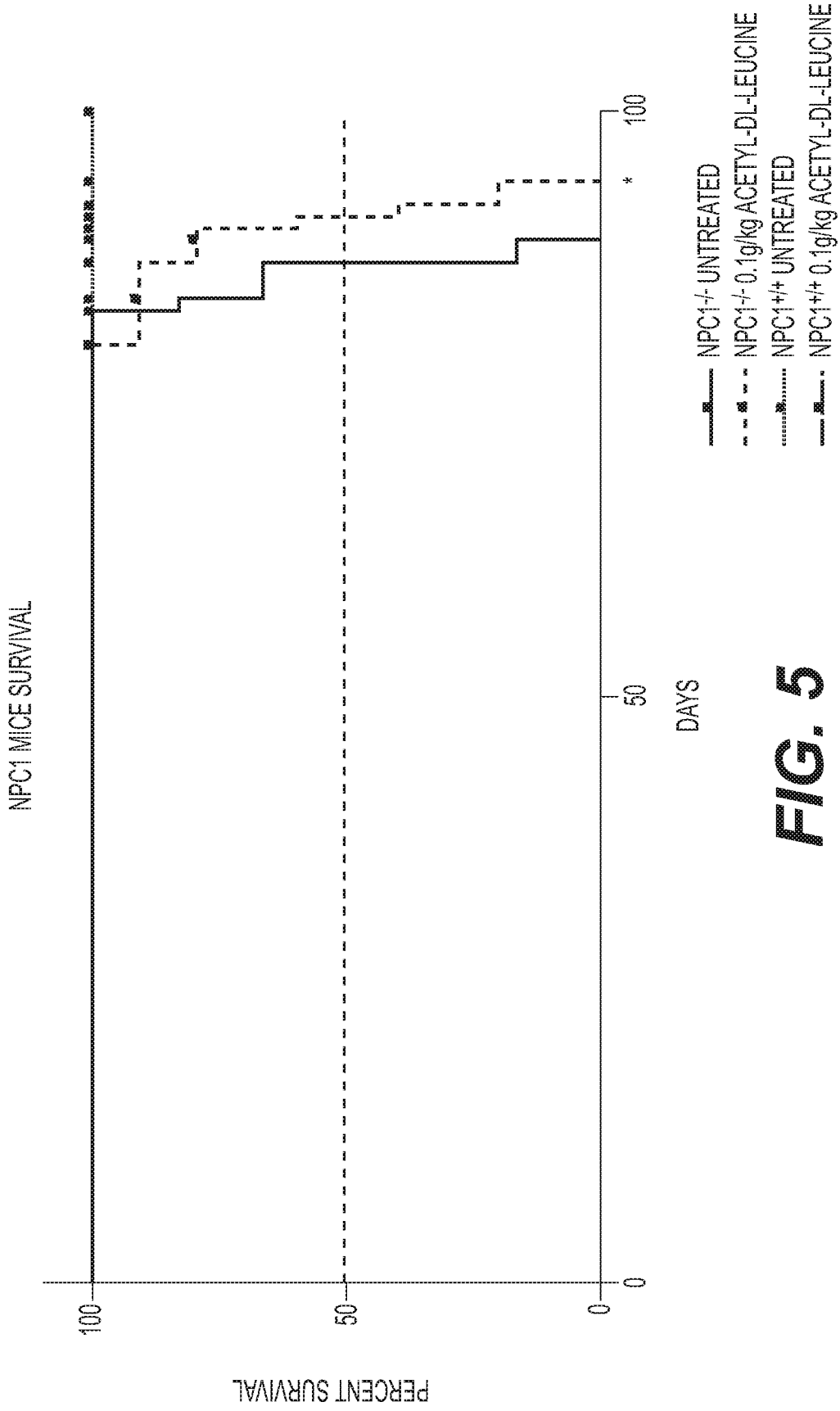

NPC1 MICE SURVIVAL
PERCENT SURVIVAL
100
50
0
DAYS
0
50
100
*
NPC1-/- UNTREATED
NPC1-/- 0.1g/kg ACETYL-DL-LEUCINE
NPC1+/+ UNTREATED
NPC1+/+ 0.1g/kg ACETYL-DL-LEUCINE

FIG. 5

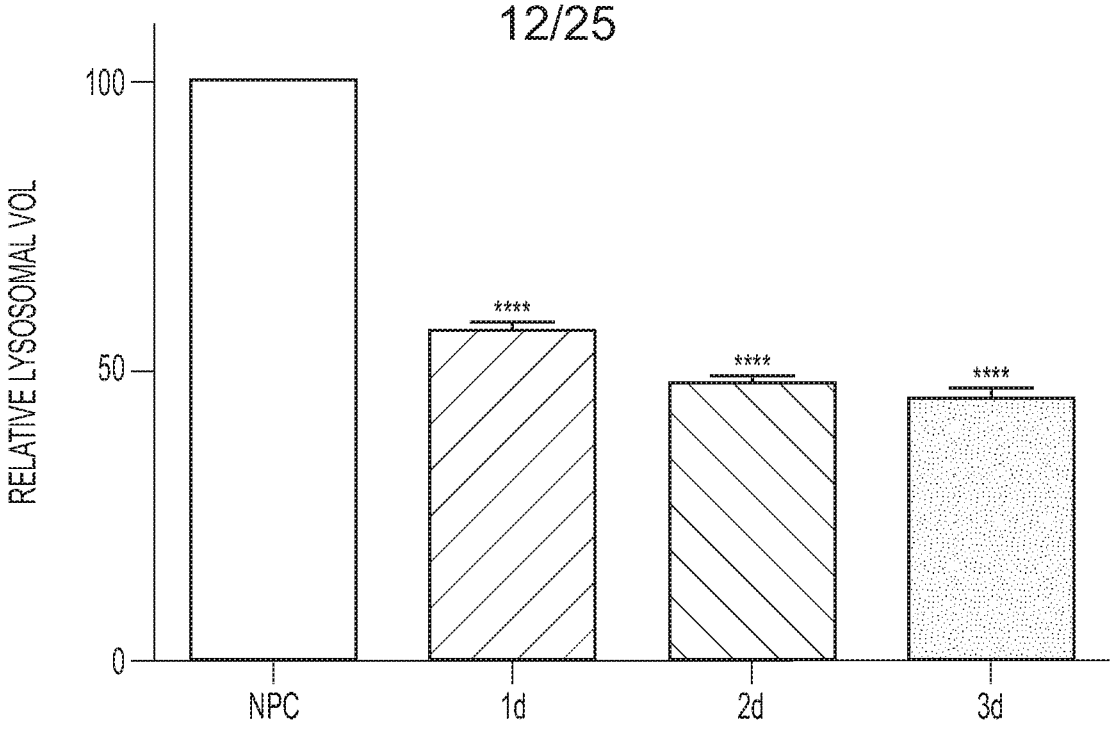

RELATIVE LYSOSOMAL VOL
100
50
0
****
****
****
NPC
1d
2d
3d

FIG. 6A

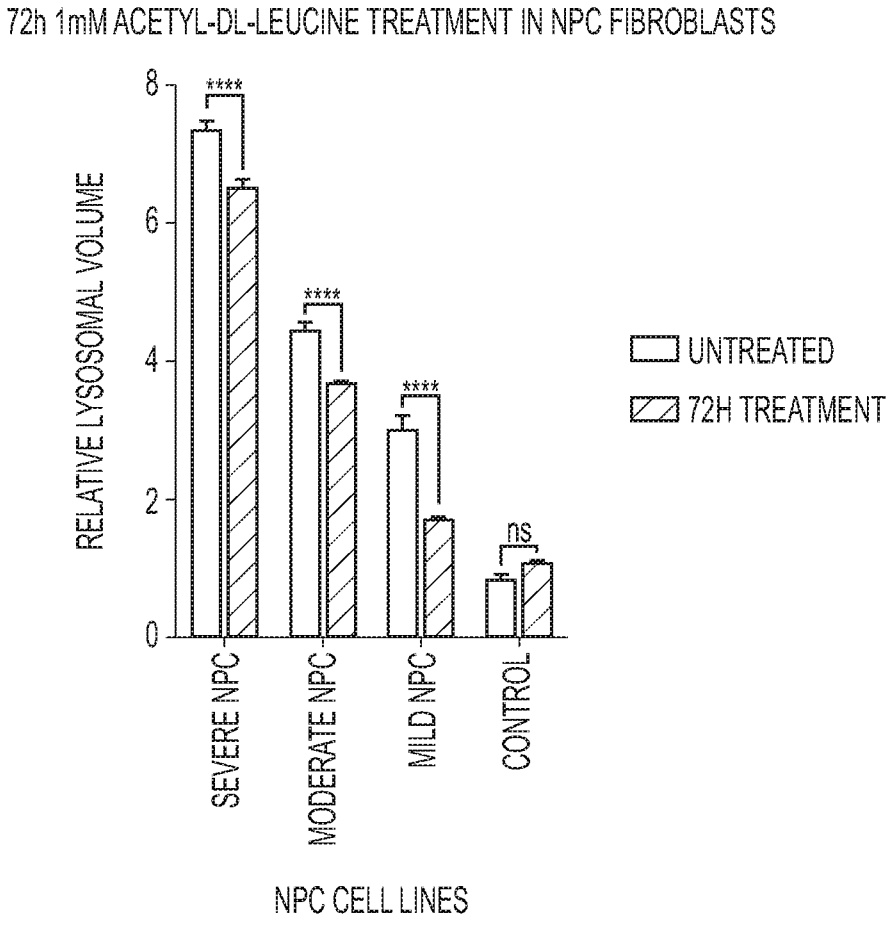

72h 1mM ACETYL-DL-LEUCINE TREATMENT IN NPC FIBROBLASTS
RELATIVE LYSOSOMAL VOLUME
8
6
4
2
0
****
****
****
ns
SEVERE NPC
MODERATE NPC
MILD NPC
CONTROL
UNTREATED
72H TREATMENT
NPC CELL LINES

FIG. 6B

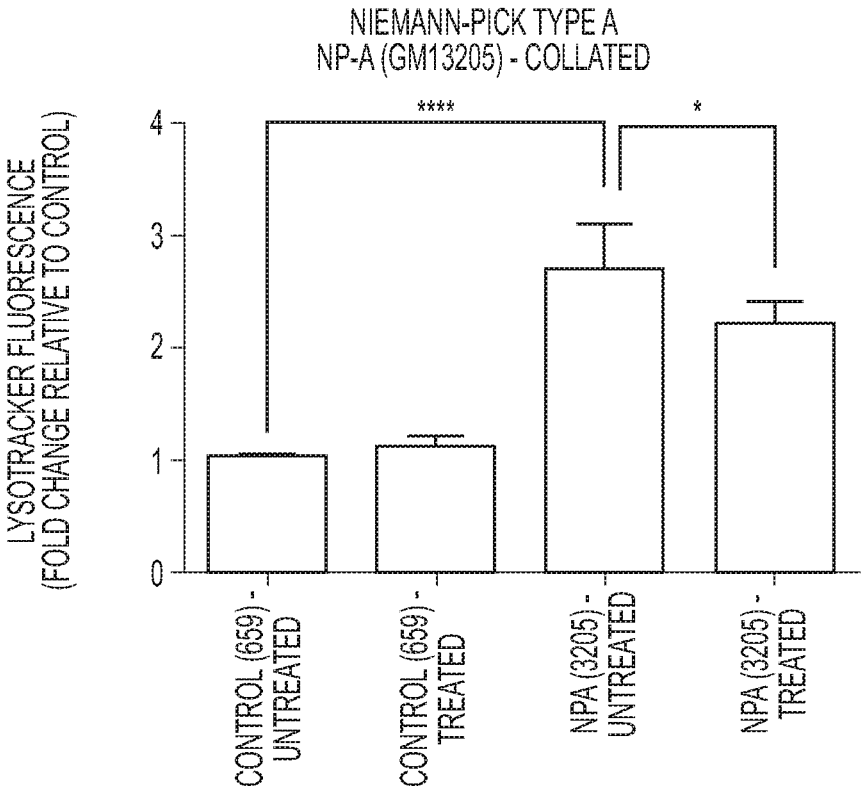

NIEMANN-PICK TYPE A
NP-A (GM13205) - COLLATED
LYSOTRACKER FLUORESCENCE
(FOLD CHANGE RELATIVE TO CONTROL)
****
*
0
1
2
3
4
CONTROL (659) - UNTREATED
CONTROL (659) - TREATED
NPA (3205) - UNTREATED
NPA (3205) - TREATED

FIG. 6C

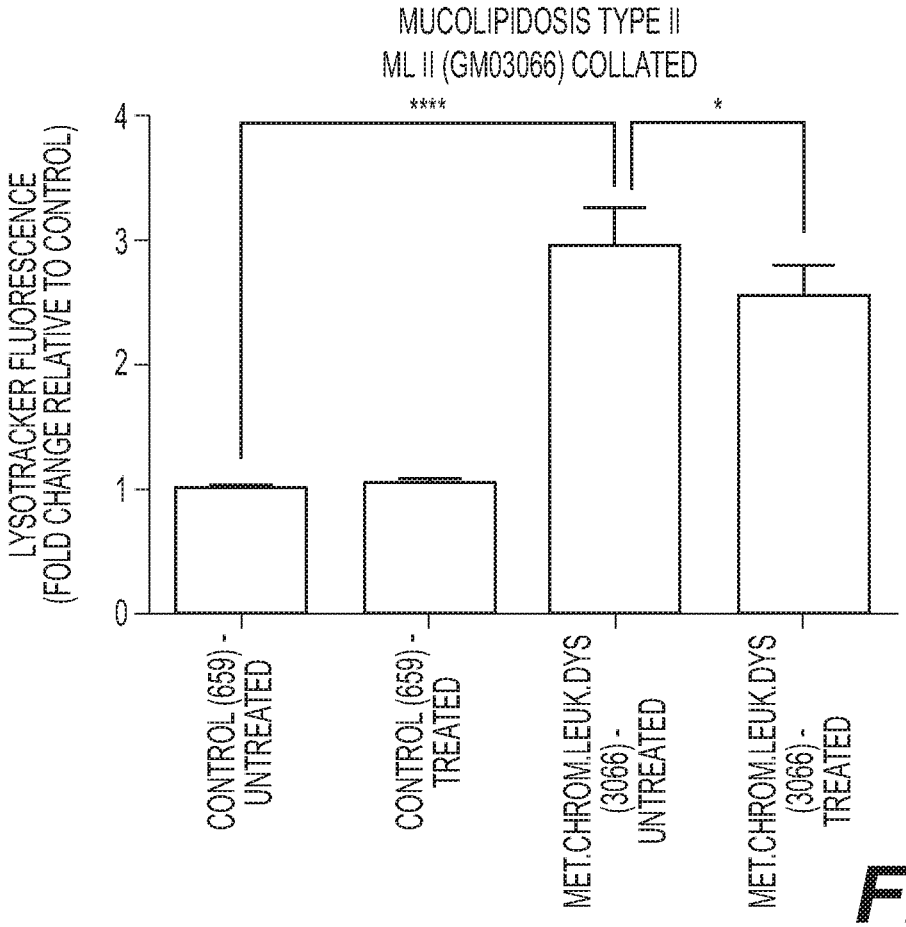

MUCOLIPIDOSIS TYPE II
ML II (GM03066) COLLATED
LYSOTRACKER FLUORESCENCE
(FOLD CHANGE RELATIVE TO CONTROL)
****
*
0
1
2
3
4
CONTROL (659) - UNTREATED
CONTROL (659) - TREATED
MET.CHROM.LEUK.DYS (3066) - UNTREATED
MET.CHROM.LEUK.DYS (3066) - TREATED

FIG. 6D

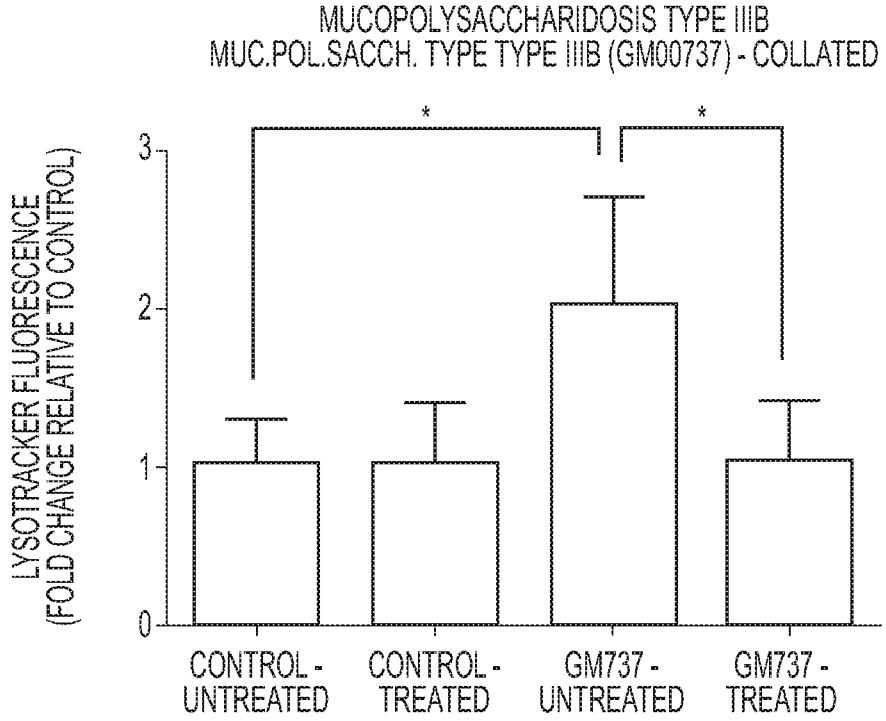

MUCOPOLYSACCHARIDOSIS TYPE IIIB
MUC.POL.SACCH. TYPE TYPE IIIB (GM00737) - COLLATED
LYSOTRACKER FLUORESCENCE
(FOLD CHANGE RELATIVE TO CONTROL)
*
*
3
2
1
0
CONTROL - UNTREATED
CONTROL - TREATED
GM737 - UNTREATED
GM737 - TREATED

FIG. 6E

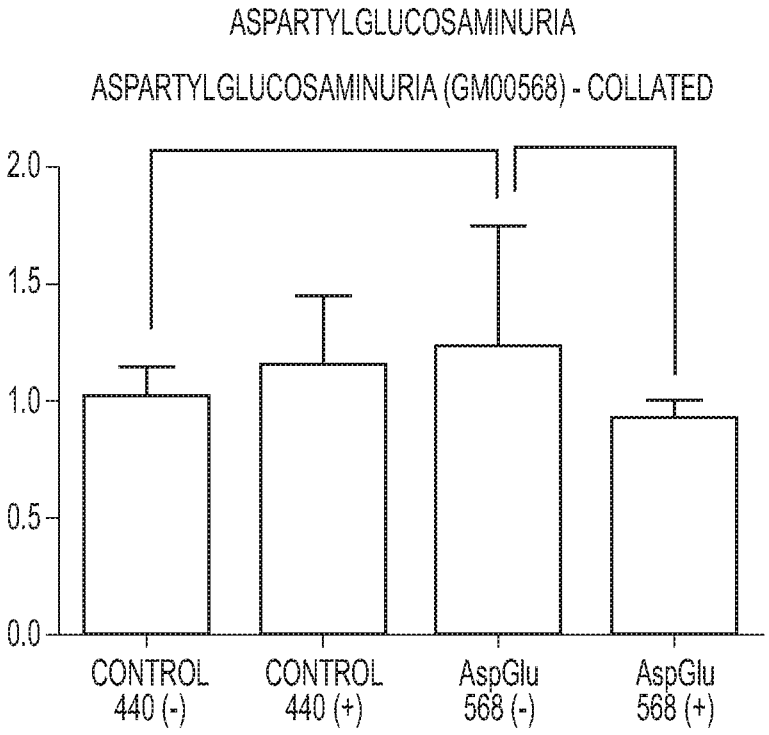

ASPARTYLGLUCOSAMINURIA
ASPARTYLGLUCOSAMINURIA (GM00568) - COLLATED
2.0
1.5
1.0
0.5
0.0
CONTROL 440 (-)
CONTROL 440 (+)
AspGlu 568 (-)
AspGlu 568 (+)

FIG. 6F

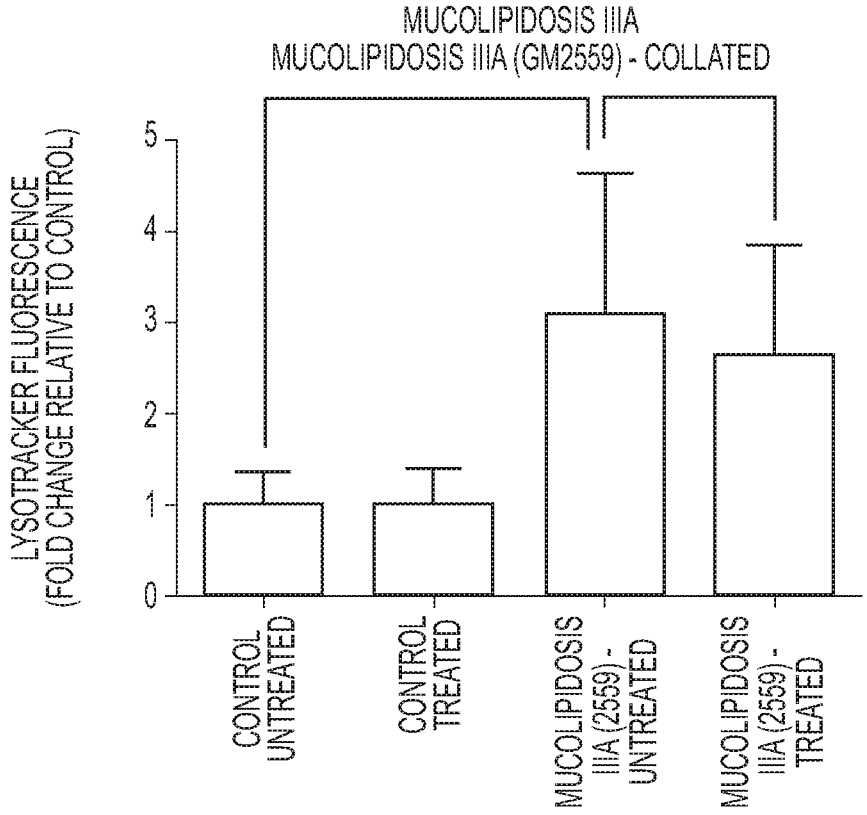

MUCOLIPIDOSIS IIIA
MUCOLIPIDOSIS IIIA (GM2559) - COLLATED
LYSOTRACKER FLUORESCENCE
(FOLD CHANGE RELATIVE TO CONTROL)
0
1
2
3
4
5
CONTROL UNTREATED
CONTROL TREATED
MUCOLIPIDOSIS IIIA (2559) - UNTREATED
MUCOLIPIDOSIS IIIA (2559) - TREATED

FIG. 6G

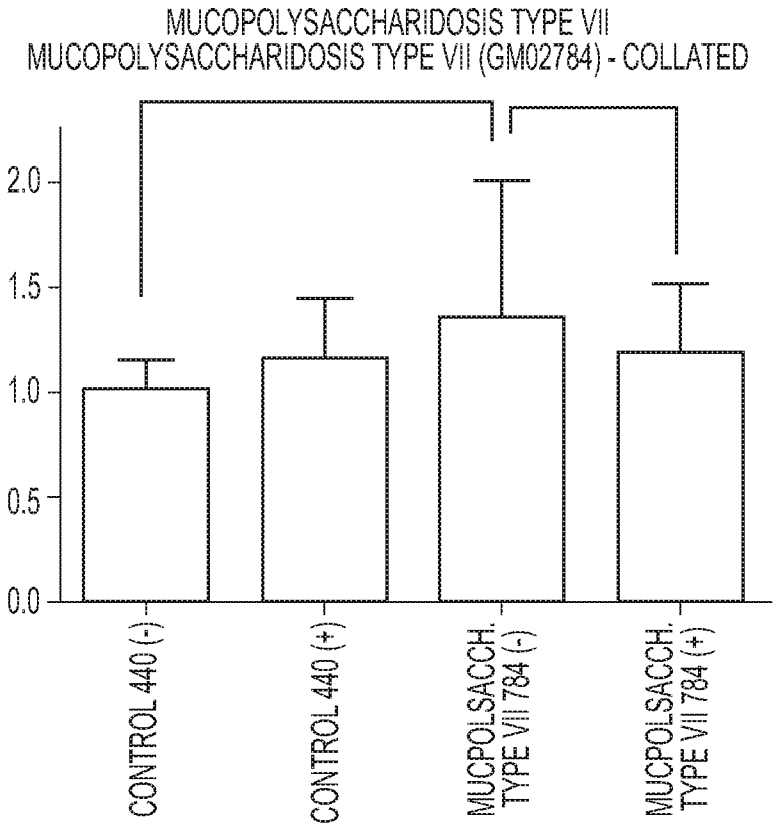
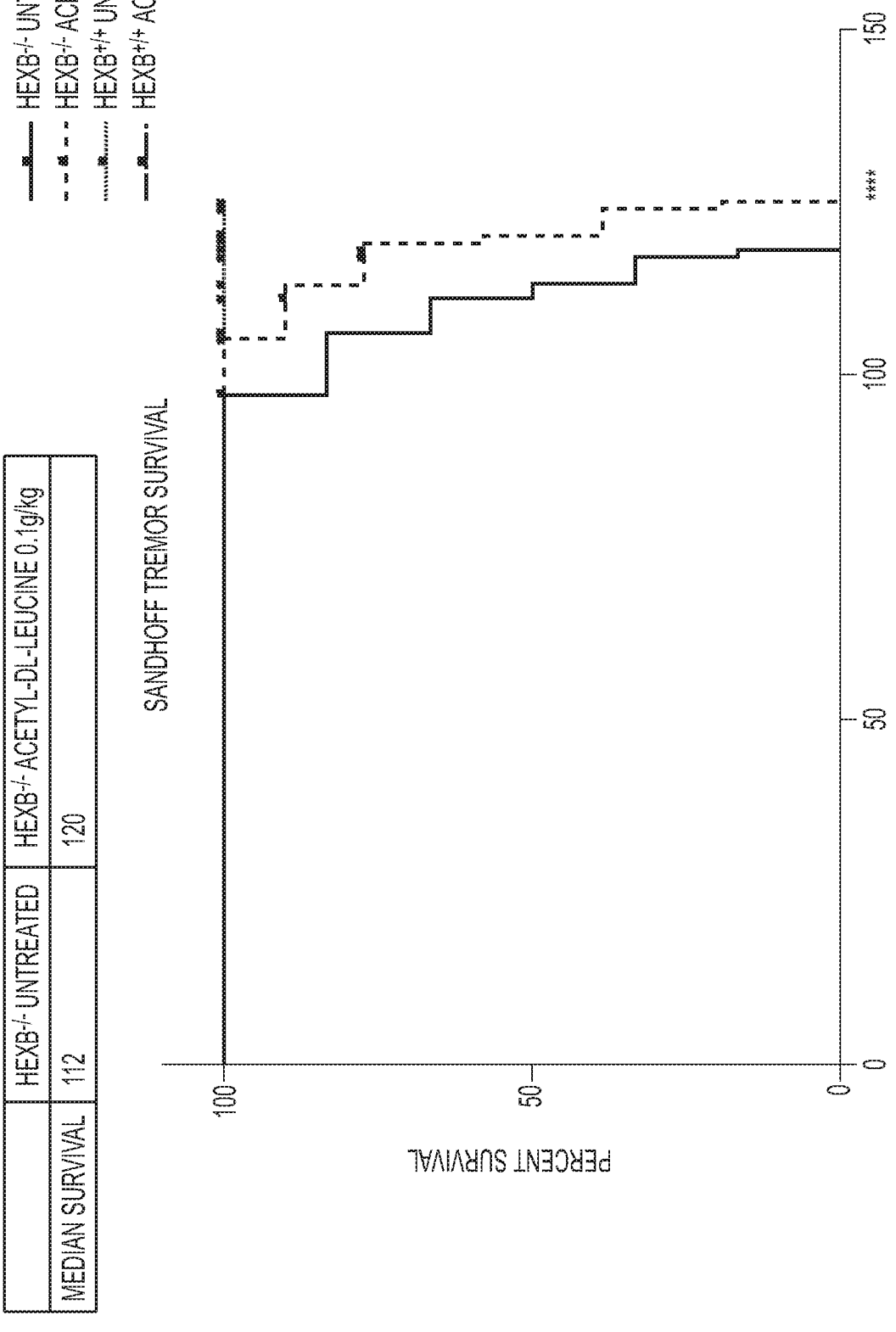

MUCOPOLYSACCHARIDOSIS TYPE VII
MUCOPOLYSACCHARIDOSIS TYPE VII (GM02784) - COLLATED
0.0
0.5
1.0
1.5
2.0
CONTROL 440 (-)
CONTROL 440 (+)
MUCPOLSACCH. TYPE VII 784 (-)
MUCPOLSACCH. TYPE VII 784 (+)

FIG. 6H



	HEXB-/- UNTREATED	HEXB-/- ACETYL-DL-LEUCINE 0.1g/kg
MEDIAN SURVIVAL	112	120

FIG. 7A

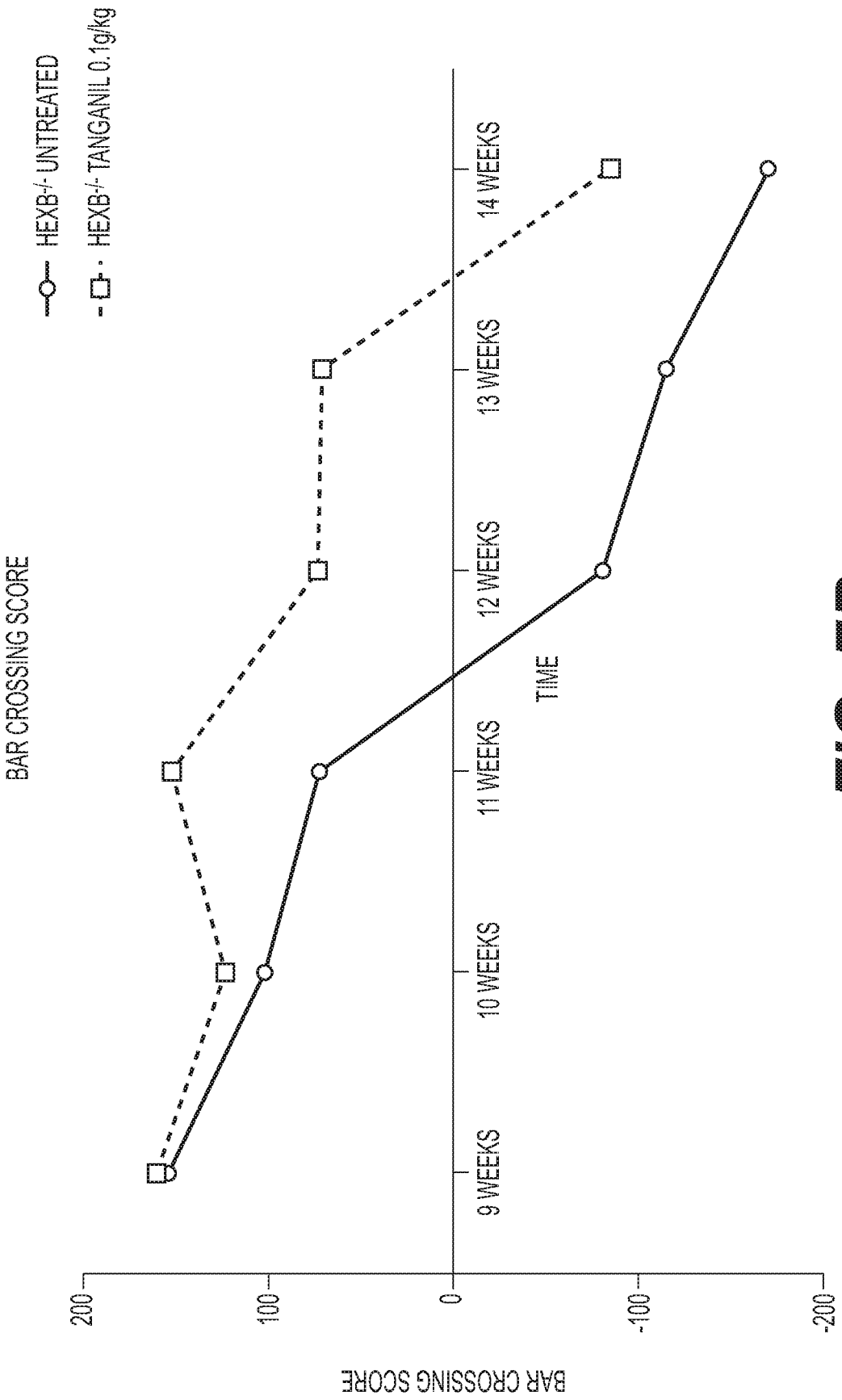

HEXB-/- UNTREATED
HEXB-/- TANGANIL 0.1g/kg
BAR CROSSING SCORE
200
100
0
-100
-200
9 WEEKS
10 WEEKS
11 WEEKS
12 WEEKS
13 WEEKS
14 WEEKS
TIME
BAR CROSSING SCORE

FIG. 7B

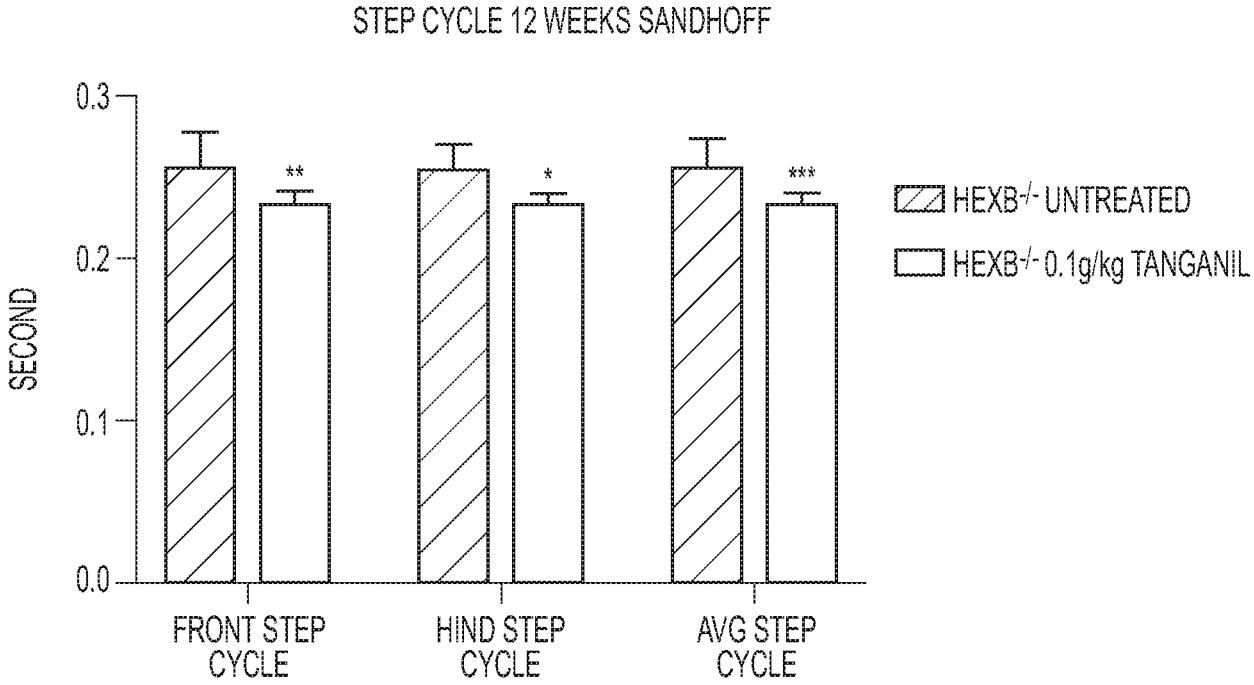

STEP CYCLE 12 WEEKS SANDHOFF
SECOND
0.3
0.2
0.1
0.0
**
*
***
FRONT STEP CYCLE
HIND STEP CYCLE
AVG STEP CYCLE
HEXB-/- UNTREATED
HEXB-/- 0.1g/kg TANGANIL

FIG. 7C

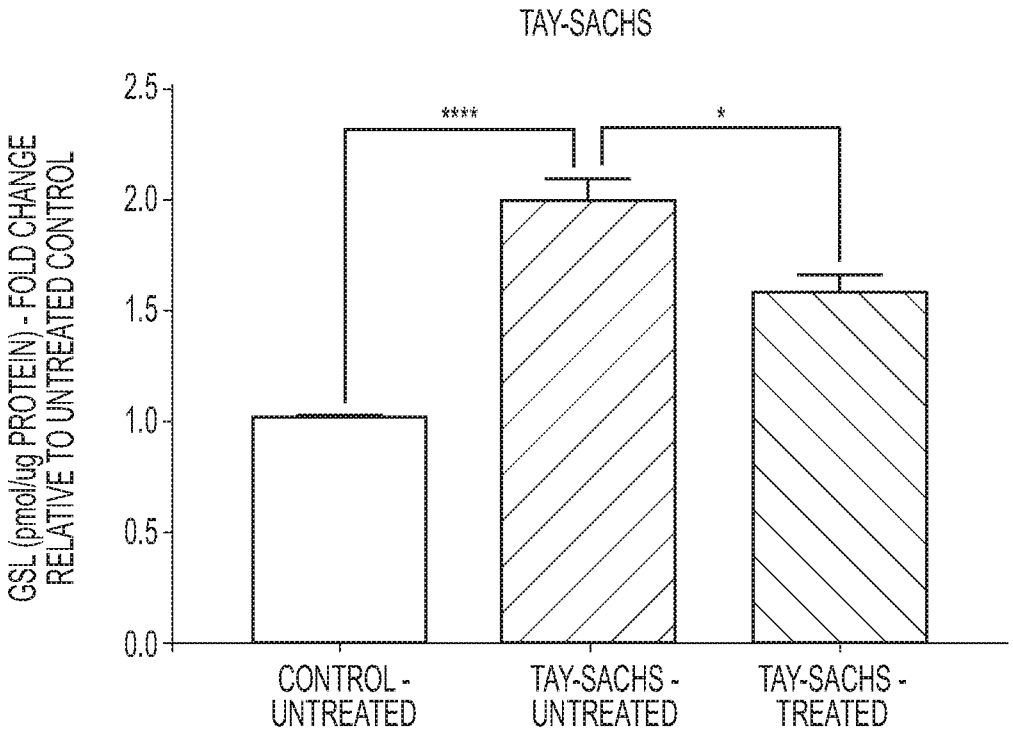

TAY-SACHS
GSL (pmol/ug PROTEIN) - FOLD CHANGE RELATIVE TO UNTREATED CONTROL
2.5
2.0
1.5
1.0
0.5
0.0
****
*
CONTROL - UNTREATED
TAY-SACHS - UNTREATED
TAY-SACHS - TREATED

FIG. 8A

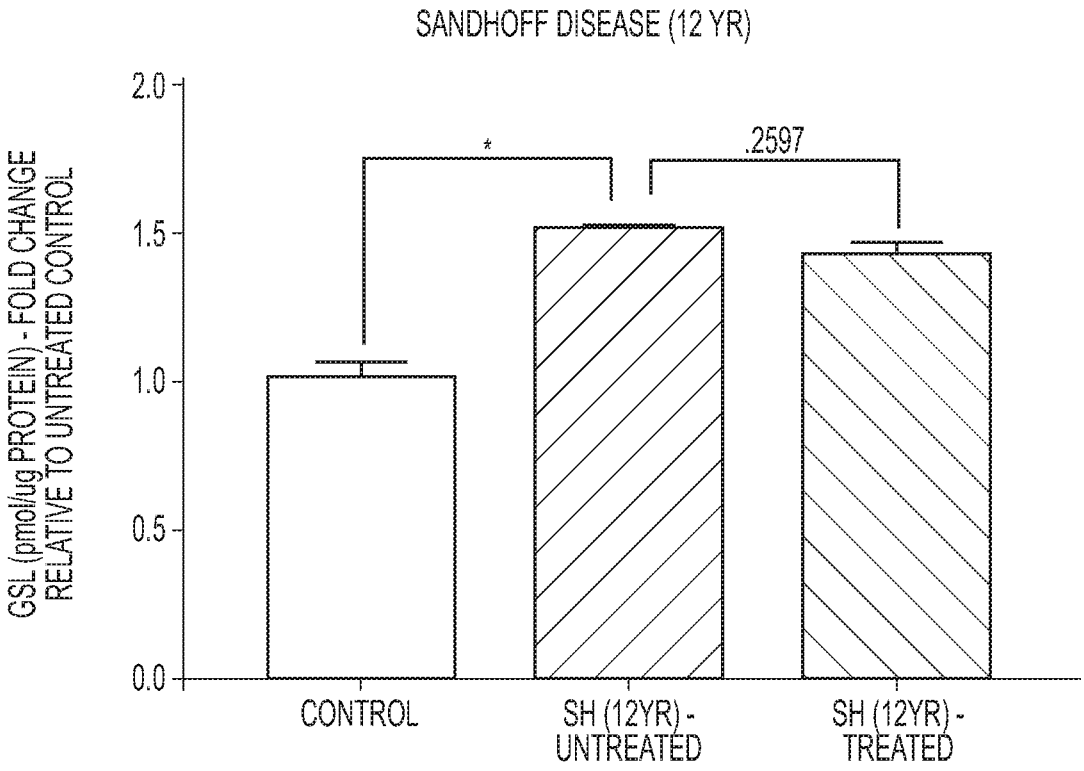

SANDHOFF DISEASE (12 YR)
GSL (pmol/ug PROTEIN) - FOLD CHANGE RELATIVE TO UNTREATED CONTROL
2.0
1.5
1.0
0.5
0.0
*
.2597
CONTROL
SH (12YR) - UNTREATED
SH (12YR) - TREATED

FIG. 8B

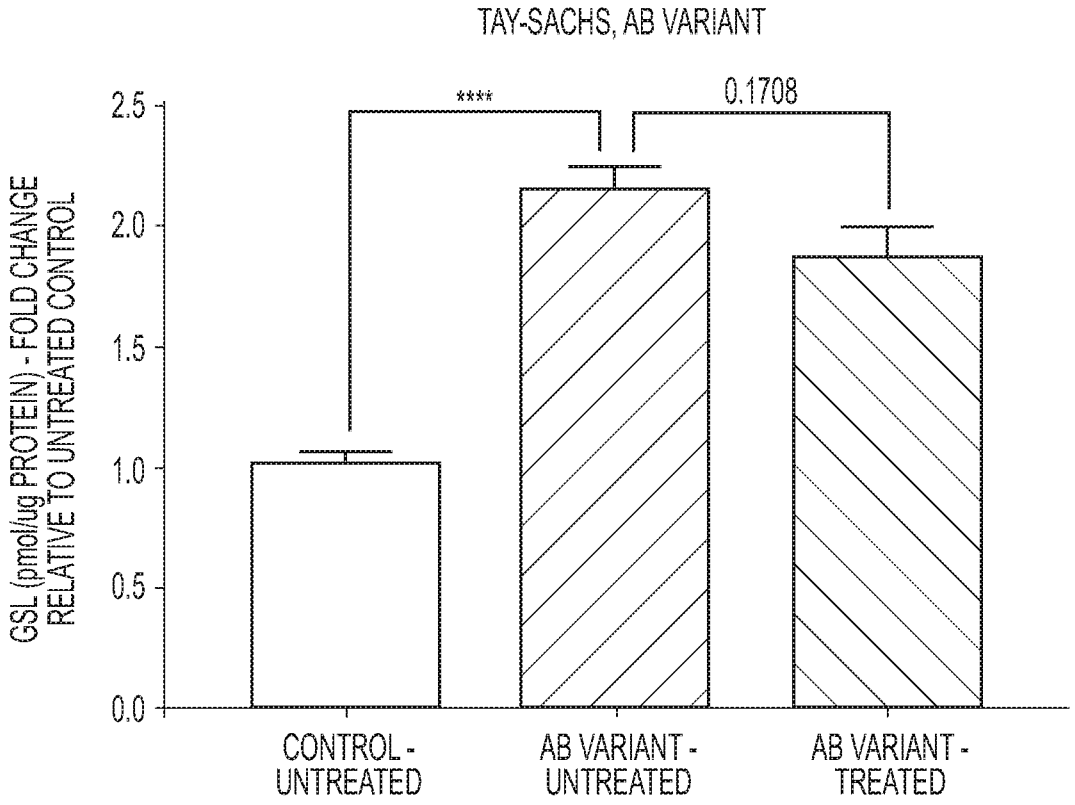

TAY-SACHS, AB VARIANT
GSL (pmol/ug PROTEIN) - FOLD CHANGE RELATIVE TO UNTREATED CONTROL
2.5
2.0
1.5
1.0
0.5
0.0
****
0.1708
CONTROL - UNTREATED
AB VARIANT - UNTREATED
AB VARIANT - TREATED

FIG. 8C

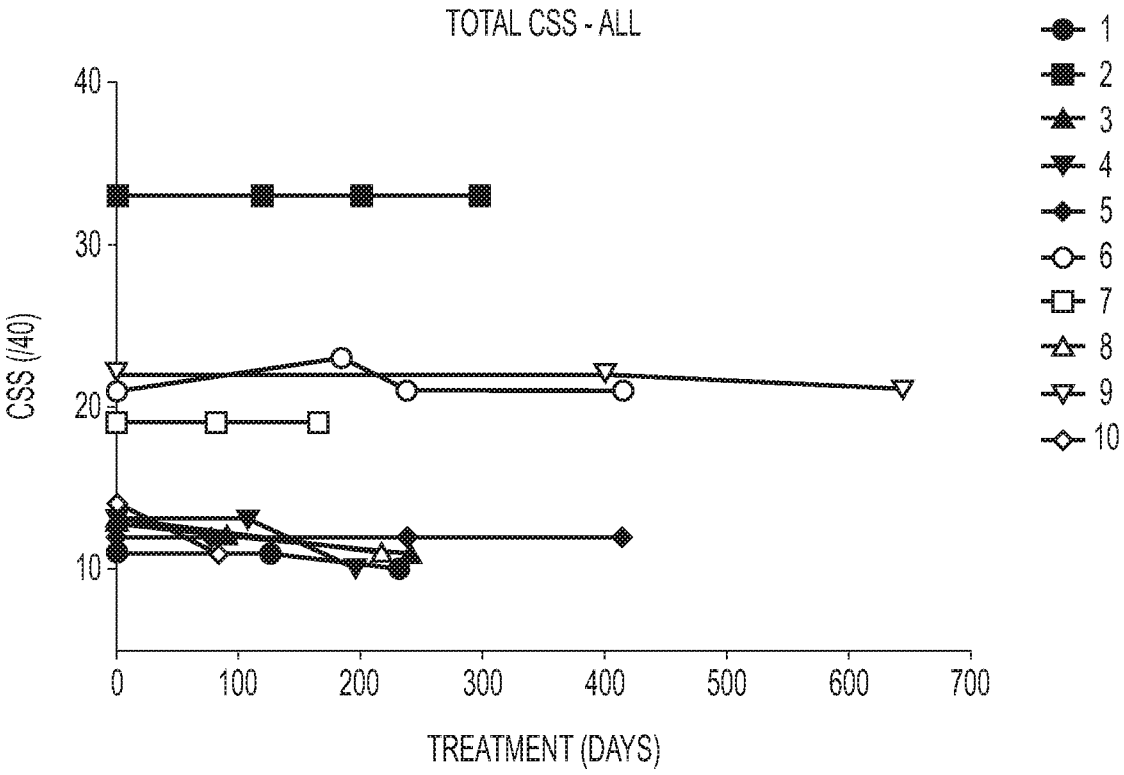

TOTAL CSS - ALL
CSS (/40)
40
30
20
10
0
100
200
300
400
500
600
700
TREATMENT (DAYS)
1
2
3
4
5
6
7
8
9
10

FIG. 9A

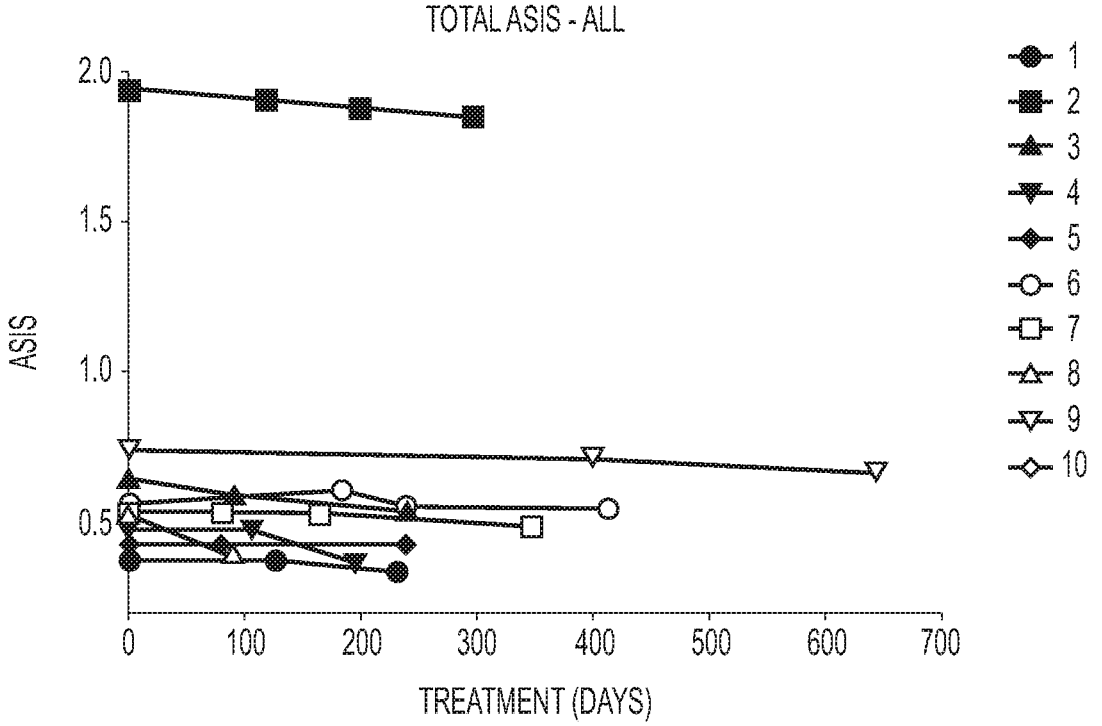

TOTAL ASIS - ALL
ASIS
2.0
1.5
1.0
0.5
0
100
200
300
400
500
600
700
TREATMENT (DAYS)
1
2
3
4
5
6
7
8
9
10

FIG. 9B

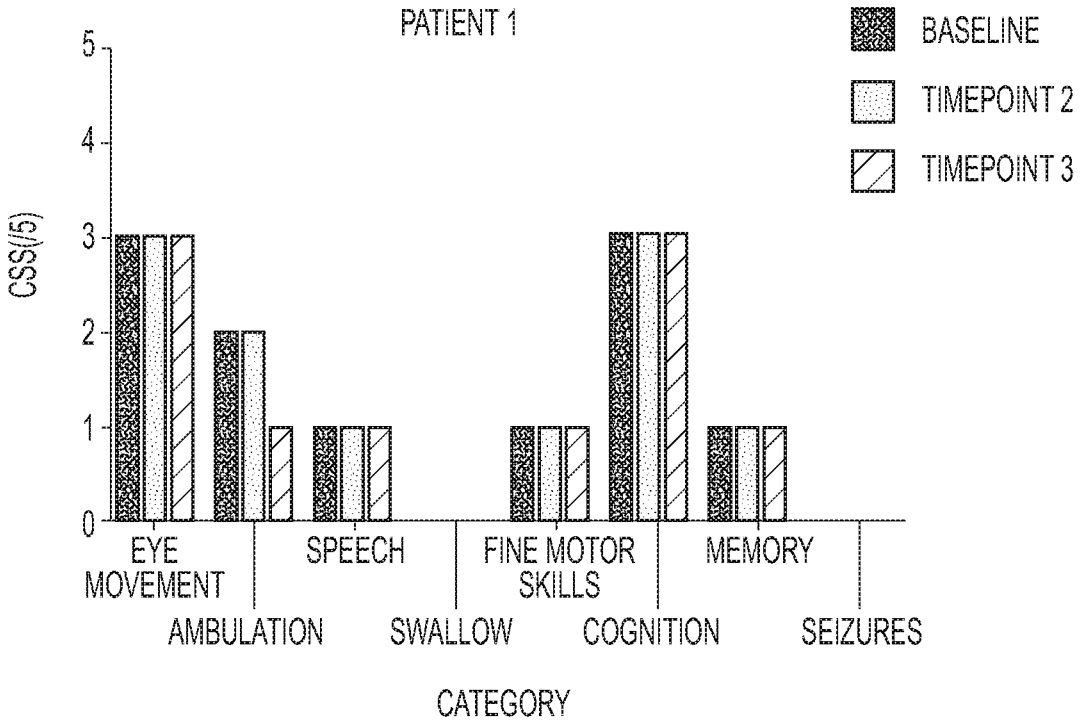


FIG. 10A

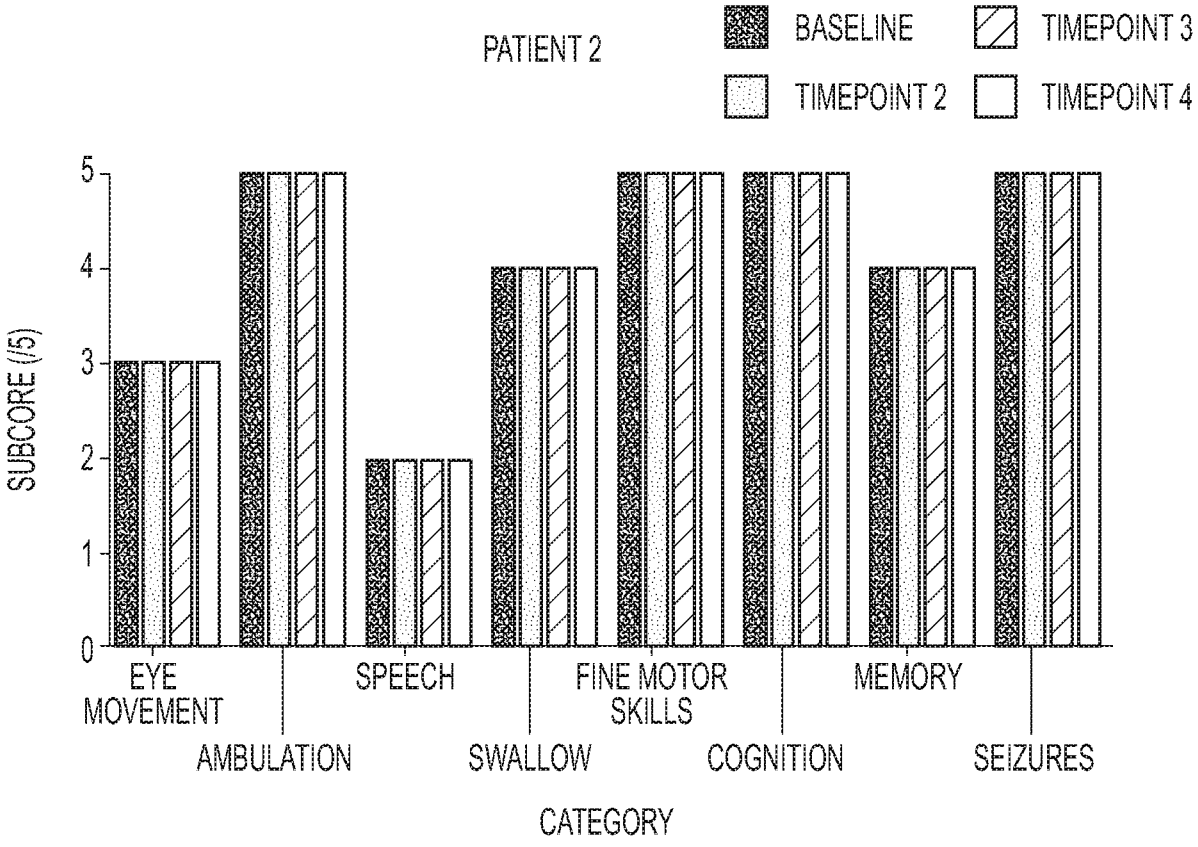


FIG. 10B

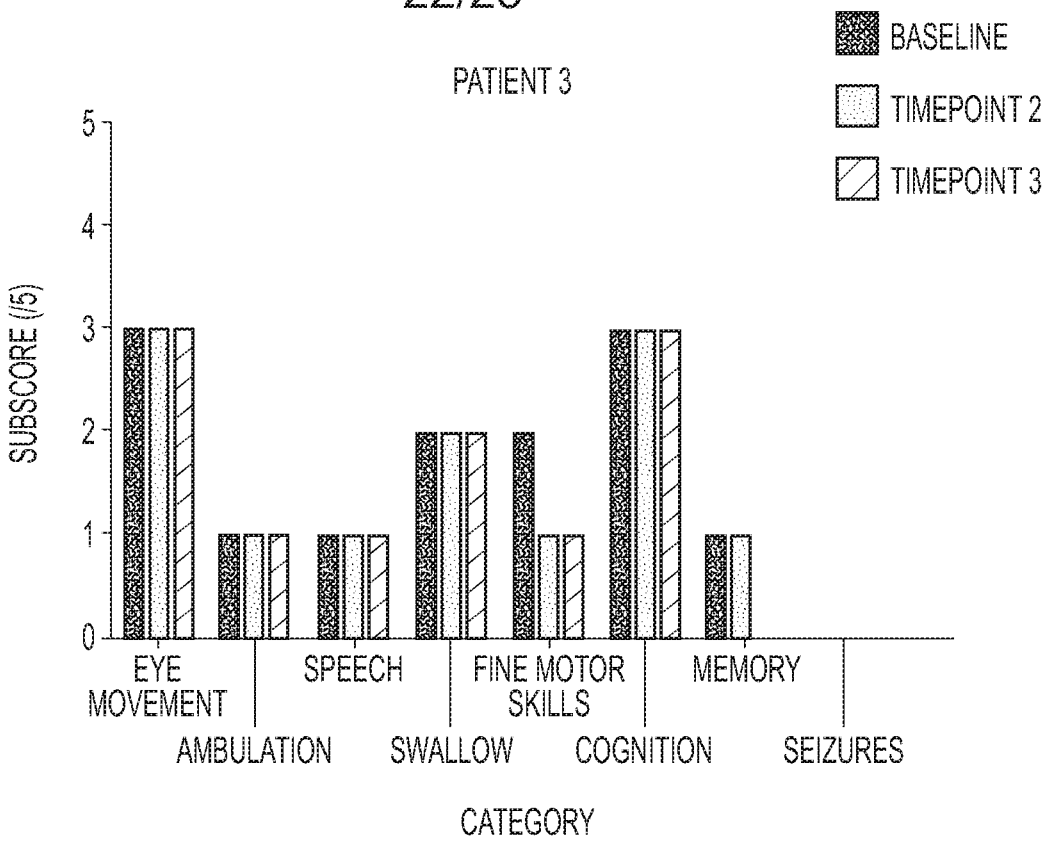


FIG. 10C

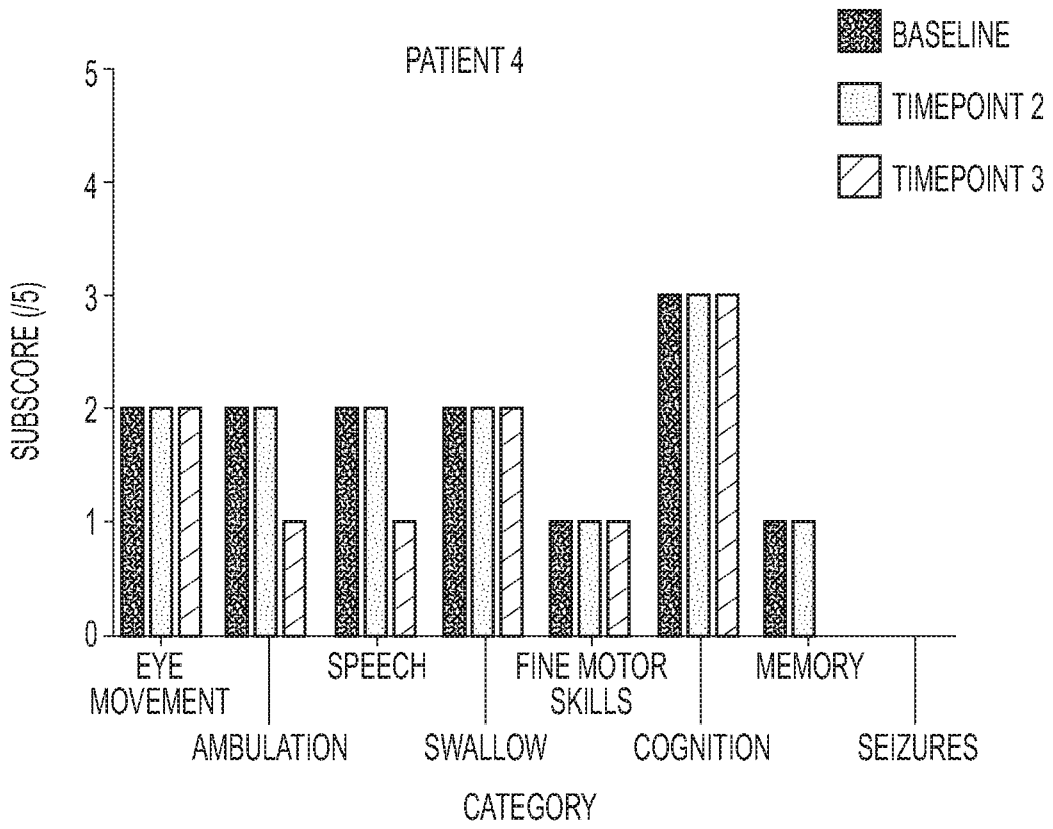


FIG. 10D

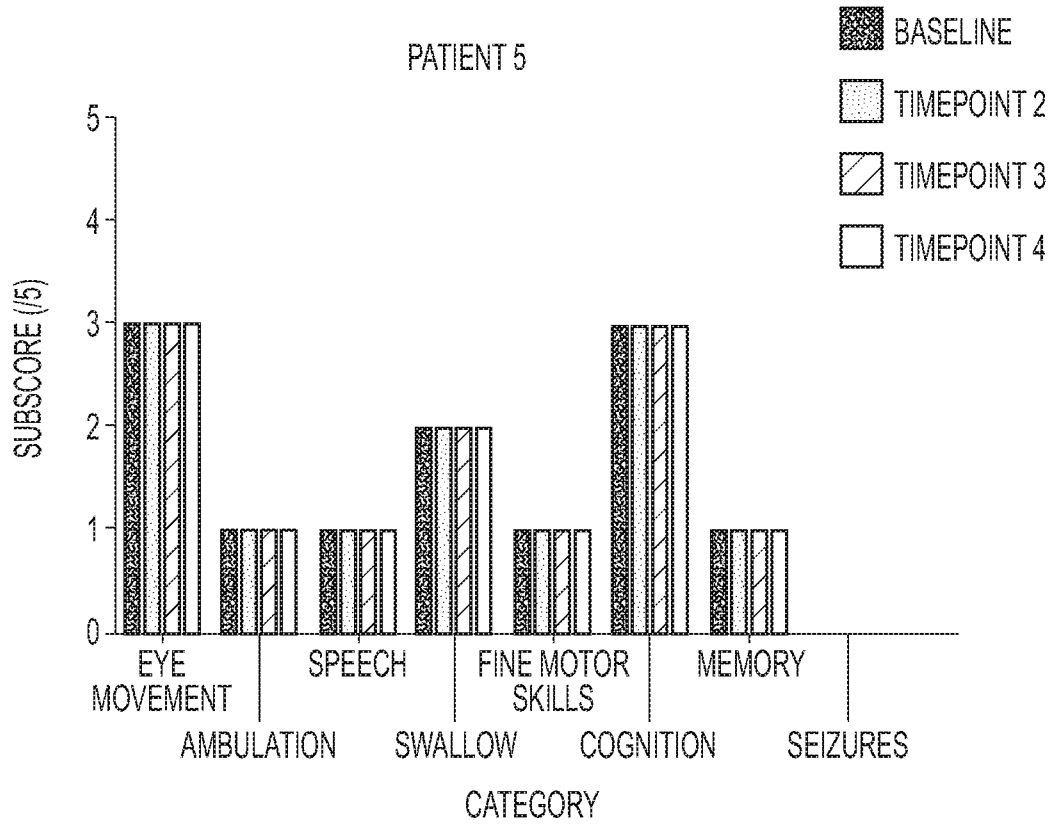


FIG. 10E

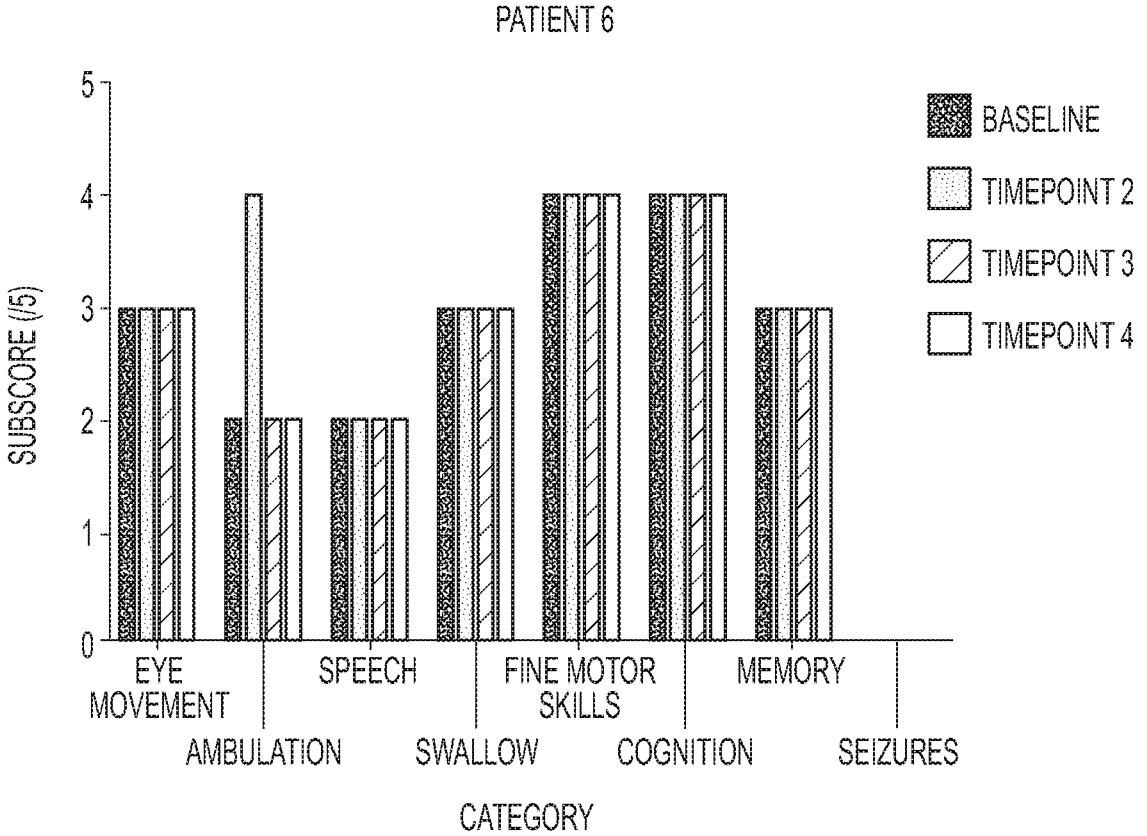


FIG. 10F

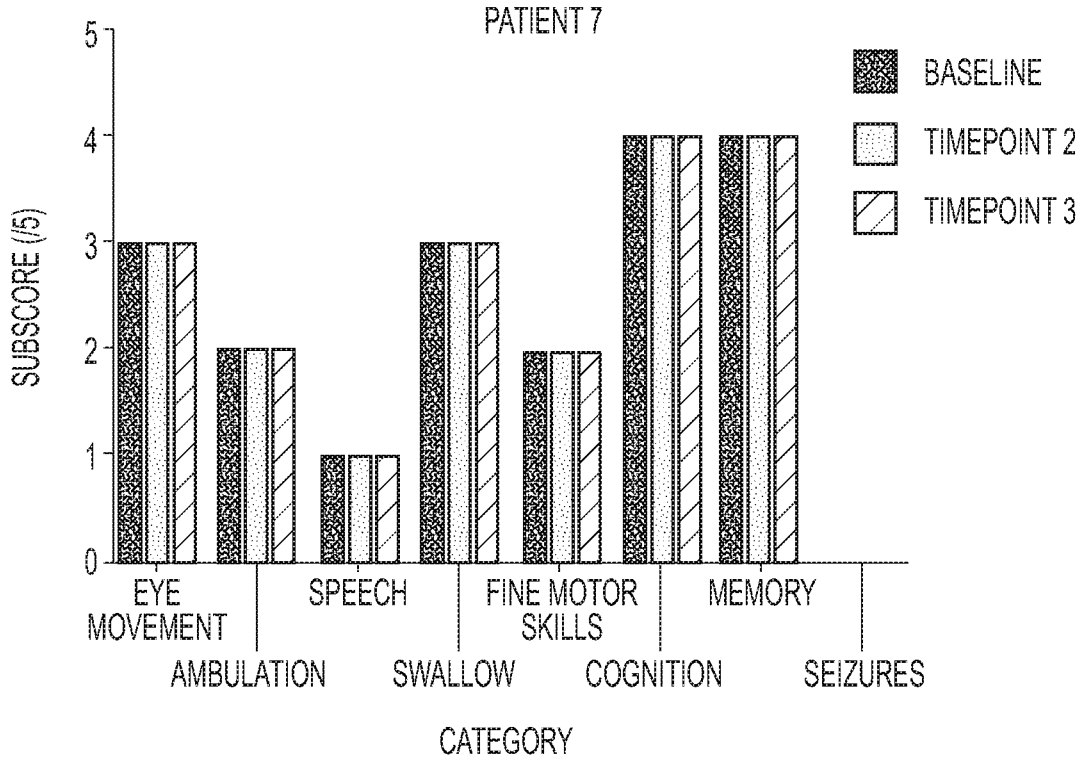


FIG. 10G

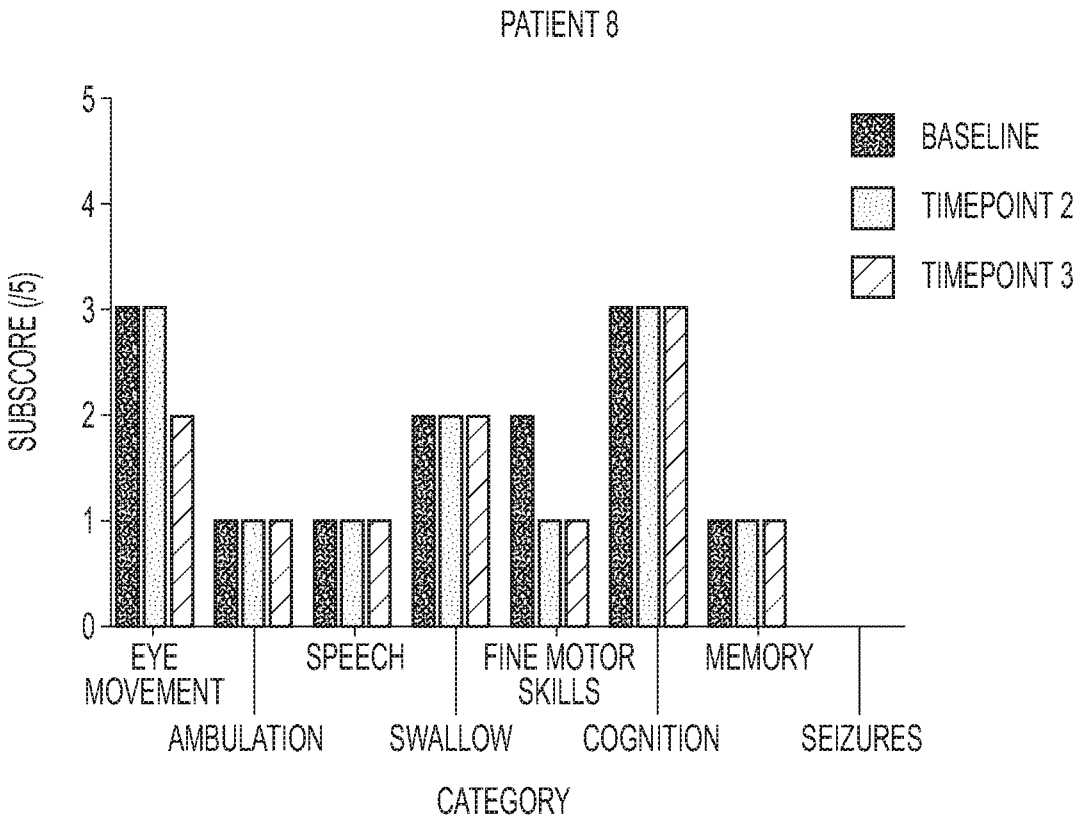


FIG. 10H

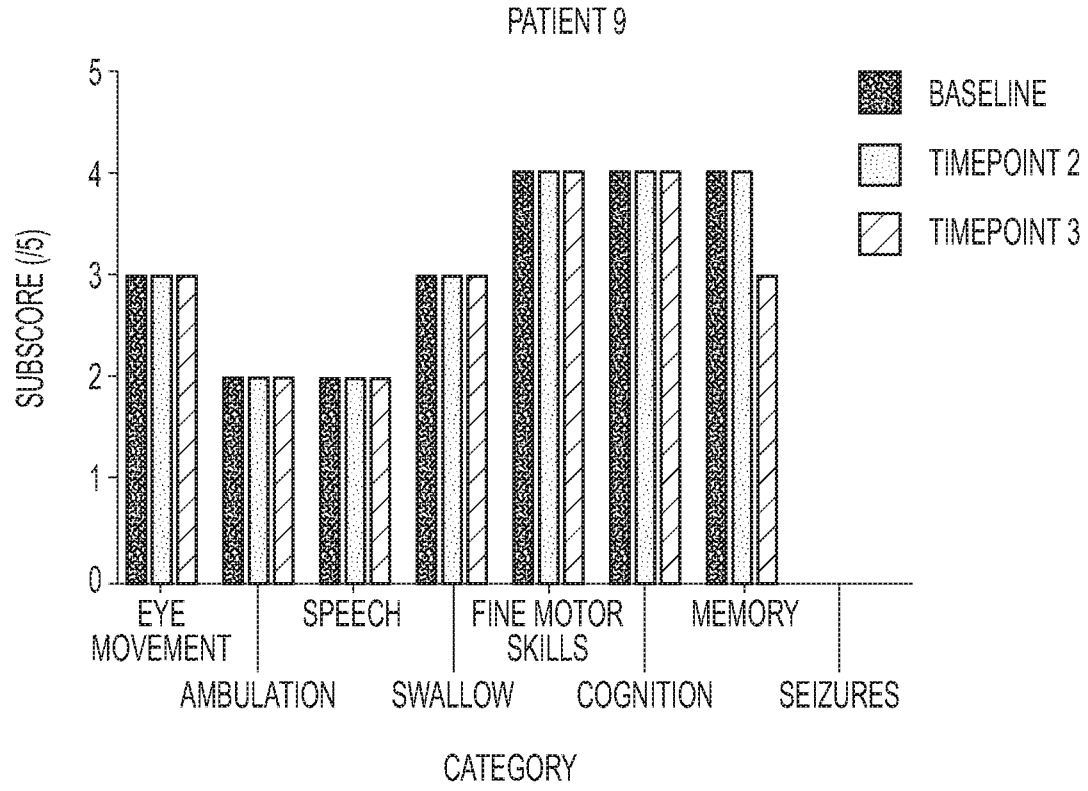


FIG. 10I

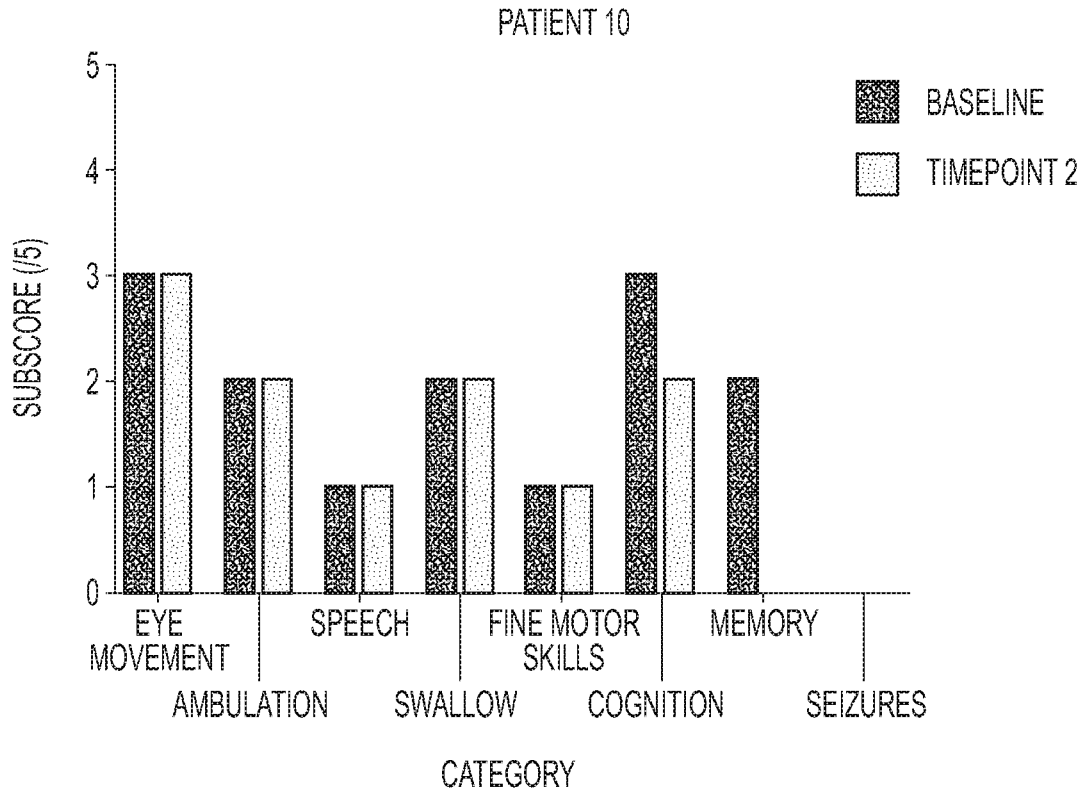


FIG. 10J