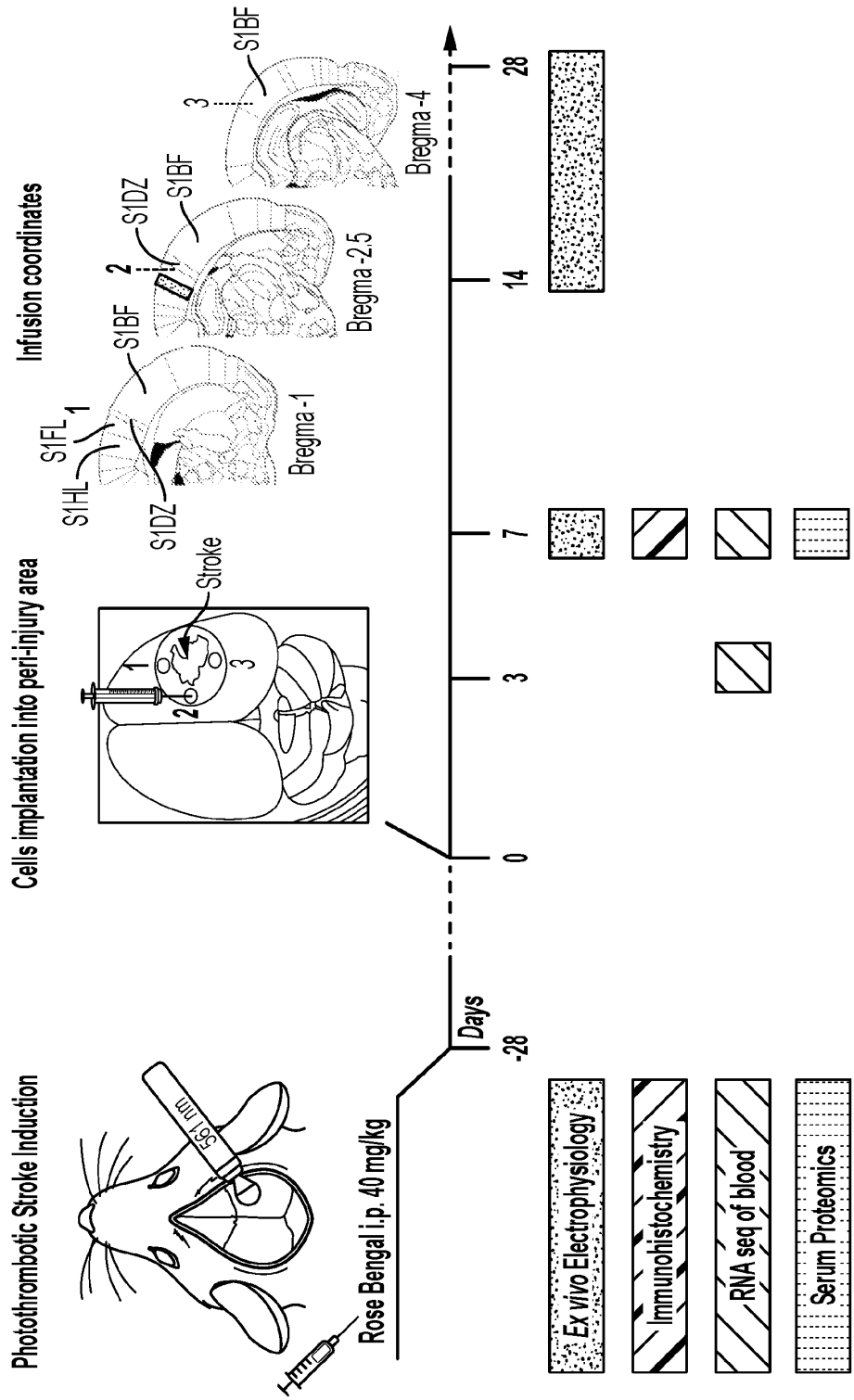

Photothrombotic Stroke Induction
561 nm
Rose Bengal i.p. 40 mg/kg
Days
-28
0
3
7
14
28
Cells implantation into peri-injury area
Stroke
Infusion coordinates
S1HL
S1FL
S1BF
S1DZ
Bregma -1
Bregma -2.5
Bregma -4
Ex vivo Electrophysiology
Immunohistochemistry
RNA seq of blood
Serum Proteomics

FIG. 1

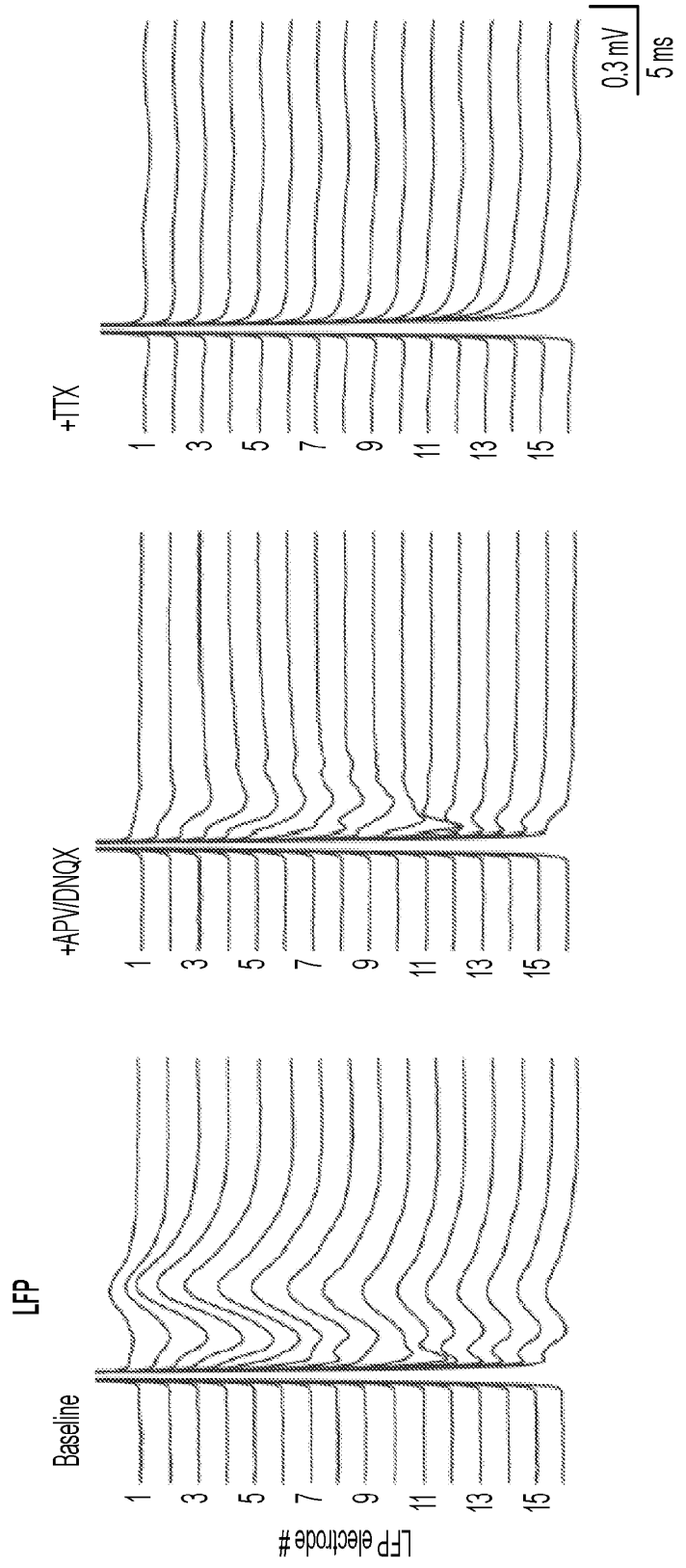

LFP
Baseline
+APV/DNQX
+TTX
0.3 mV
5 ms
1
3
5
7
9
11
13
15
LFP electrode #

FIG. 2A

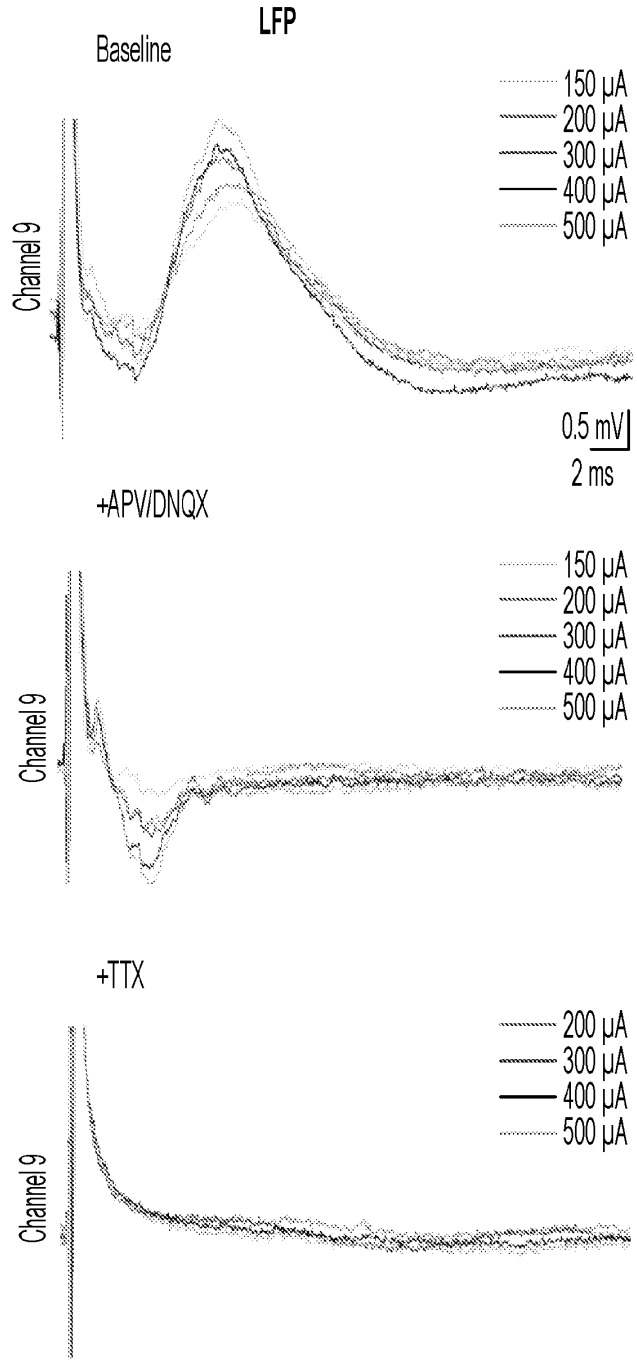

LFP
Baseline
150 µA
200 µA
300 µA
400 µA
500 µA
Channel 9
0.5 mV
2 ms
+APV/DNQX
150 µA
200 µA
300 µA
400 µA
500 µA
Channel 9
+TTX
200 µA
300 µA
400 µA
500 µA
Channel 9

FIG. 2B

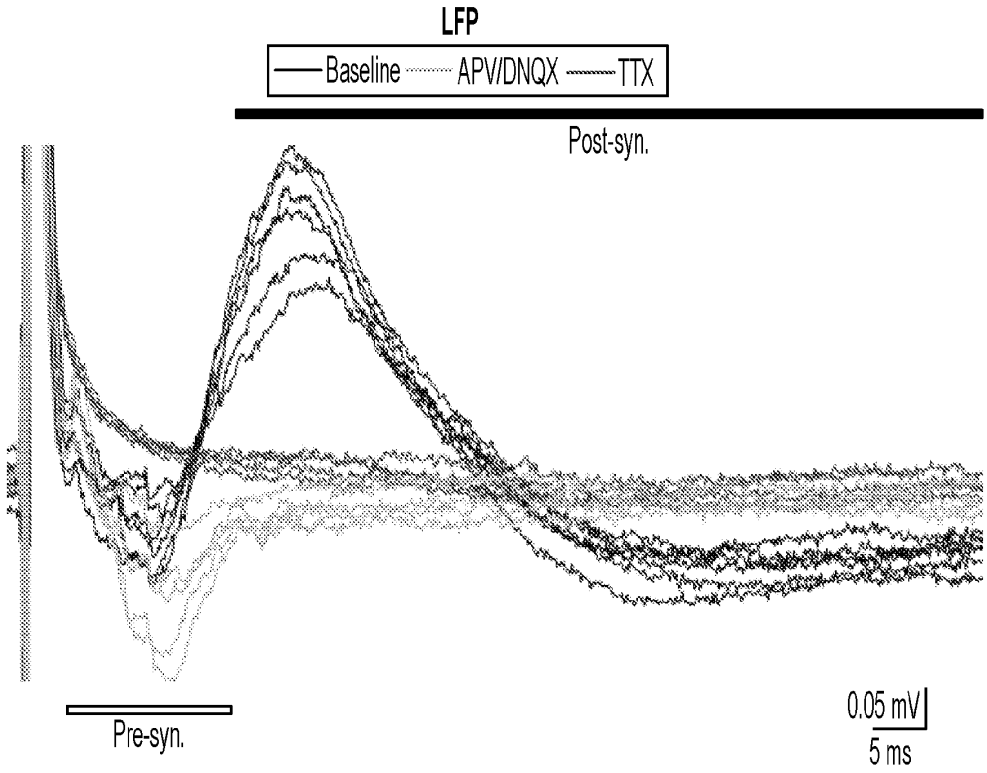


FIG. 2C

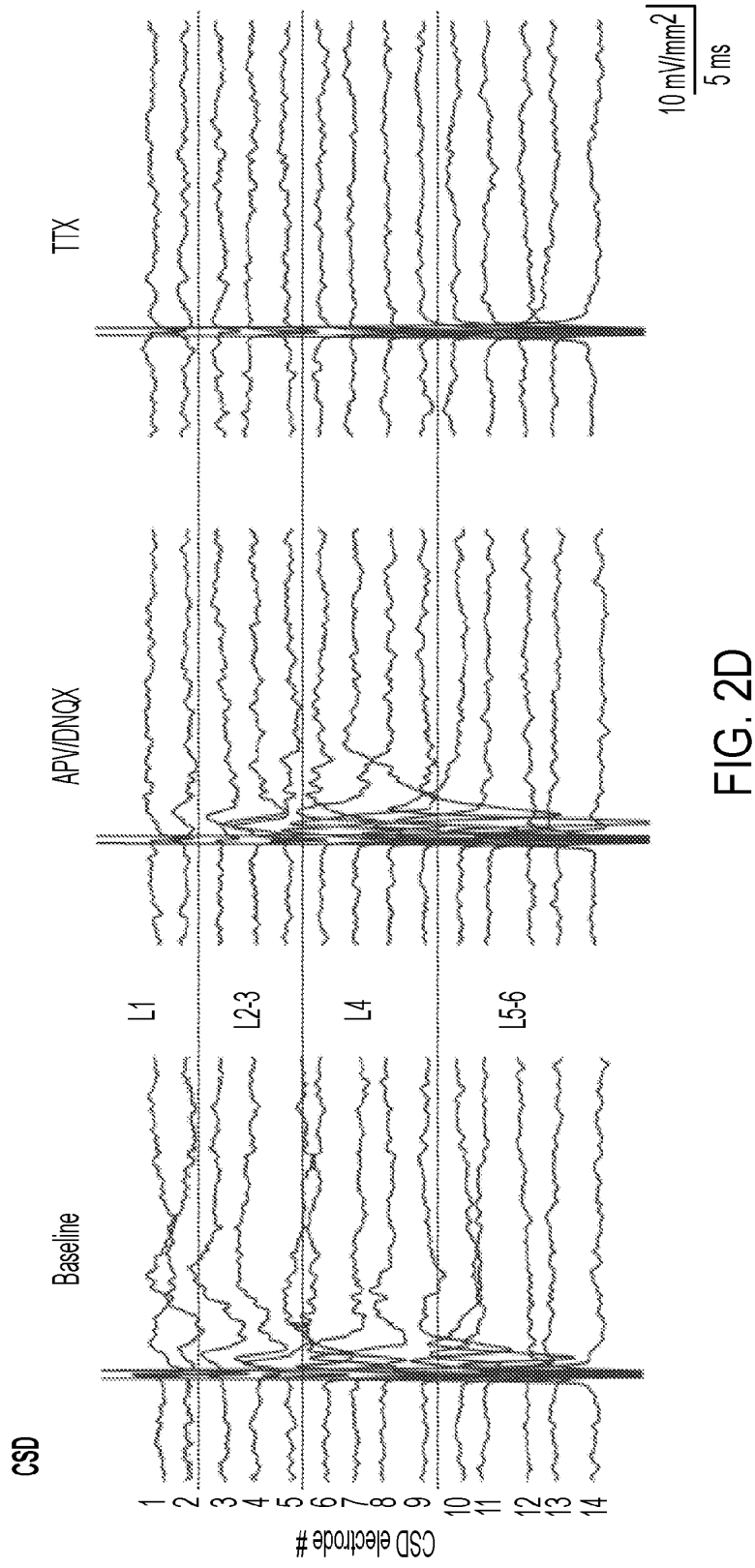

CSD
Baseline
APV/DNQX
TTX
L1
L2-3
L4
L5-6
1 2 3 4 5 6 7 8 9 10 11 12 13 14
CSD electrode #
10 mV/mm2
5 ms

FIG. 2D

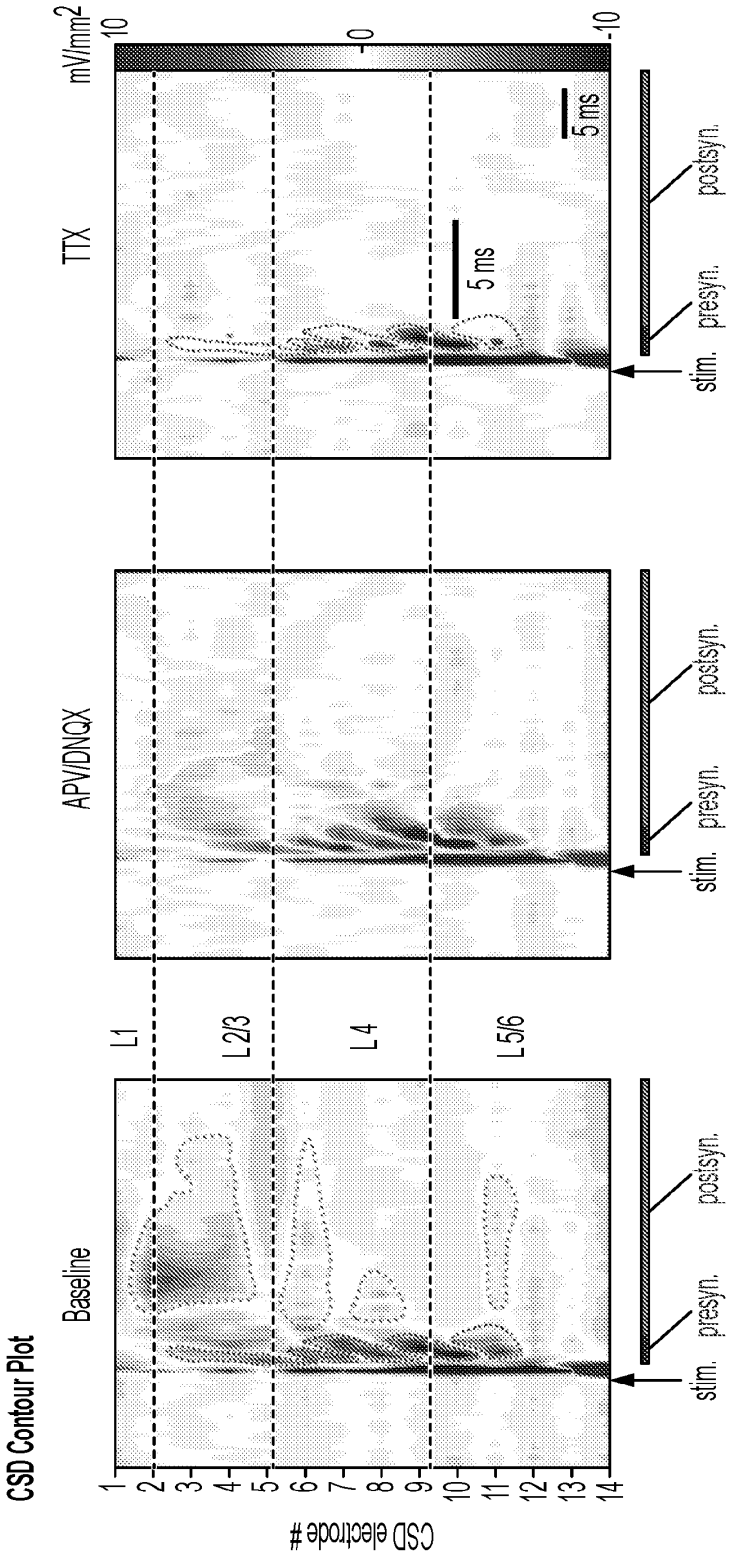

CSD Contour Plot
Baseline
APV/DNQX
TTX
mV/mm2
10
0
-10
5 ms
5 ms
stim.
presyn.
postsyn.
L1
L2/3
L4
L5/6
1
2
3
4
5
6
7
8
9
10
11
12
13
14
CSD electrode #

FIG. 2E

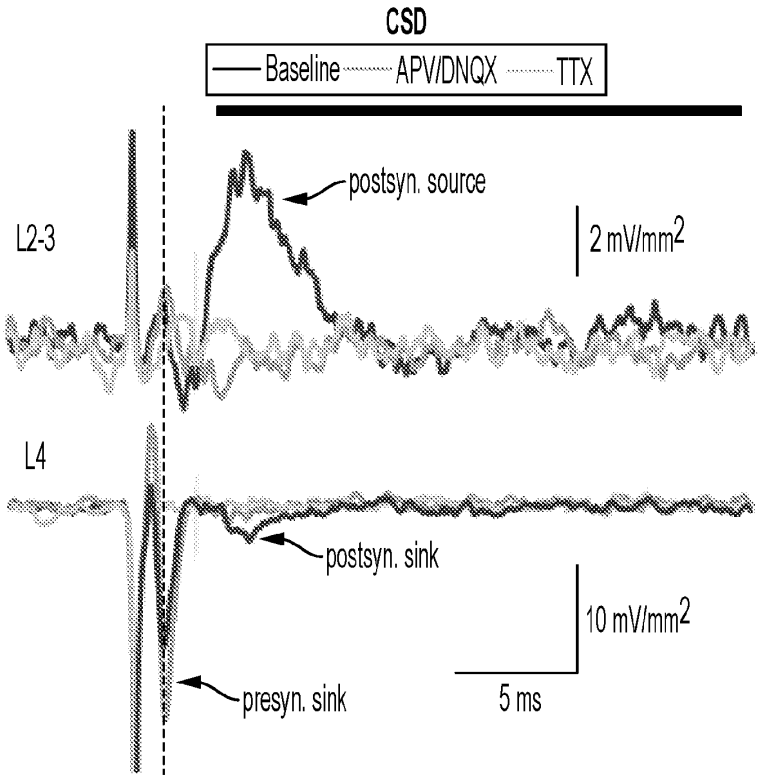

CSD
Baseline
APV/DNQX
TTX
postsyn. source
2 mV/mm2
L2-3
L4
postsyn. sink
10 mV/mm2
presyn. sink
5 ms

FIG. 2F

TO FIG. 3B

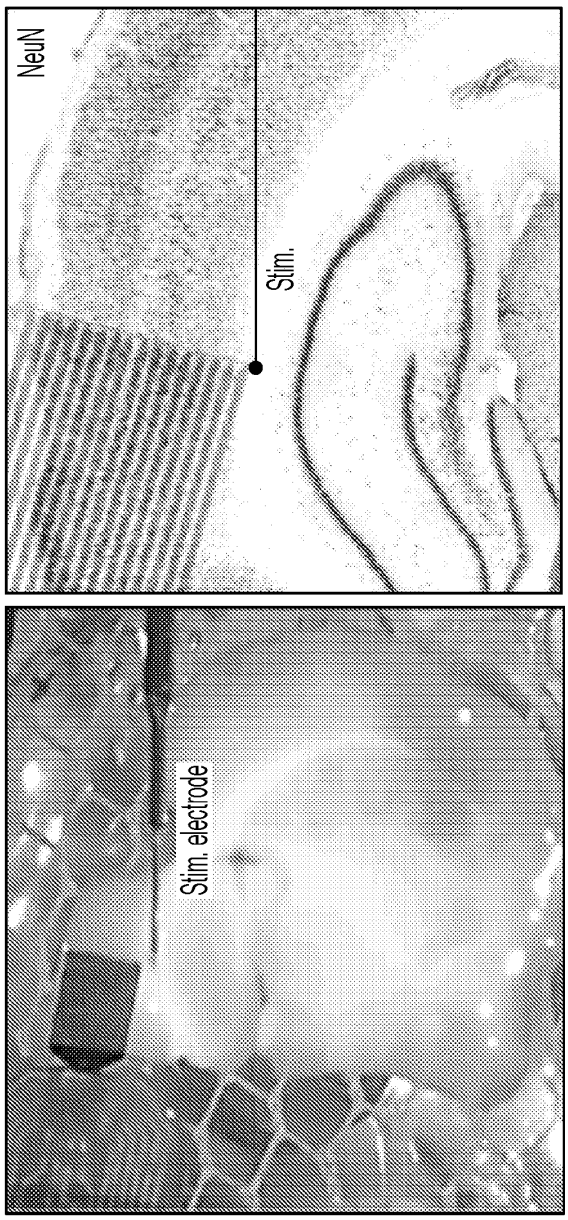


FIG. 3A

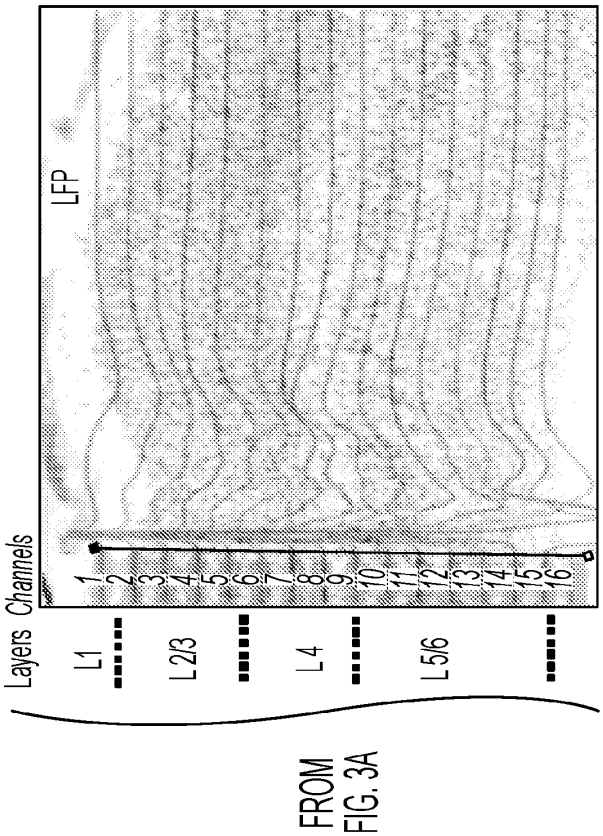

LFP
Channels
Layers
L1
L2/3
L4
L5/6
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
FROM FIG. 3A

FIG. 3B

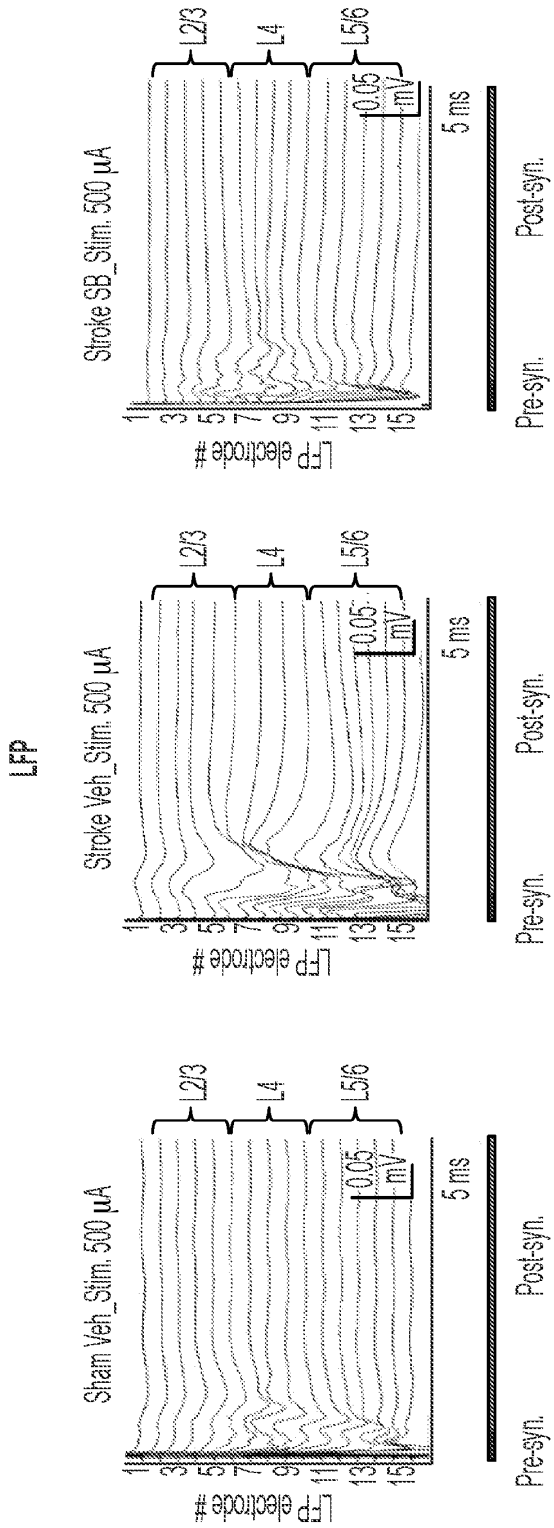

LFP
Stroke SB_Stim. 500 µA
Stroke Veh_Stim. 500 µA
Sham Veh_Stim. 500 µA
L2/3
L4
L5/6
0.05 mV
5 ms
Pre-syn.
Post-syn.
LFP electrode #
1
3
5
7
9
11
13
15

FIG. 3C

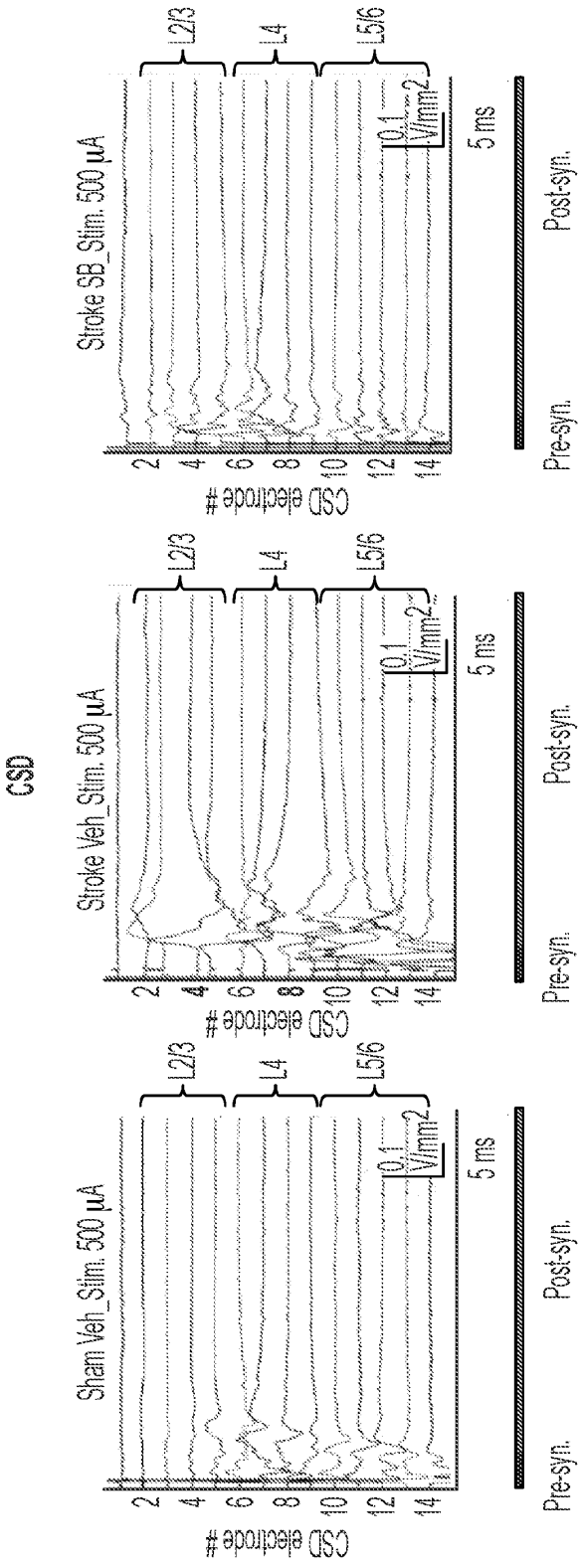

CSD
Sham Veh_Stim. 500 µA
Stroke Veh_Stim. 500 µA
Stroke SB_Stim. 500 µA
L2/3
L4
L5/6
0.1 V/mm2
5 ms
Pre-syn.
Post-syn.
CSD electrode #
2
4
6
8
10
12
14

FIG. 3D

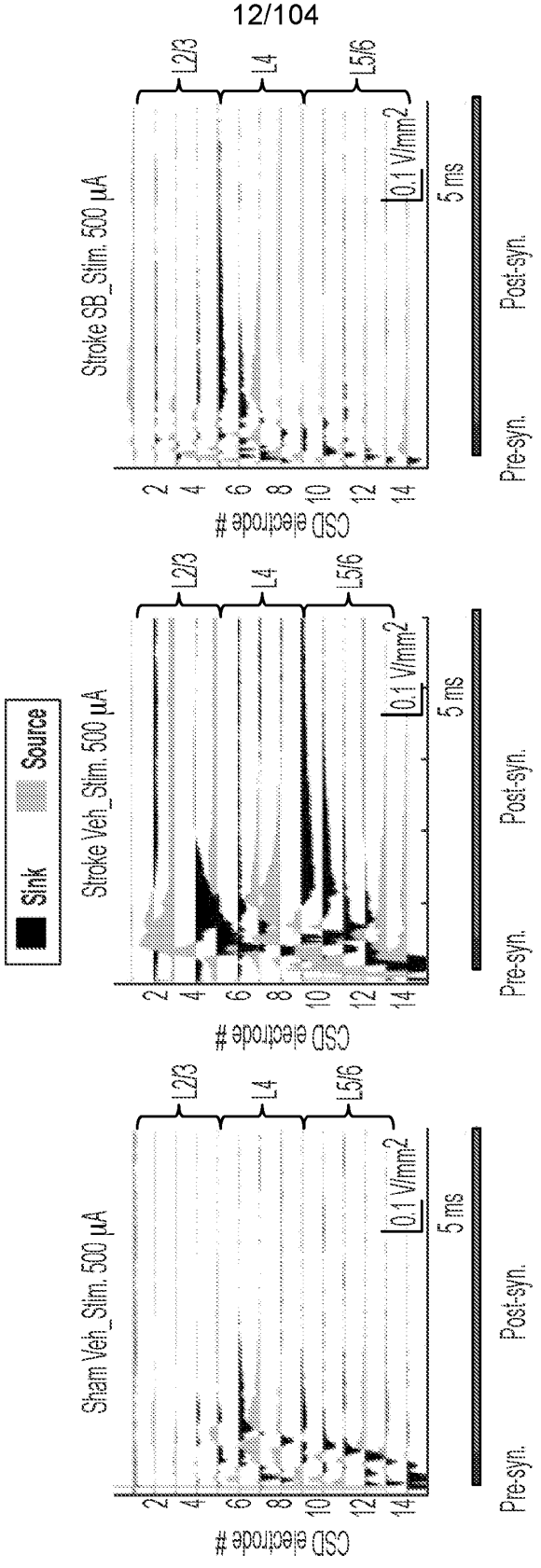

Sham Veh_Stim. 500 µA
Stroke Veh_Stim. 500 µA
Stroke SB_Stim. 500 µA
L2/3
L4
L5/6
0.1 V/mm2
5 ms
Pre-syn.
Post-syn.
CSD electrode #
Sink
Source

FIG. 3E

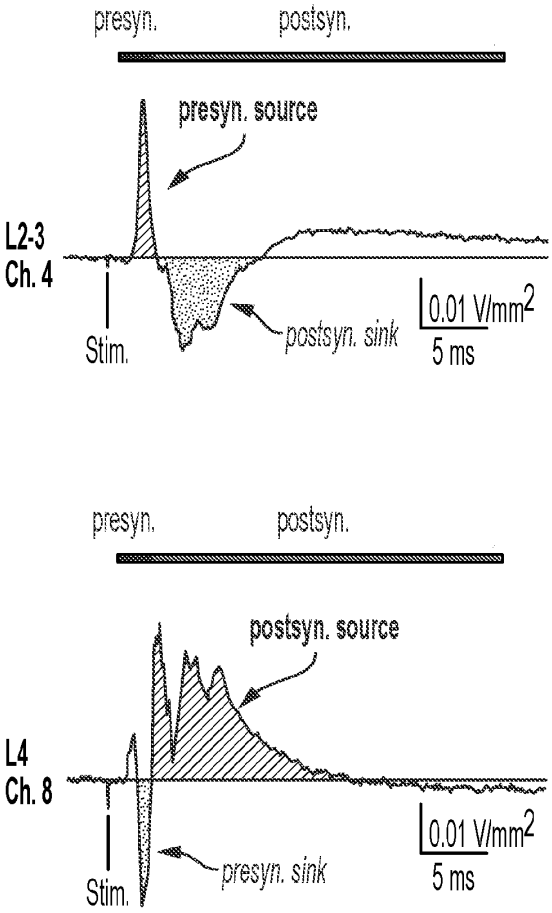

presyn.
postsyn.
presyn. source
L2-3
Ch. 4
Stim.
postsyn. sink
0.01 V/mm2
5 ms
presyn.
postsyn.
postsyn. source
L4
Ch. 8
Stim.
presyn. sink
0.01 V/mm2
5 ms

FIG. 3F

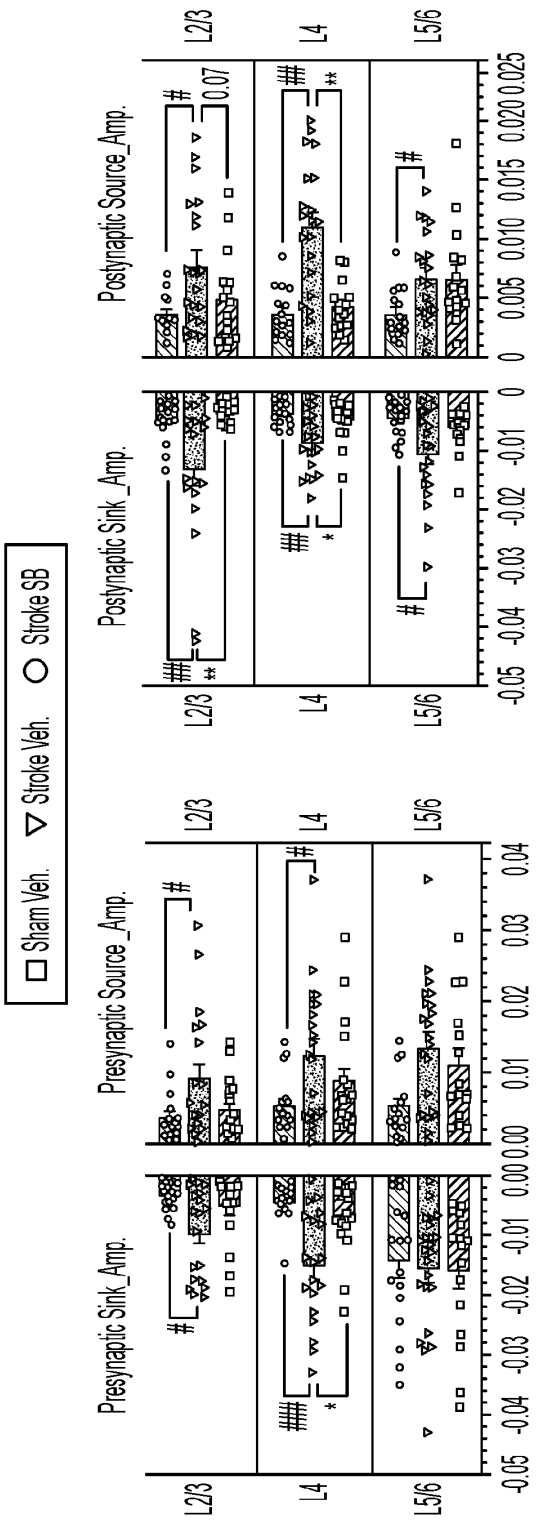

Sham Veh.
Stroke Veh.
Stroke SB
Presynaptic Sink_Amp.
Presynaptic Source_Amp.
Postsynaptic Sink_Amp.
Postsynaptic Source_Amp.
L2/3
L4
L5/6
Amplitude (V/mm2)
-0.05
-0.04
-0.03
-0.02
-0.01
0.00
0.01
0.02
0.03
0.04
0.005
0.010
0.015
0.020
0.025
0.07

FIG. 3G

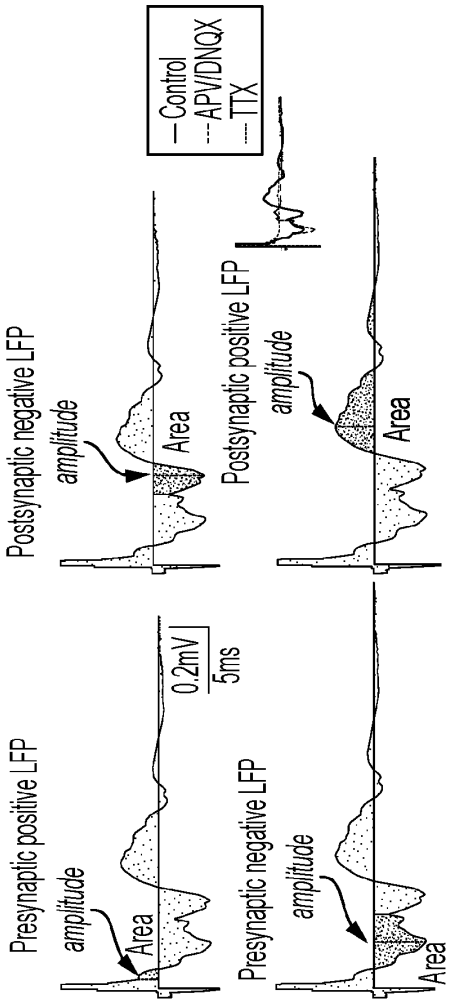

Control
APV/DNQX
TTX
Postsynaptic negative LFP
amplitude
Area
Postsynaptic positive LFP
amplitude
Area
0.2mV
5ms
Presynaptic positive LFP
amplitude
Area
Presynaptic negative LFP
amplitude
Area

FIG. 4A

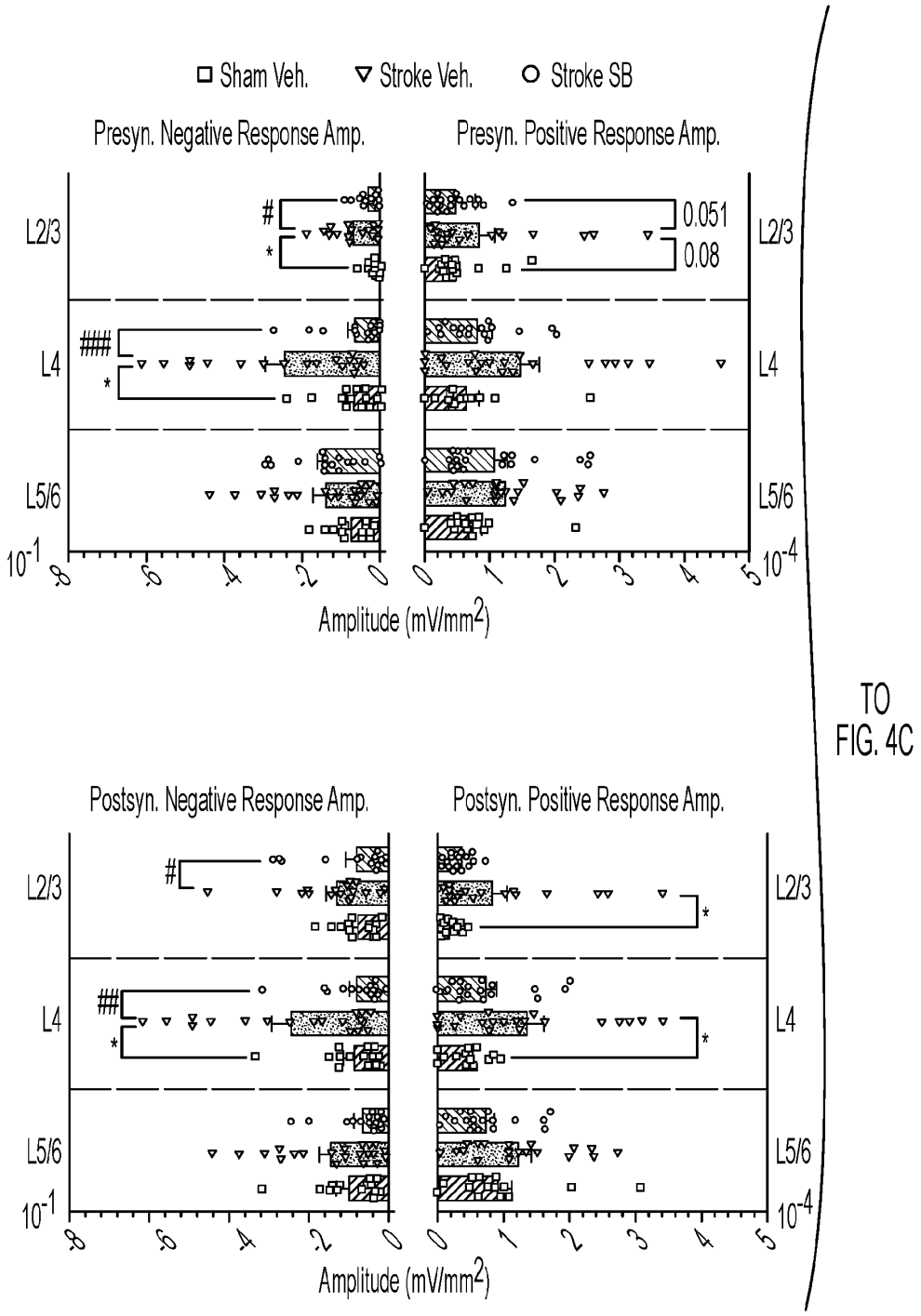

Sham Veh.
Stroke Veh.
Stroke SB
Presyn. Negative Response Amp.
Presyn. Positive Response Amp.
L2/3
L4
L5/6
#
*
###
0.051
0.08
10^{-1}
10^{-4}
Amplitude (mV/mm^2)
Postsyn. Negative Response Amp.
Postsyn. Positive Response Amp.
TO FIG. 4C

FIG. 4B

FROM FIG. 4B

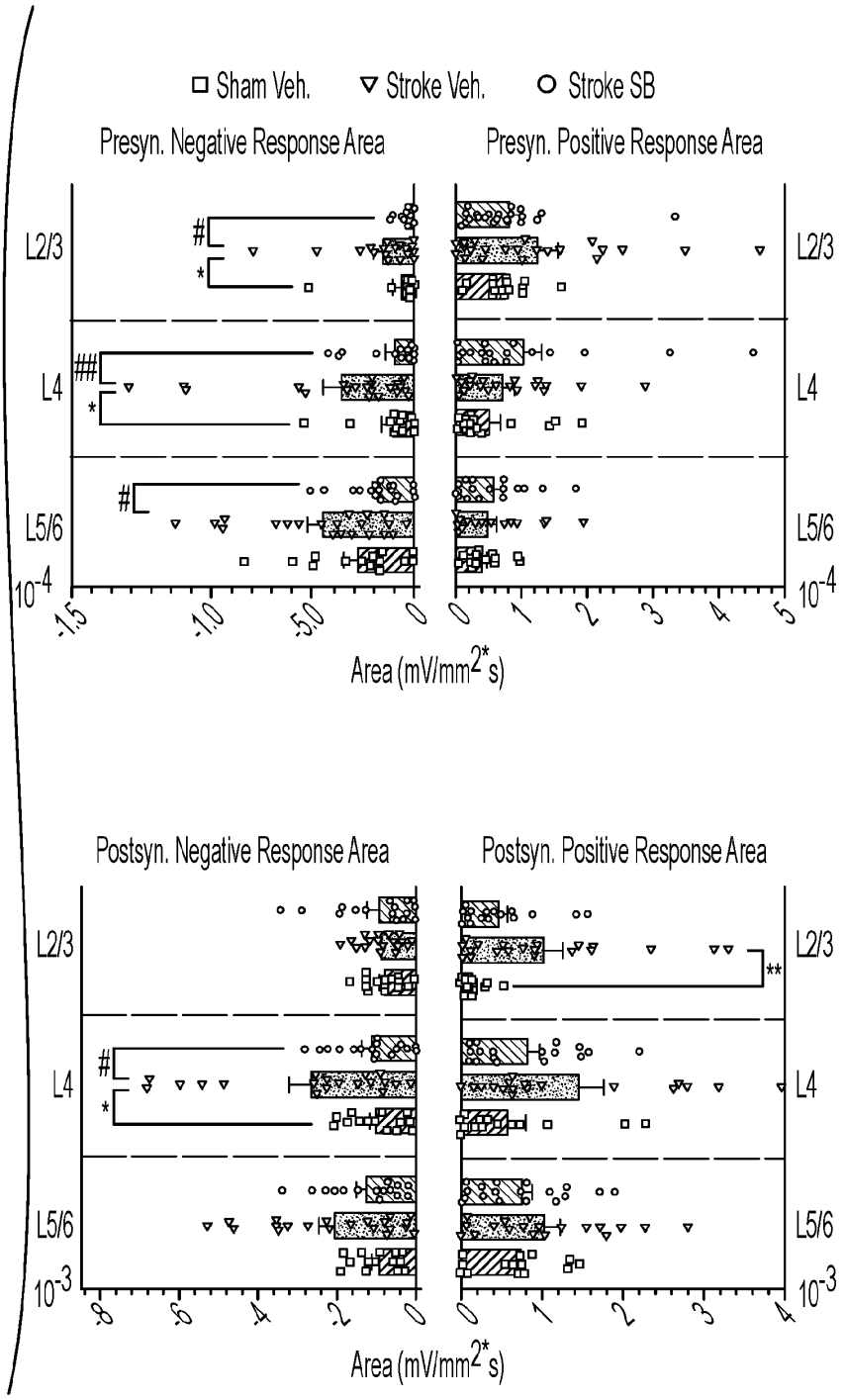


FIG. 4C

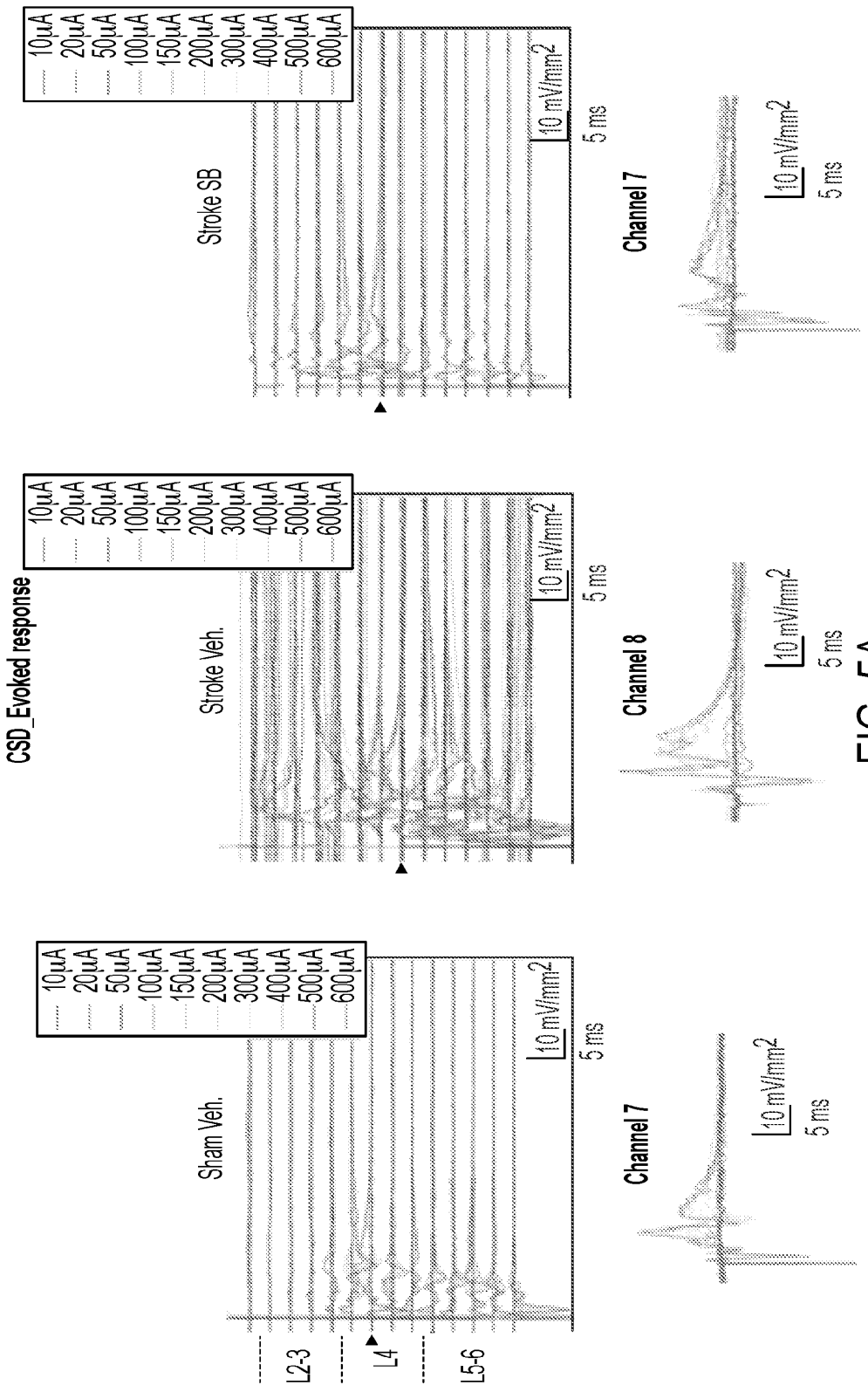

CSD_Evoked response
10µA
20µA
50µA
100µA
150µA
200µA
300µA
400µA
500µA
600µA
Sham Veh.
Stroke Veh.
Stroke SB
10 mV/mm2
5 ms
Channel 7
Channel 8
L2-3
L4
L5-6

FIG. 5A

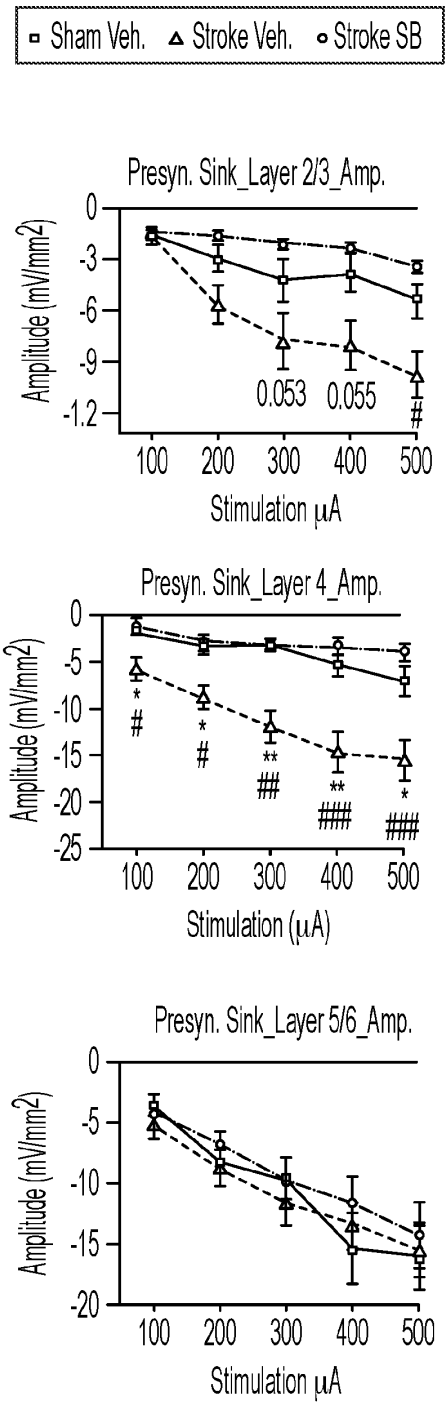

Sham Veh.
Stroke Veh.
Stroke SB
Presyn. Sink_Layer 2/3_Amp.
Amplitude (mV/mm2)
0
-3
-6
-9
-1.2
0.053
0.055
#
100
200
300
400
500
Stimulation μA
Presyn. Sink_Layer 4_Amp.
Amplitude (mV/mm2)
0
-5
-10
-15
-20
-25
*
#
*
#
**
##
**
###
*
###
100
200
300
400
500
Stimulation (μA)
Presyn. Sink_Layer 5/6_Amp.
Amplitude (mV/mm2)
0
-5
-10
-15
-20
100
200
300
400
500
Stimulation μA

FIG. 5B

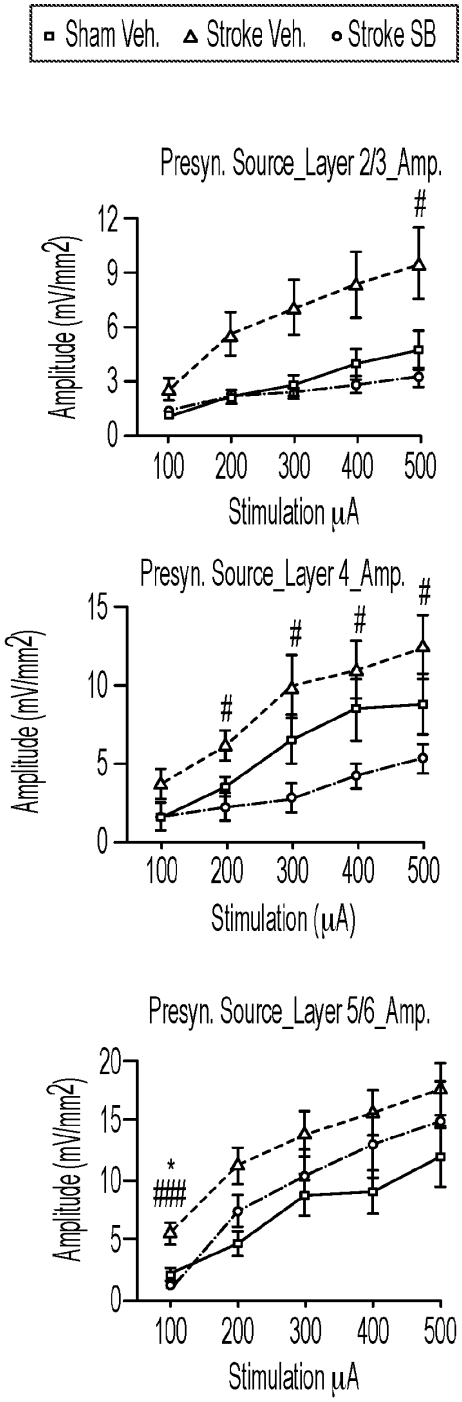

Sham Veh.
Stroke Veh.
Stroke SB
Presyn. Source_Layer 2/3_Amp.
Amplitude (mV/mm2)
Stimulation μA
Presyn. Source_Layer 4_Amp.
Amplitude (mV/mm2)
Stimulation (μA)
Presyn. Source_Layer 5/6_Amp.
Amplitude (mV/mm2)
Stimulation μA

FIG. 5C

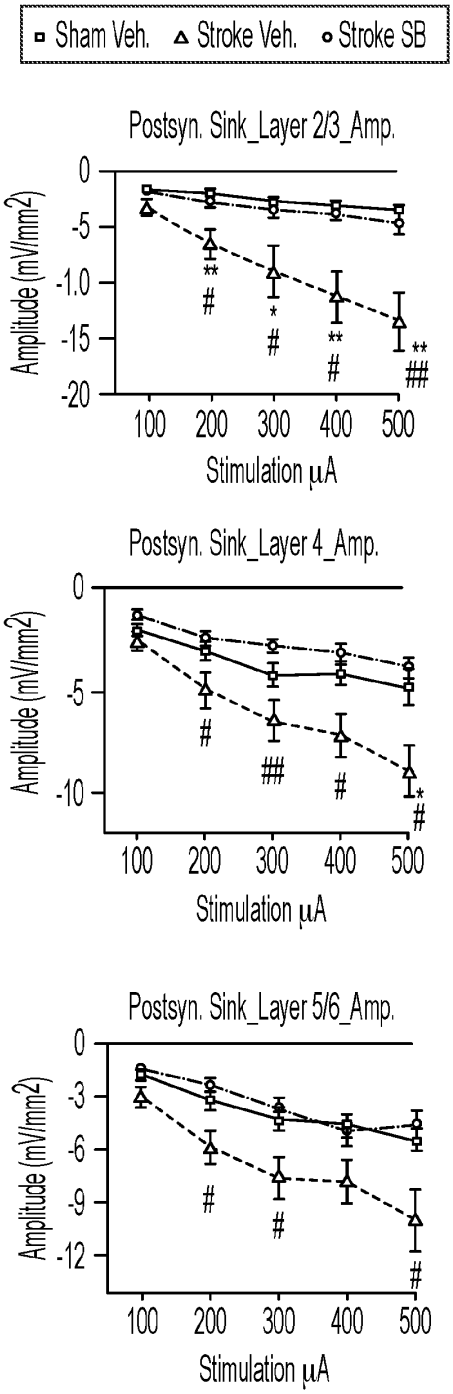

Sham Veh.
Stroke Veh.
Stroke SB
Postsyn. Sink_Layer 2/3_Amp.
Amplitude (mV/mm2)
0
-5
-1.0
-15
-20
100
200
300
400
500
Stimulation µA
Postsyn. Sink_Layer 4_Amp.
Amplitude (mV/mm2)
0
-5
-10
100
200
300
400
500
Stimulation µA
Postsyn. Sink_Layer 5/6_Amp.
Amplitude (mV/mm2)
0
-3
-6
-9
-12
100
200
300
400
500
Stimulation µA

FIG. 5D

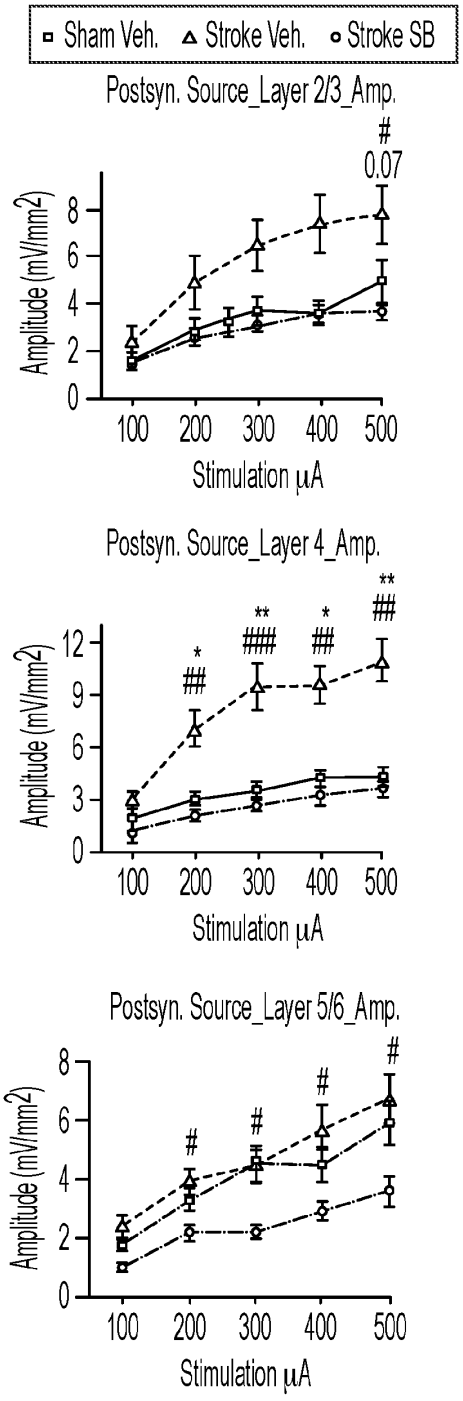

Sham Veh.
Stroke Veh.
Stroke SB
Postsyn. Source_Layer 2/3_Amp.
Amplitude (mV/mm2)
Stimulation µA
0.07
Postsyn. Source_Layer 4_Amp.
Amplitude (mV/mm2)
Stimulation µA
Postsyn. Source_Layer 5/6_Amp.
Amplitude (mV/mm2)
Stimulation µA

FIG. 5E

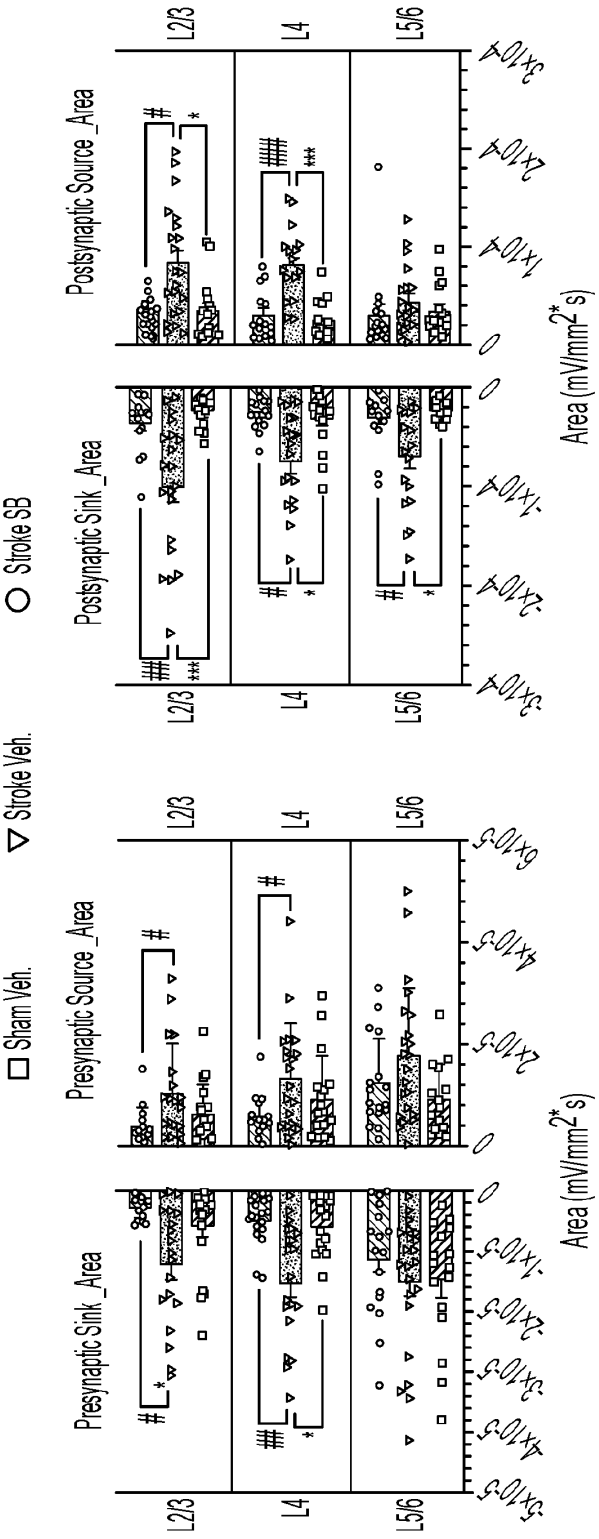

Sham Veh.
Stroke Veh.
Stroke SB
Presynaptic Sink_Area
Presynaptic Source_Area
Postsynaptic Sink_Area
Postsynaptic Source_Area
L2/3
L4
L5/6
Area (mV/mm^2*s)

FIG. 6A

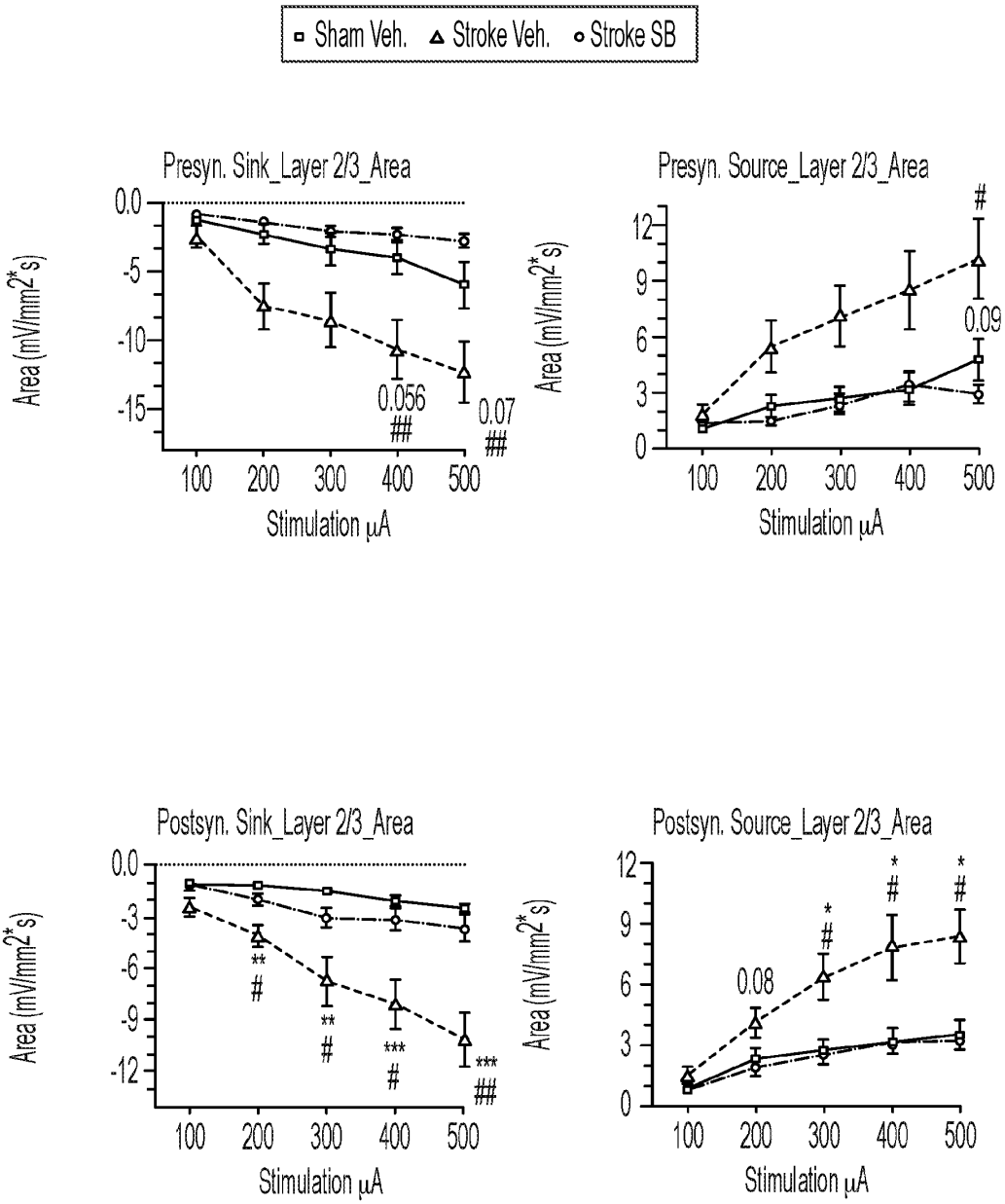

Sham Veh.
Stroke Veh.
Stroke SB
Presyn. Sink_Layer 2/3_Area
Area (mV/mm2*s)
0.0
-5
-10
-15
0.056
##
0.07
##
100
200
300
400
500
Stimulation μA
Presyn. Source_Layer 2/3_Area
Area (mV/mm2*s)
12
9
6
3
0
#
0.09
100
200
300
400
500
Stimulation μA
Postsyn. Sink_Layer 2/3_Area
Area (mV/mm2*s)
0.0
-3
-6
-9
-12
**
#
**
#
***
#
***
##
100
200
300
400
500
Stimulation μA
Postsyn. Source_Layer 2/3_Area
Area (mV/mm2*s)
12
9
6
3
0
0.08
*
#
*
#
*
#
100
200
300
400
500
Stimulation μA

FIG. 6B

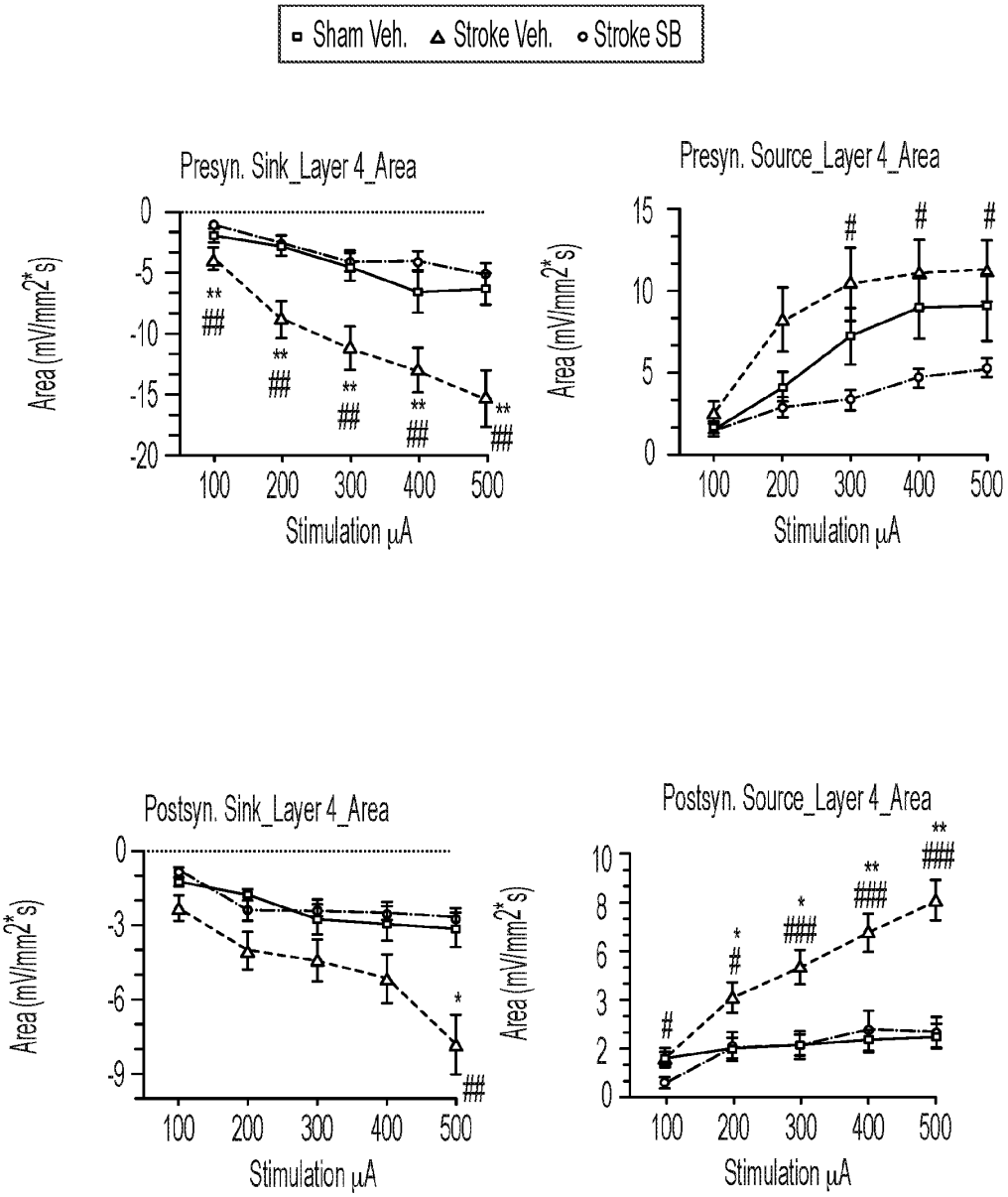

Sham Veh.
Stroke Veh.
Stroke SB
Presyn. Sink_Layer 4_Area
Area (mV/mm2*s)
Stimulation µA
Presyn. Source_Layer 4_Area
Area (mV/mm2*s)
Stimulation µA
Postsyn. Sink_Layer 4_Area
Area (mV/mm2*s)
Stimulation µA
Postsyn. Source_Layer 4_Area
Area (mV/mm2*s)
Stimulation µA

FIG. 6C

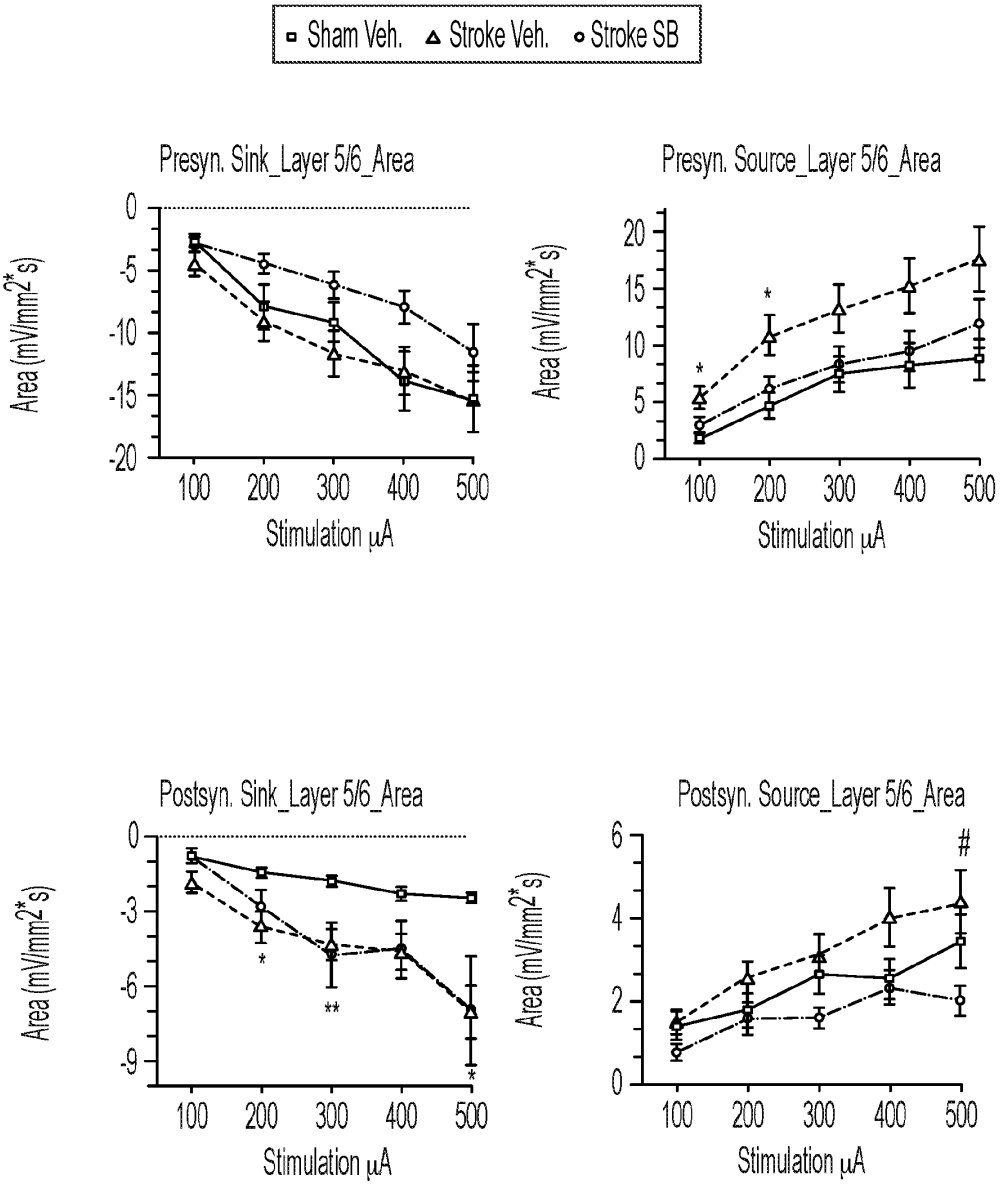

Sham Veh.
Stroke Veh.
Stroke SB
Presyn. Sink_Layer 5/6_Area
Area (mV/mm2*s)
0
-5
-10
-15
-20
100
200
300
400
500
Stimulation μA
Presyn. Source_Layer 5/6_Area
Area (mV/mm2*s)
20
15
10
5
0
*
Stimulation μA
Postsyn. Sink_Layer 5/6_Area
Area (mV/mm2*s)
0
-3
-6
-9
*
**
*
Stimulation μA
Postsyn. Source_Layer 5/6_Area
Area (mV/mm2*s)
6
4
2
0
#
Stimulation μA

FIG. 6D

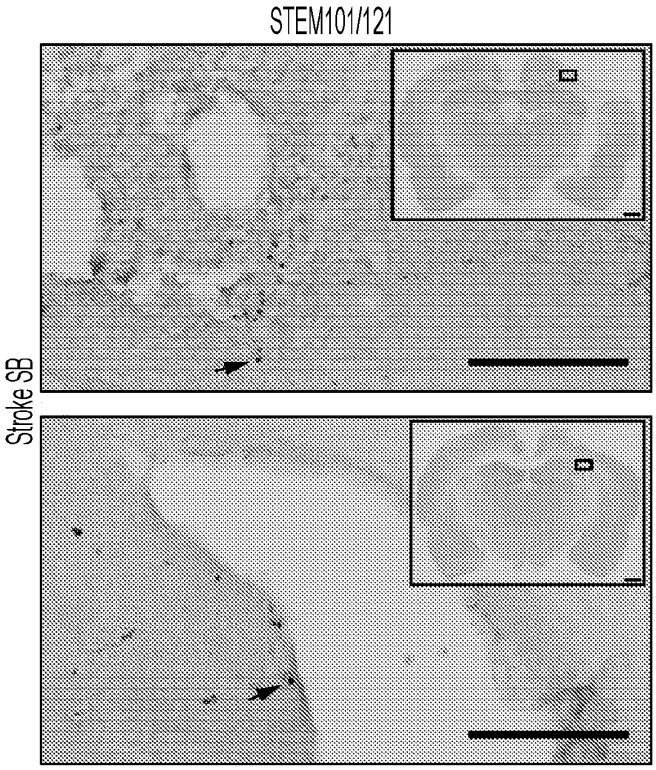


FIG. 7A

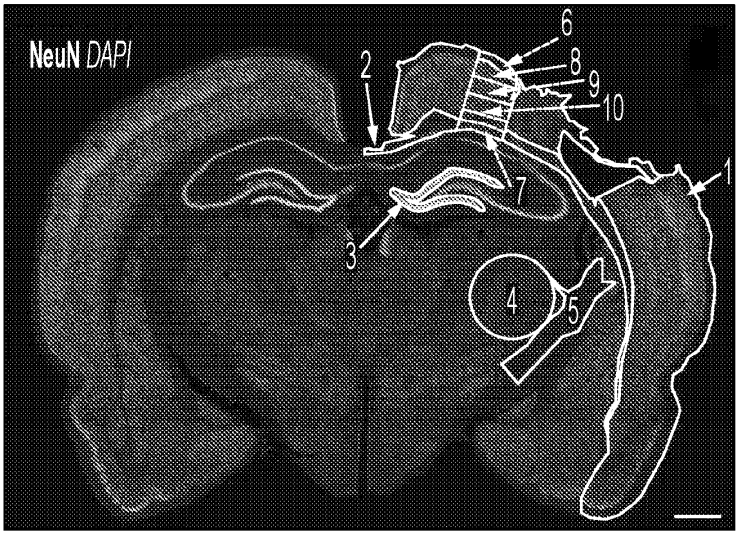


FIG. 7B

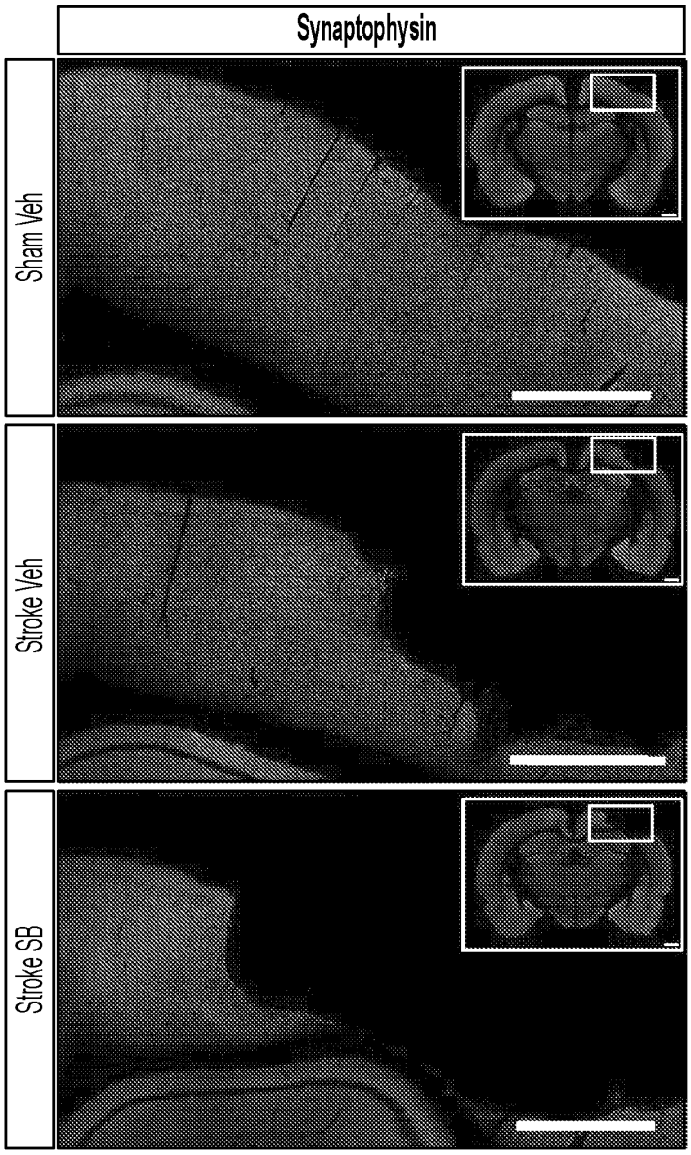


FIG. 7C

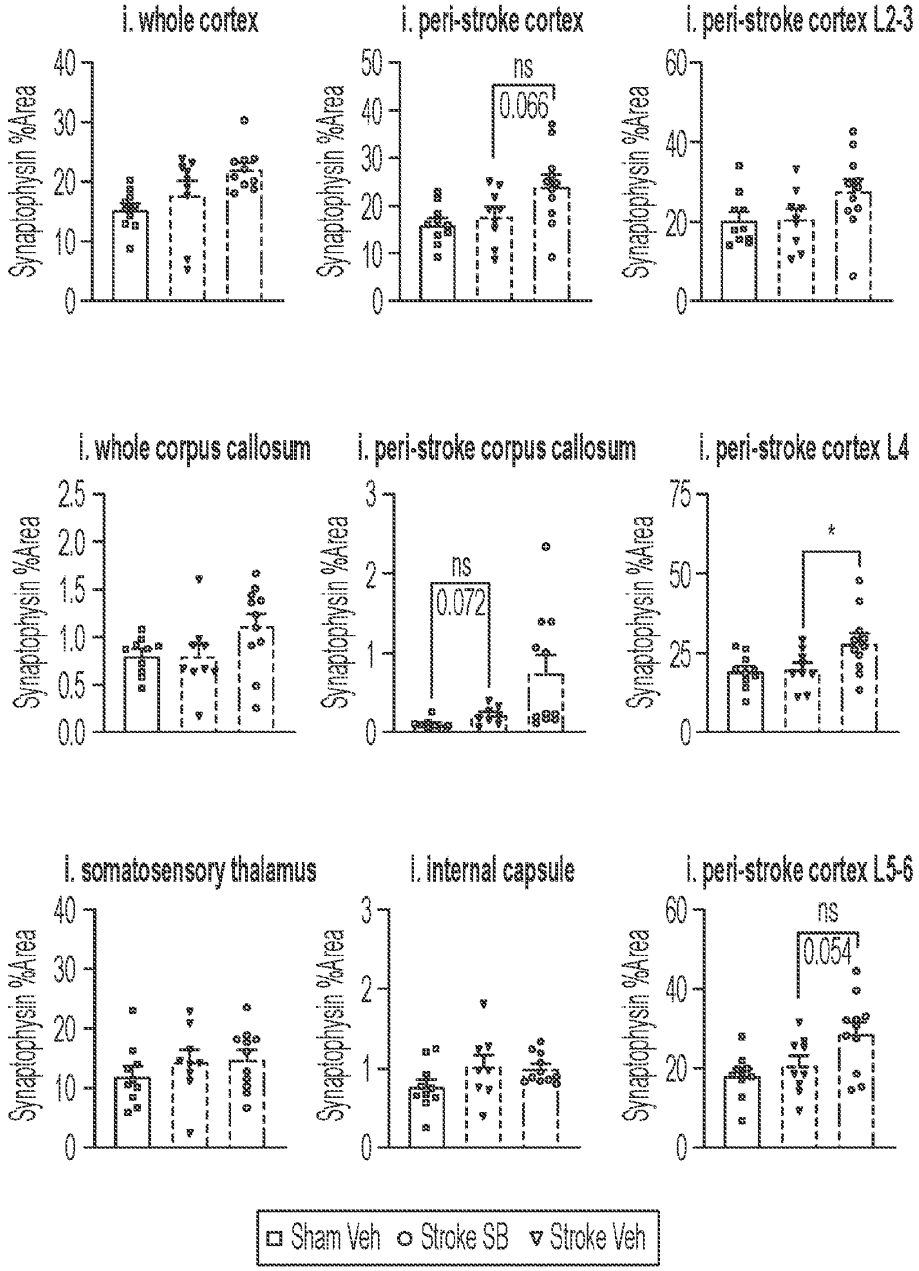

i. whole cortex
i. peri-stroke cortex
i. peri-stroke cortex L2-3
i. whole corpus callosum
i. peri-stroke corpus callosum
i. peri-stroke cortex L4
i. somatosensory thalamus
i. internal capsule
i. peri-stroke cortex L5-6
Synaptophysin %Area
ns
0.066
ns
0.072
*
ns
0.054
Sham Veh
Stroke SB
Stroke Veh

FIG. 7D

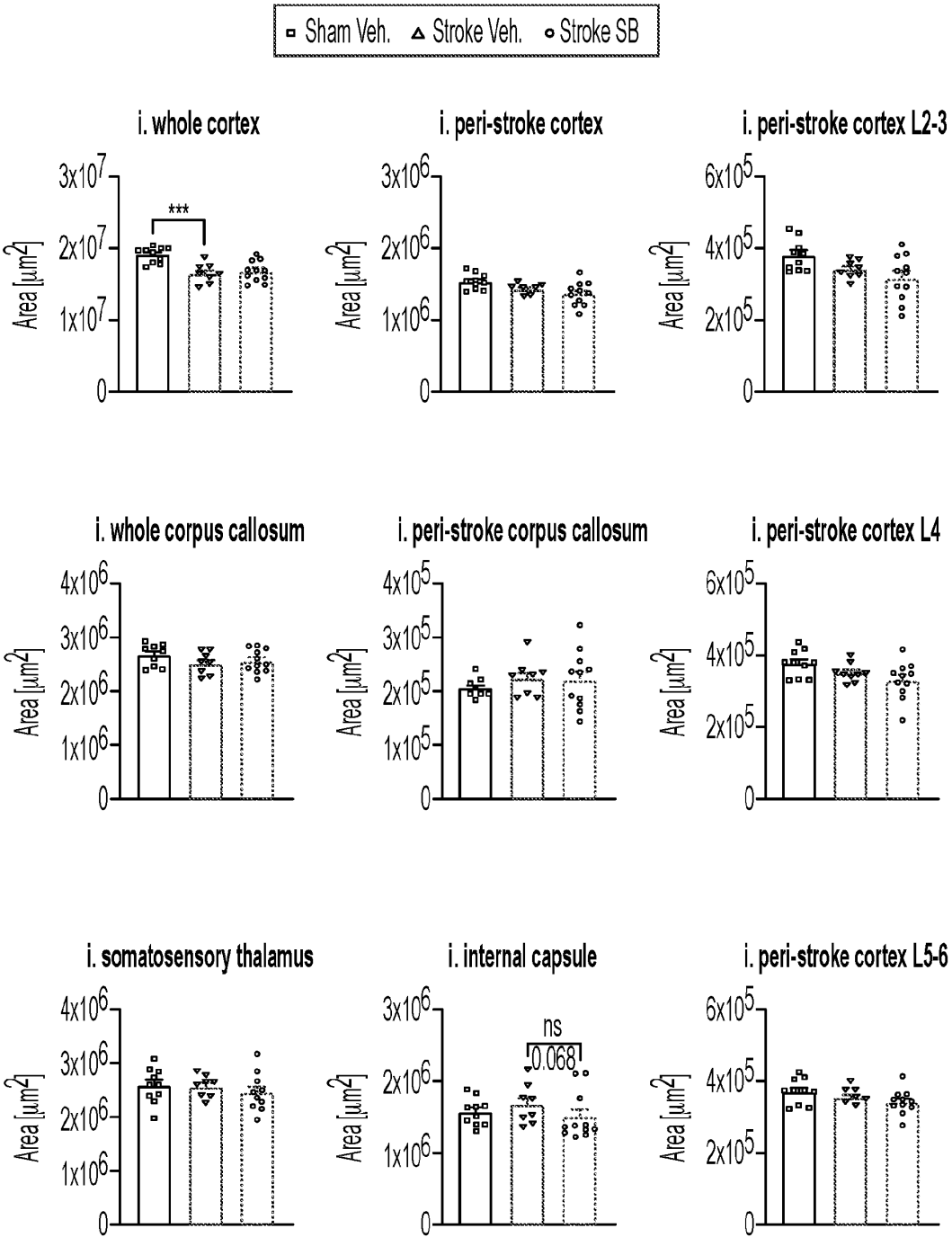

Sham Veh.
Stroke Veh.
Stroke SB
i. whole cortex
i. peri-stroke cortex
i. peri-stroke cortex L2-3
i. whole corpus callosum
i. peri-stroke corpus callosum
i. peri-stroke cortex L4
i. somatosensory thalamus
i. internal capsule
i. peri-stroke cortex L5-6
Area [µm2]
***
ns
0.068

FIG. 8A

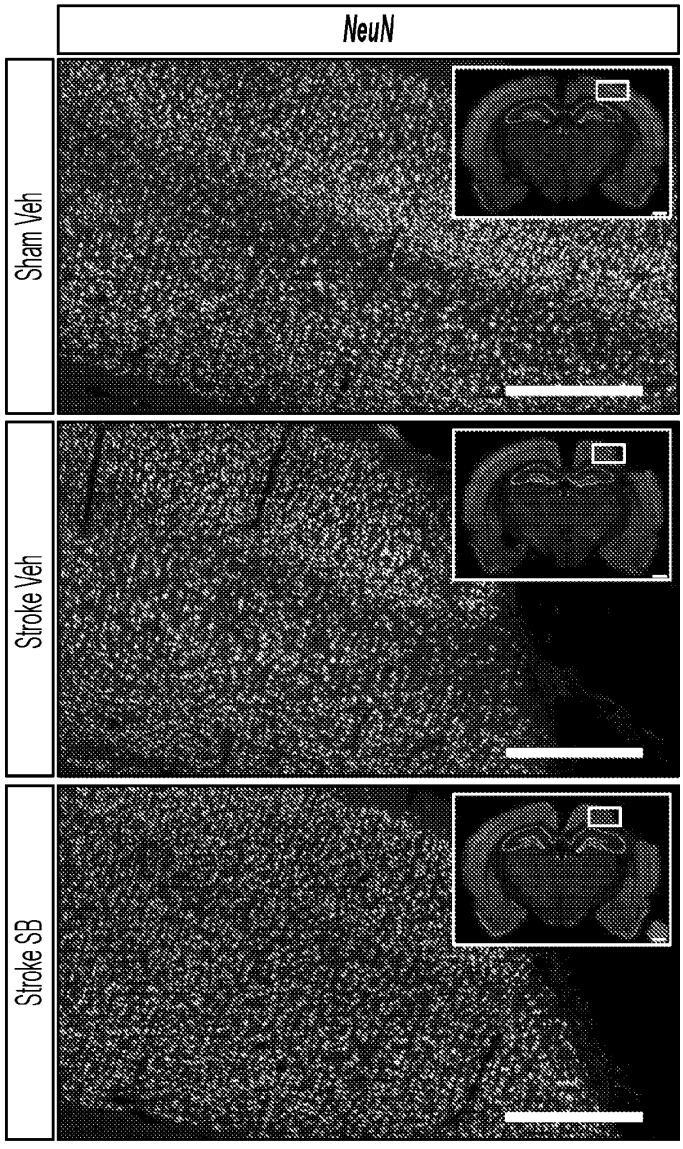


FIG. 8B

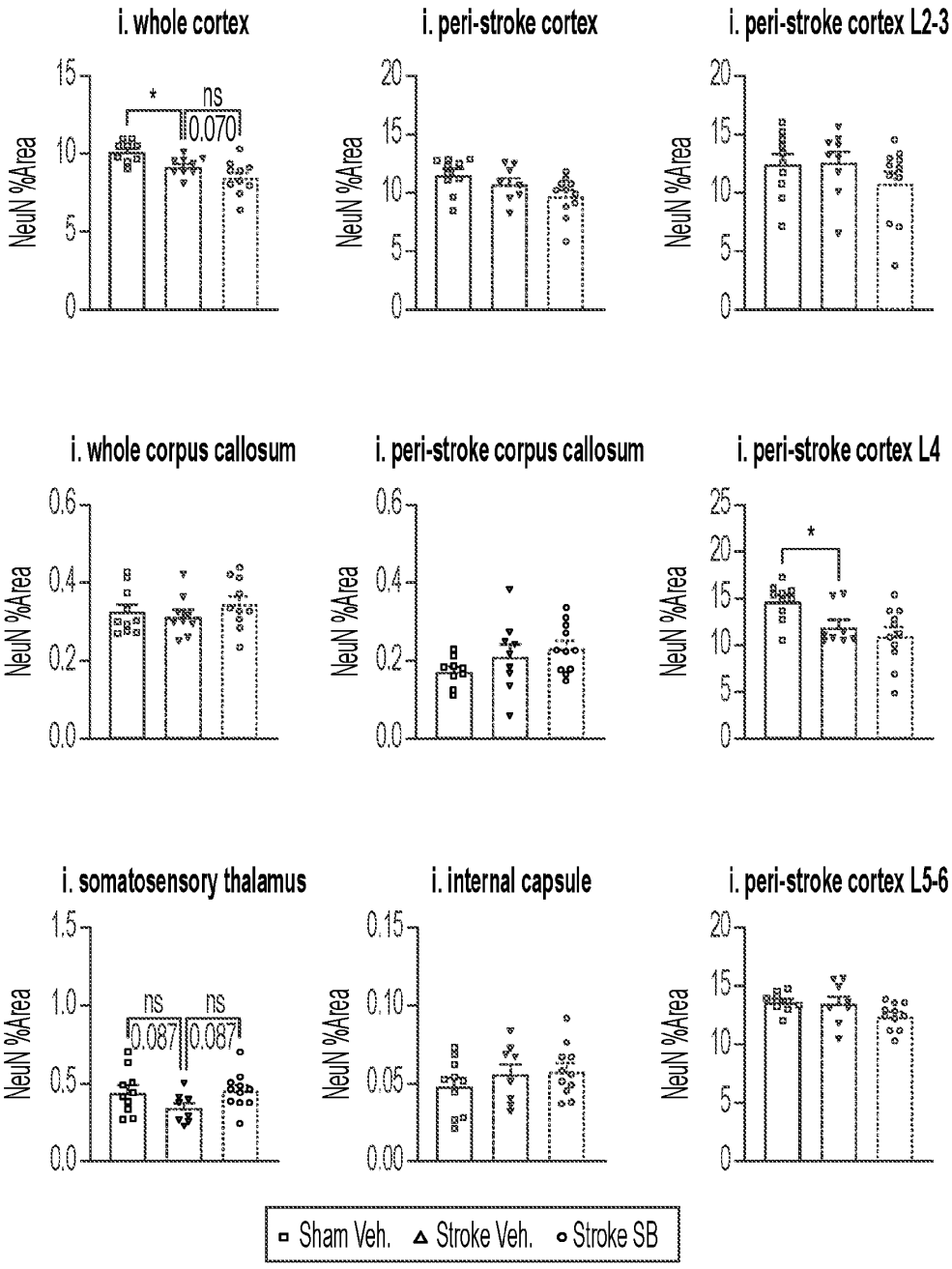

i. whole cortex
i. peri-stroke cortex
i. peri-stroke cortex L2-3
i. whole corpus callosum
i. peri-stroke corpus callosum
i. peri-stroke cortex L4
i. somatosensory thalamus
i. internal capsule
i. peri-stroke cortex L5-6
NeuN %Area
*
ns
0.070
0.087
Sham Veh.
Stroke Veh.
Stroke SB

FIG. 8C

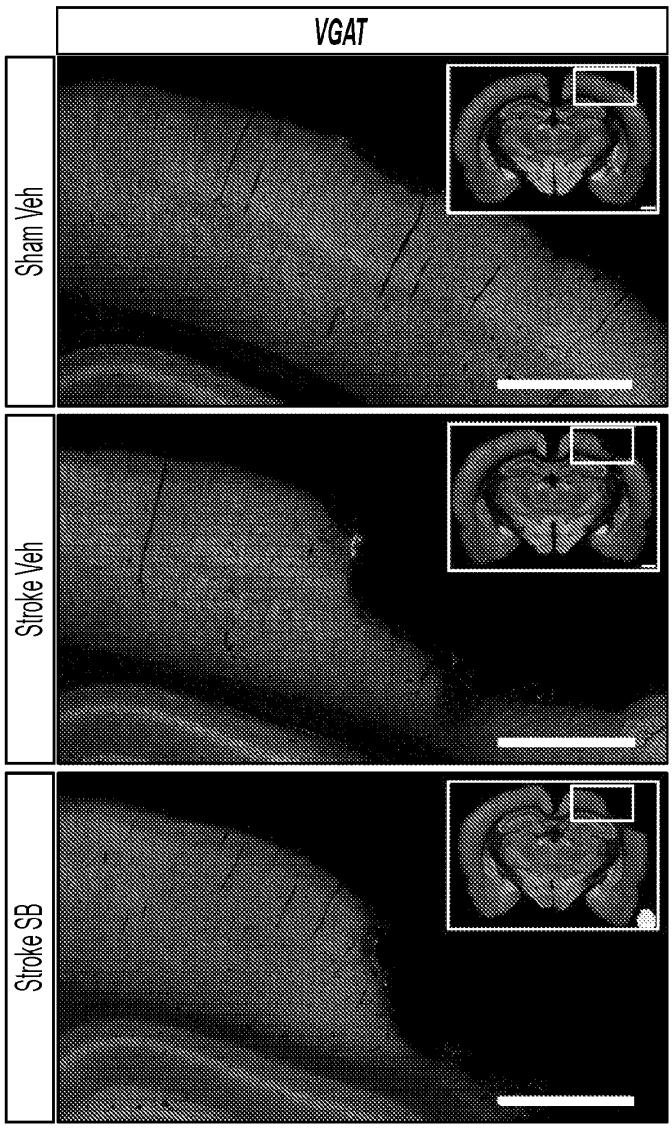


FIG. 9A

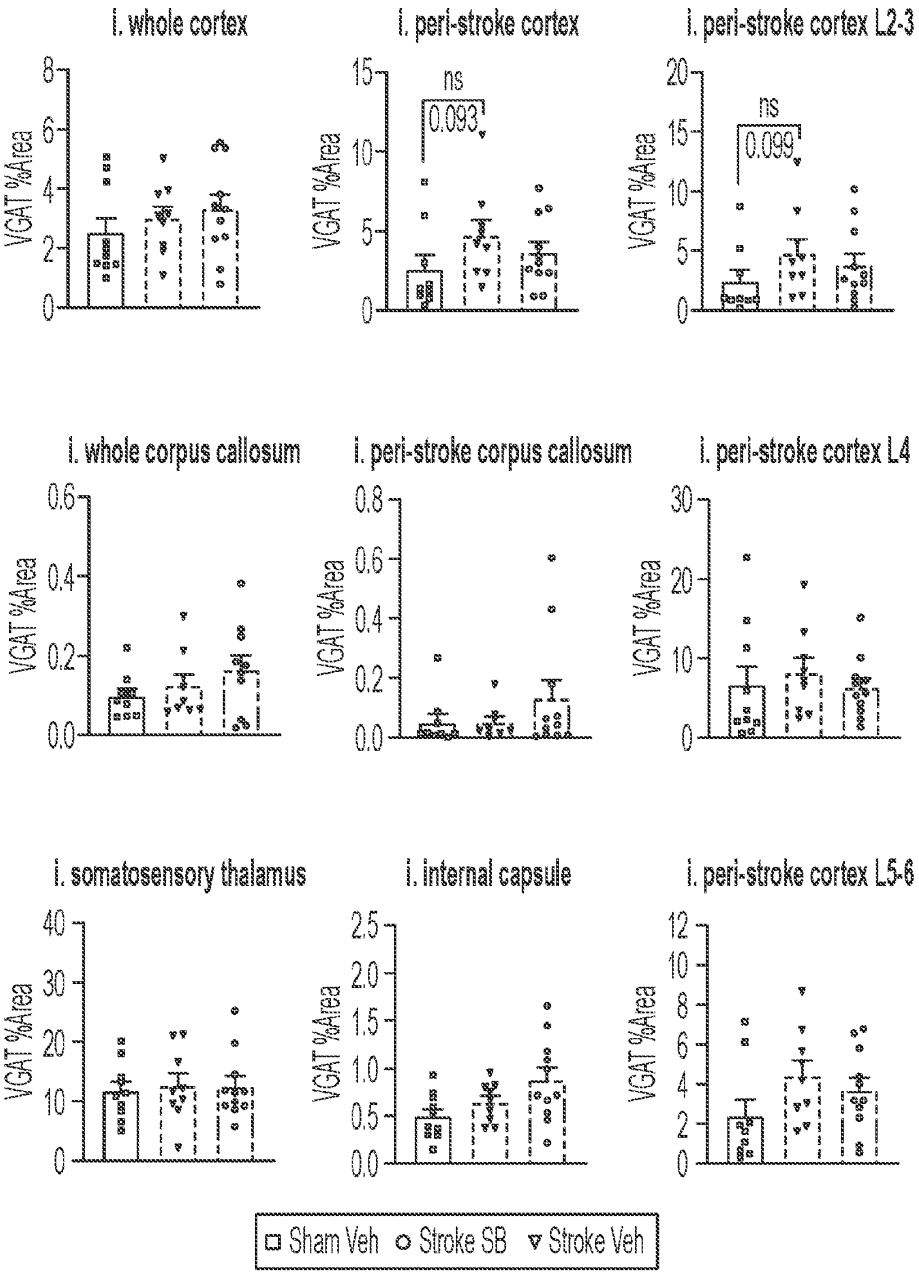

i. whole cortex
i. peri-stroke cortex
i. peri-stroke cortex L2-3
i. whole corpus callosum
i. peri-stroke corpus callosum
i. peri-stroke cortex L4
i. somatosensory thalamus
i. internal capsule
i. peri-stroke cortex L5-6
VGAT %Area
ns
0.093
0.099
Sham Veh
Stroke SB
Stroke Veh

FIG. 9B

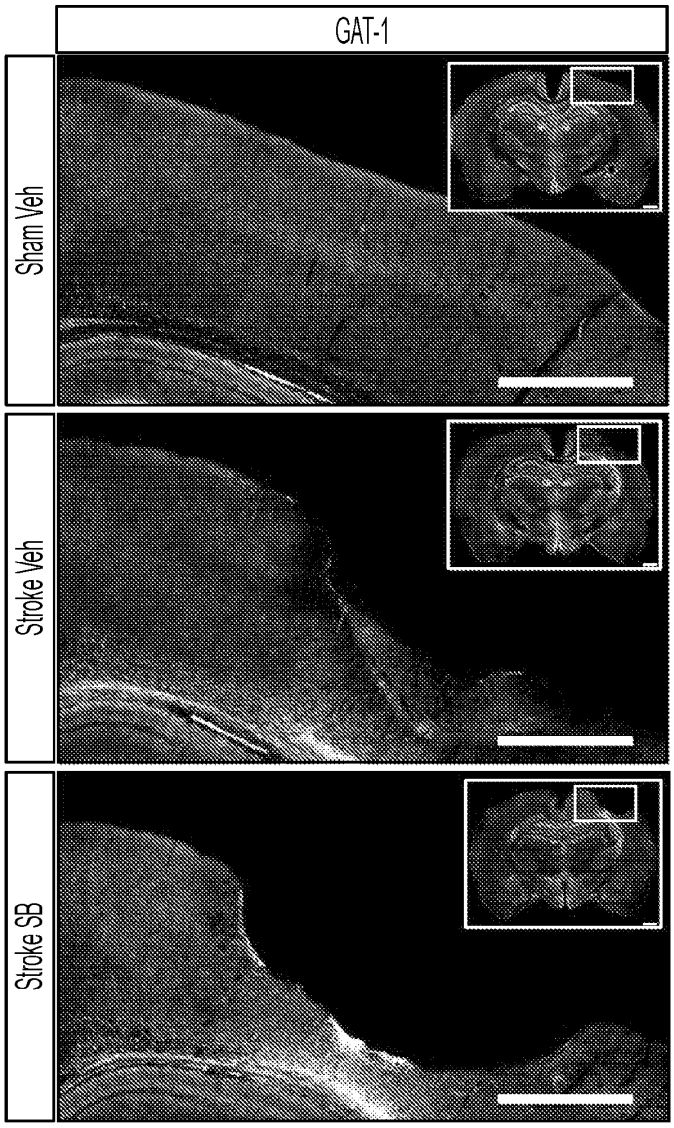


FIG. 9C

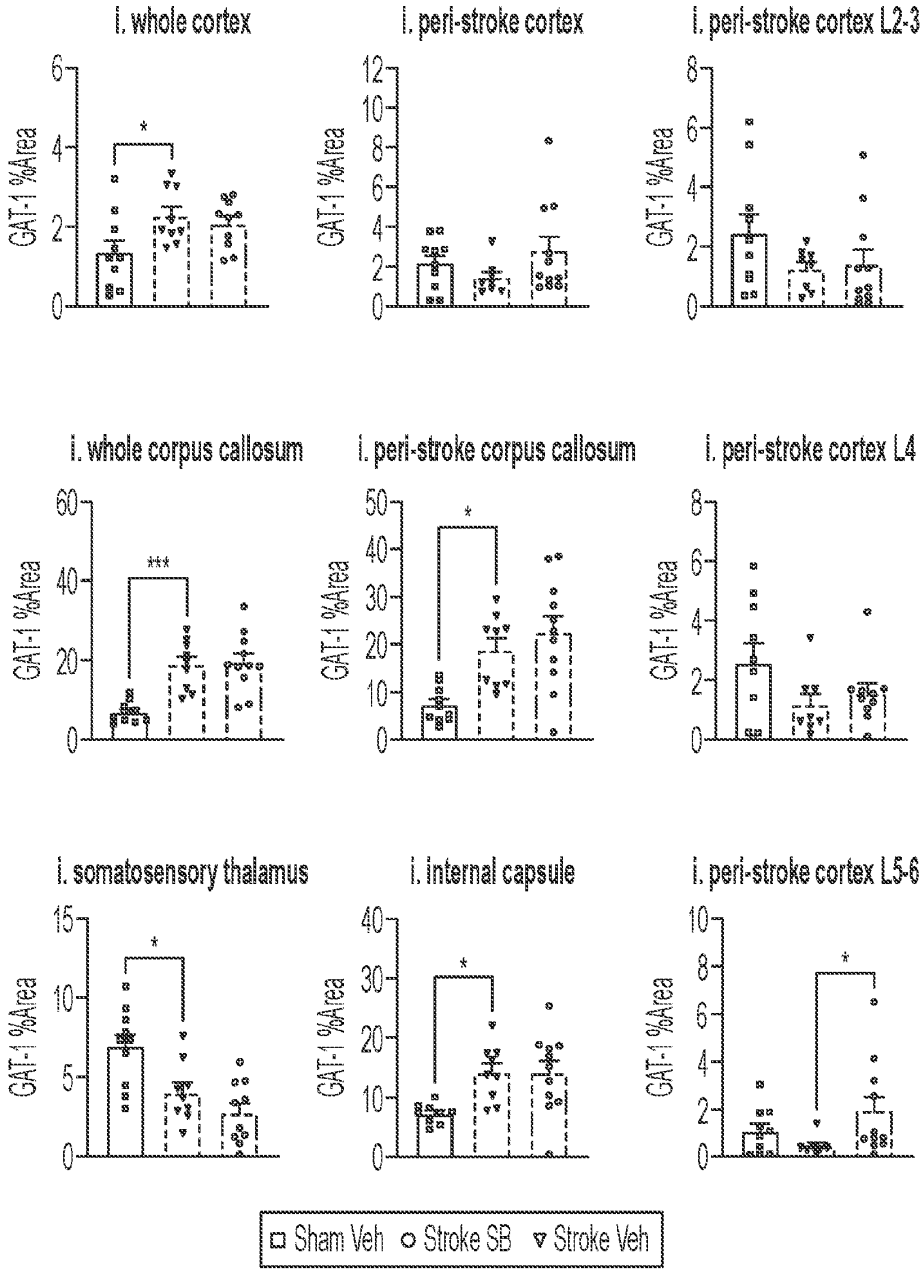

i. whole cortex
i. peri-stroke cortex
i. peri-stroke cortex L2-3
i. whole corpus callosum
i. peri-stroke corpus callosum
i. peri-stroke cortex L4
i. somatosensory thalamus
i. internal capsule
i. peri-stroke cortex L5-6
GAT-1 %Area
Sham Veh
Stroke SB
Stroke Veh

FIG. 9D

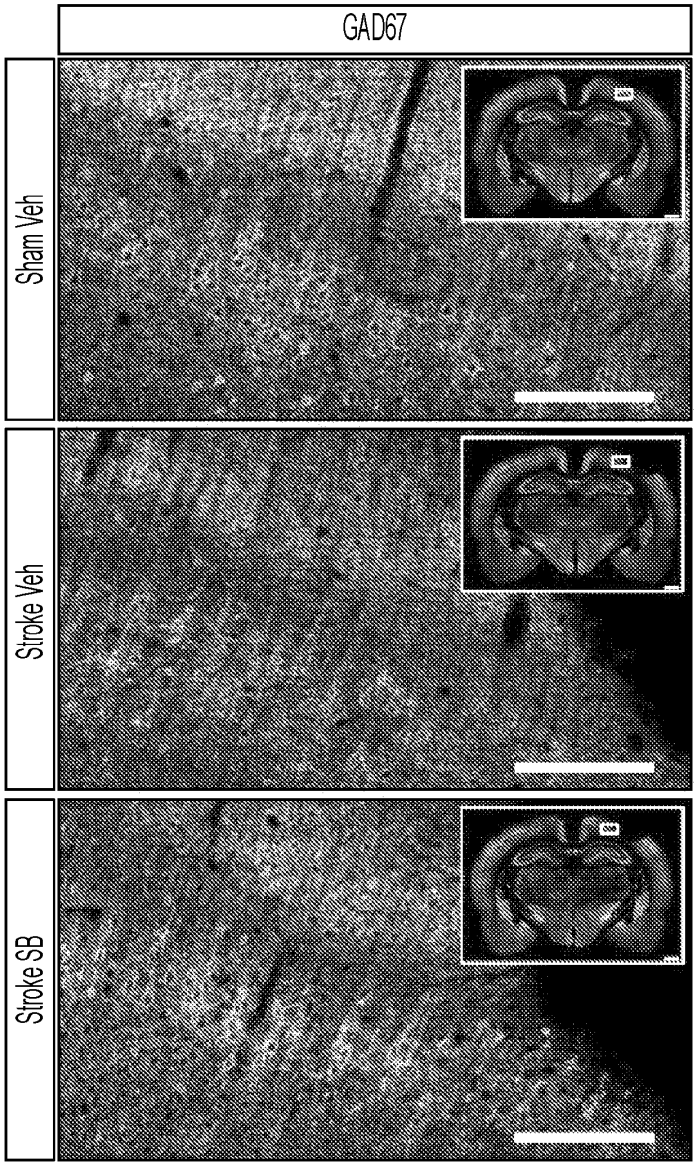


FIG. 10A

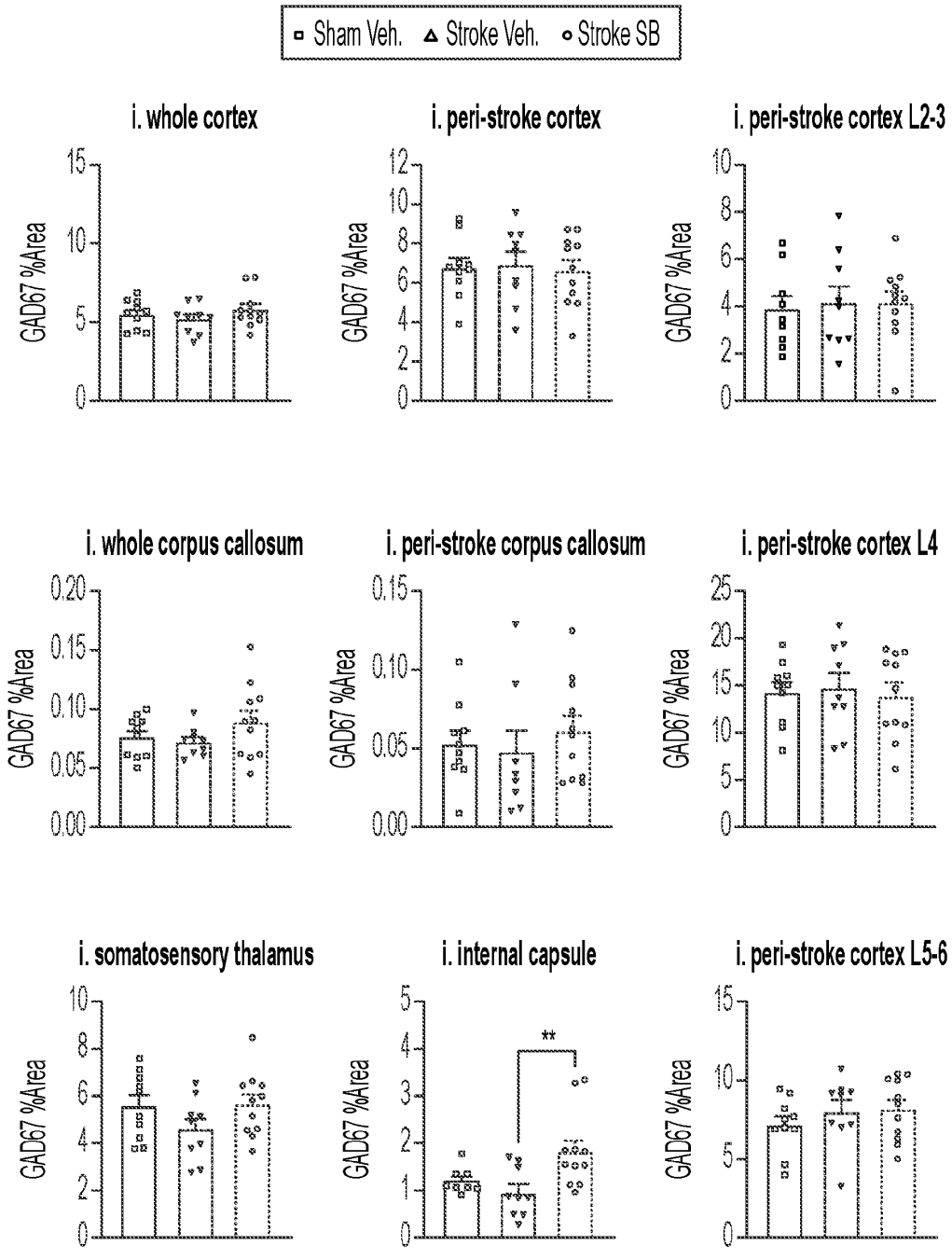

Sham Veh.
Stroke Veh.
Stroke SB
i. whole cortex
i. peri-stroke cortex
i. peri-stroke cortex L2-3
i. whole corpus callosum
i. peri-stroke corpus callosum
i. peri-stroke cortex L4
i. somatosensory thalamus
i. internal capsule
i. peri-stroke cortex L5-6
GAD67 %Area
**

FIG. 10B

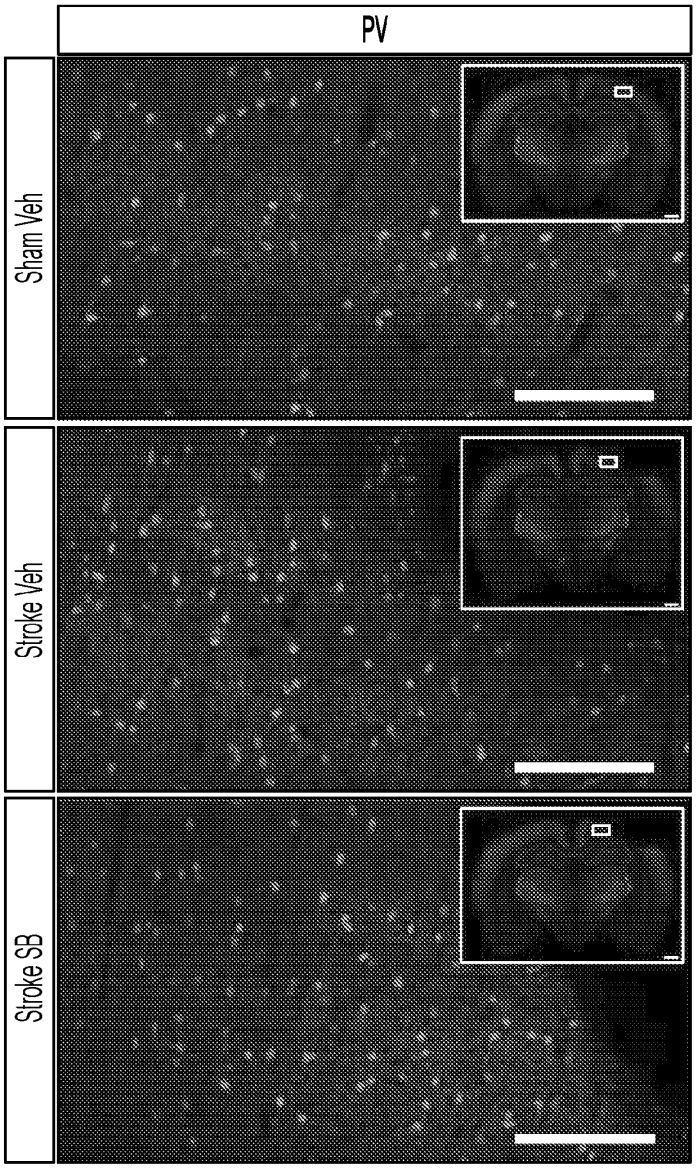


FIG. 10C

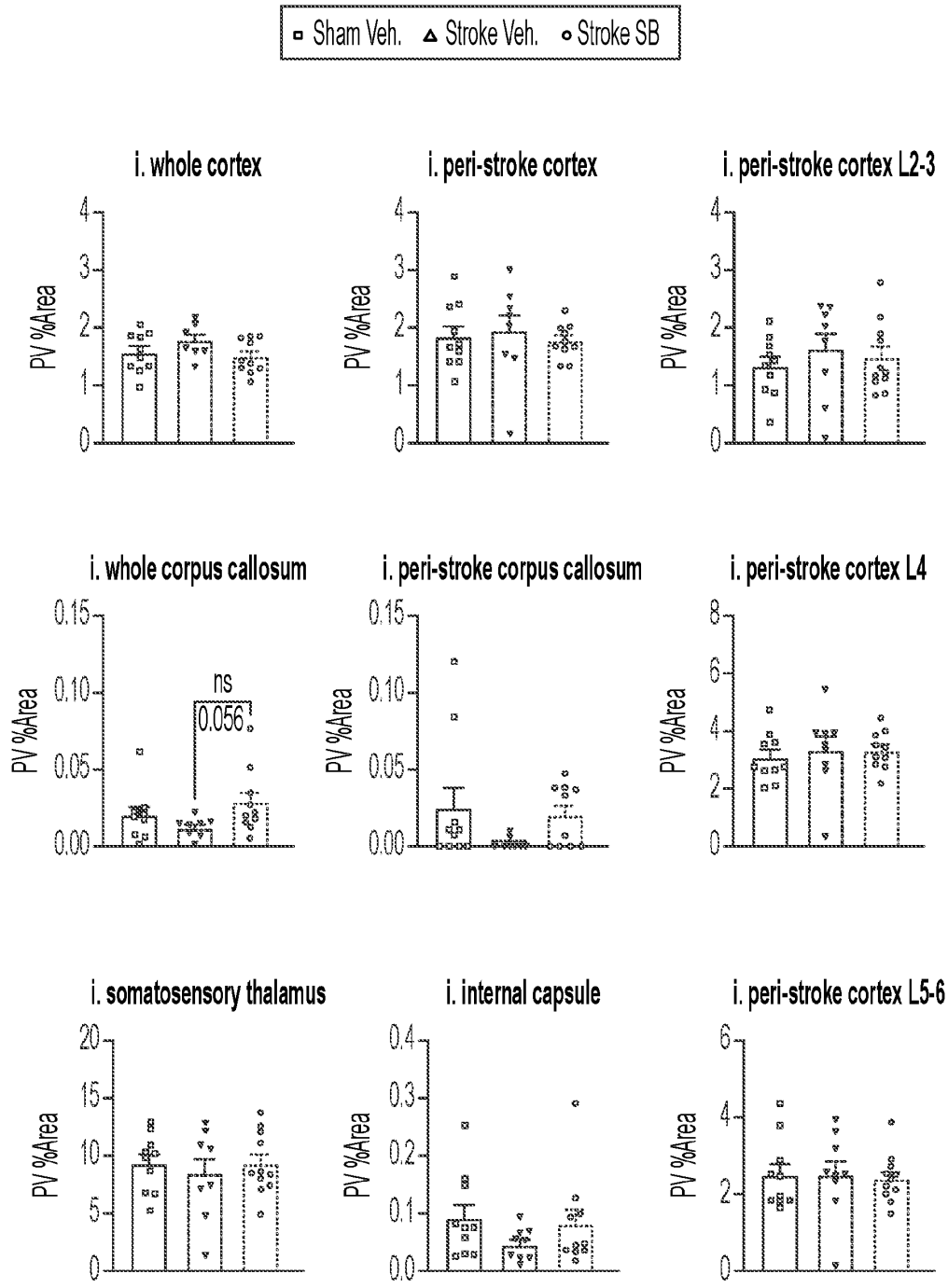

Sham Veh.
Stroke Veh.
Stroke SB
i. whole cortex
i. peri-stroke cortex
i. peri-stroke cortex L2-3
i. whole corpus callosum
i. peri-stroke corpus callosum
i. peri-stroke cortex L4
i. somatosensory thalamus
i. internal capsule
i. peri-stroke cortex L5-6
PV %Area
ns
0.056

FIG. 10D

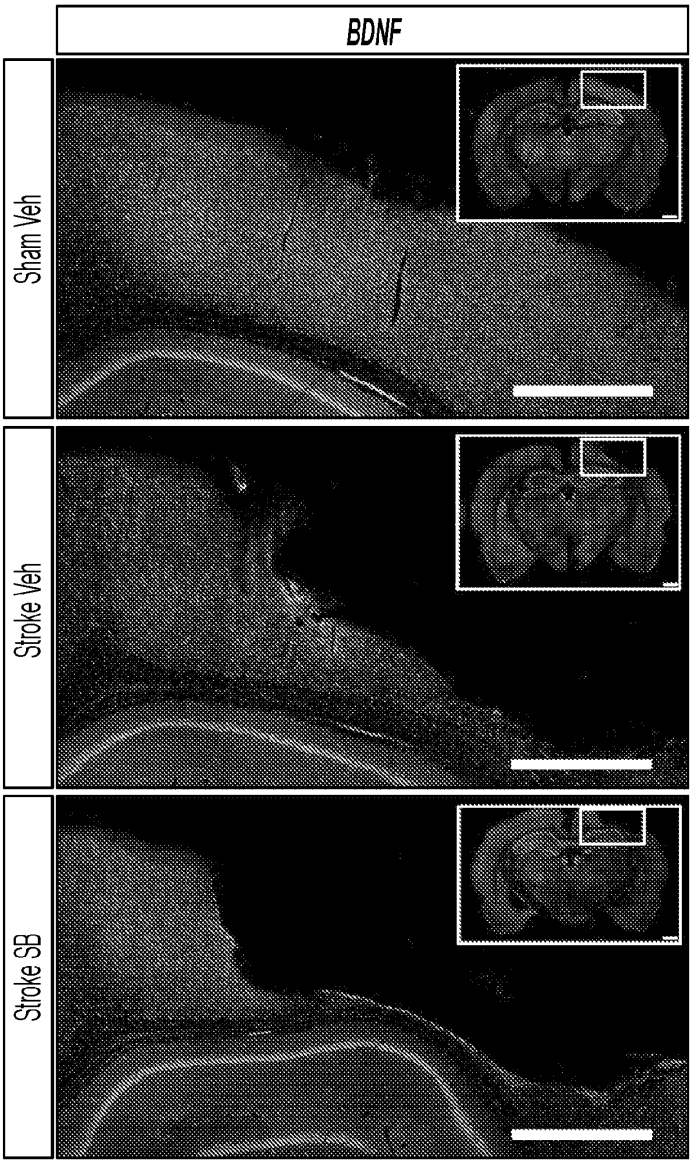


FIG. 11A

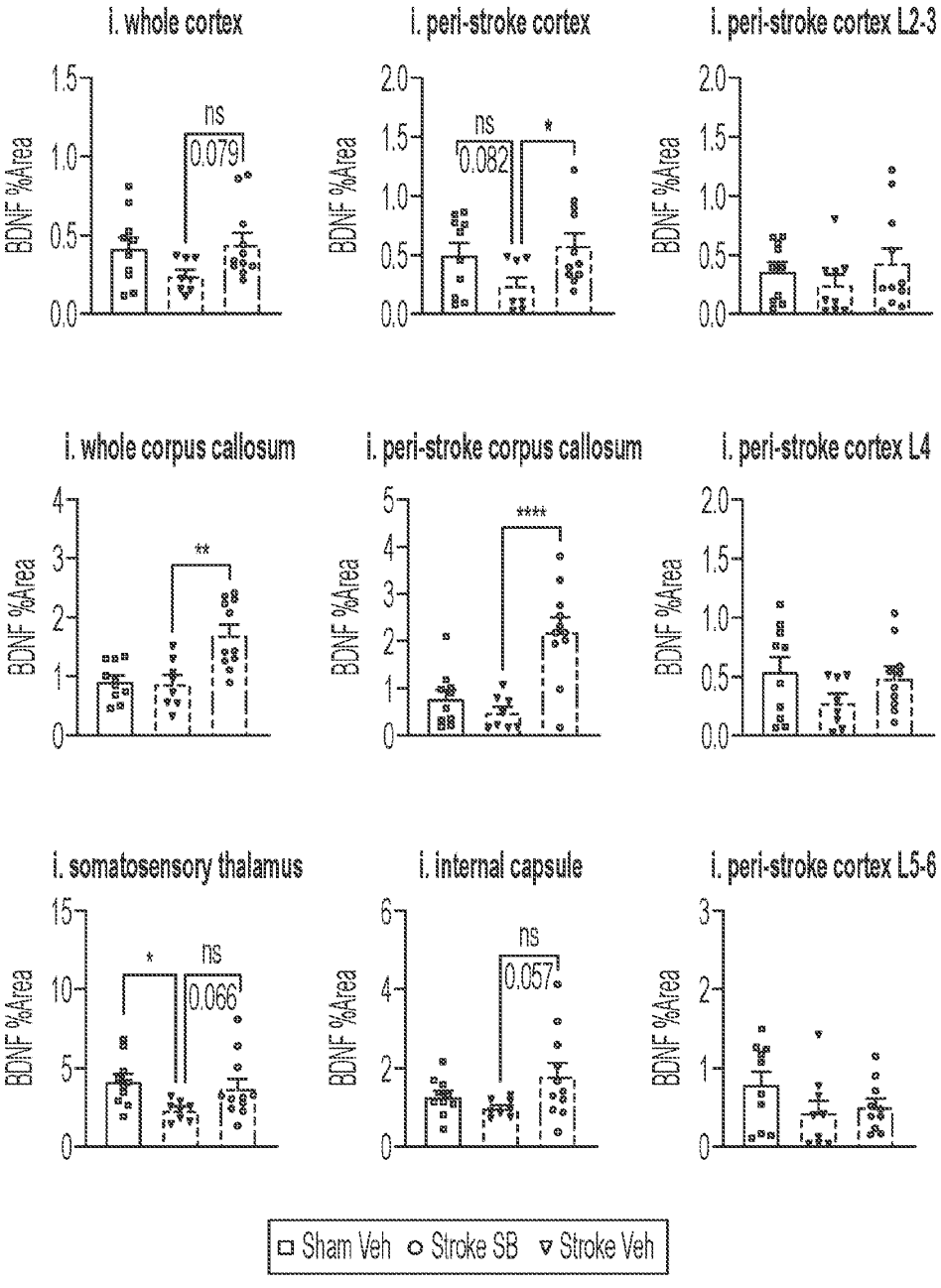

i. whole cortex
i. peri-stroke cortex
i. peri-stroke cortex L2-3
i. whole corpus callosum
i. peri-stroke corpus callosum
i. peri-stroke cortex L4
i. somatosensory thalamus
i. internal capsule
i. peri-stroke cortex L5-6
BDNF %Area
ns
0.079
0.082
0.066
0.057
*
**
****
Sham Veh
Stroke SB
Stroke Veh

FIG. 11B

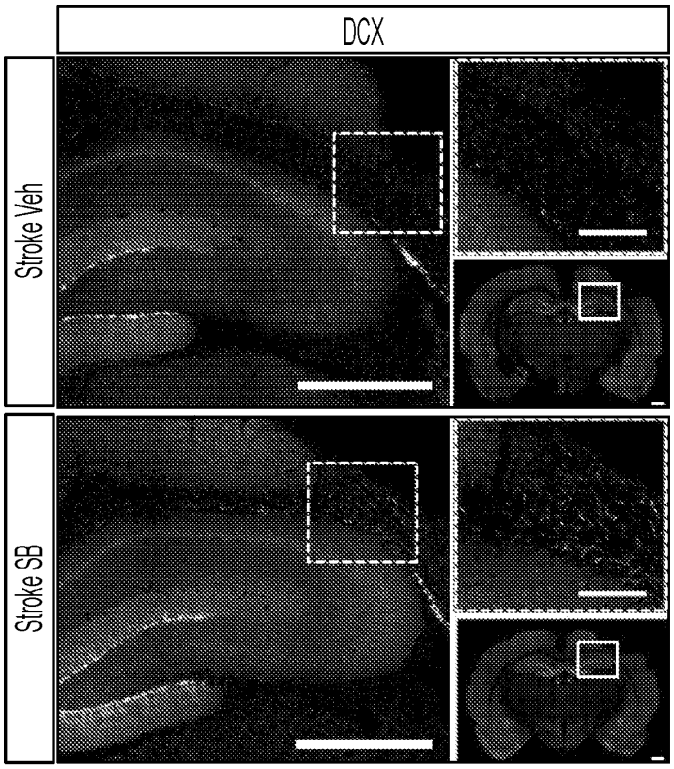


FIG. 11C

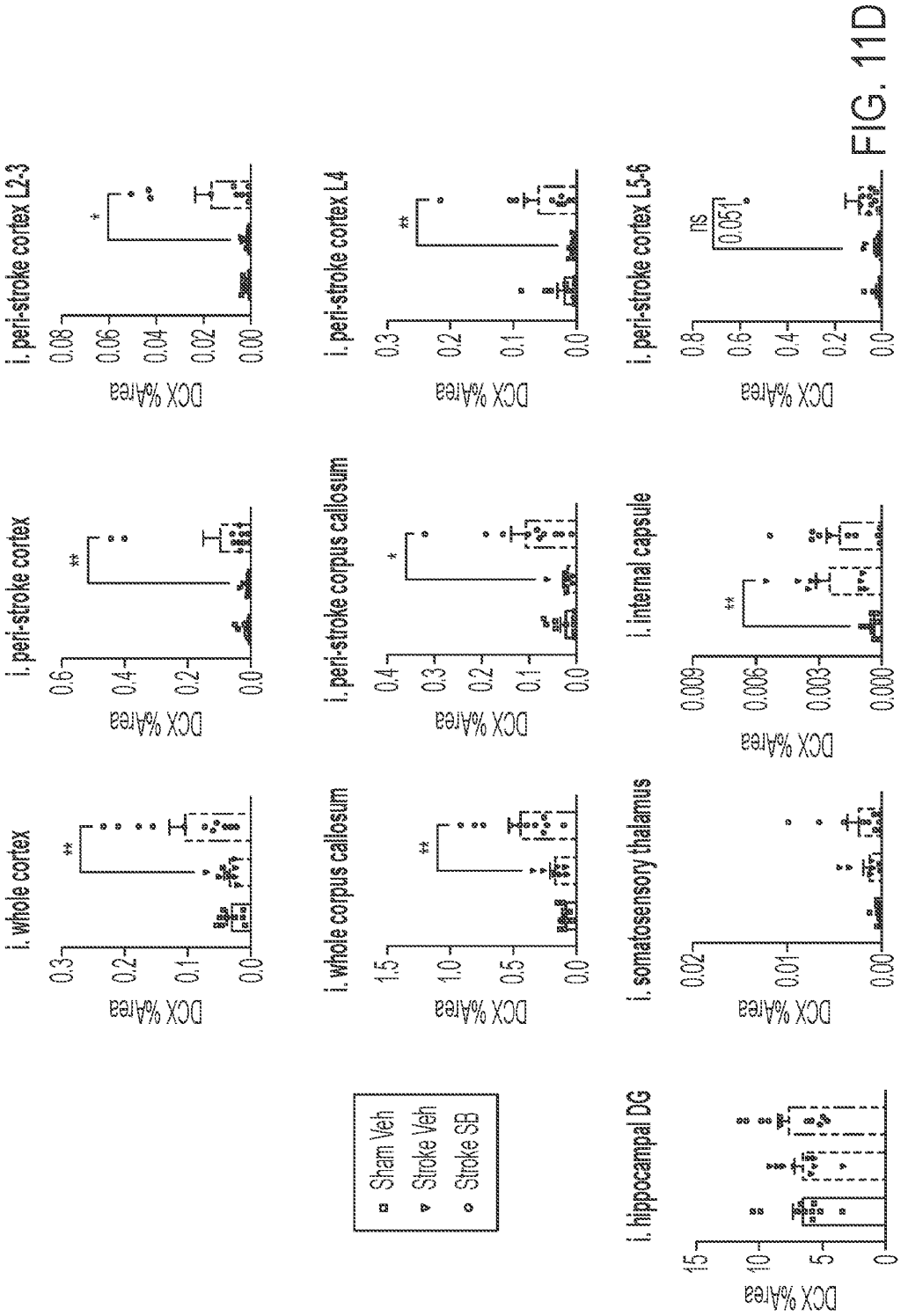

i. whole cortex
i. peri-stroke cortex
i. peri-stroke cortex L2-3
i. whole corpus callosum
i. peri-stroke corpus callosum
i. peri-stroke cortex L4
i. somatosensory thalamus
i. internal capsule
i. peri-stroke cortex L5-6
i. hippocampal DG
DCX %Area
Sham Veh
Stroke Veh
Stroke SB
NS
0.051

FIG. 11D

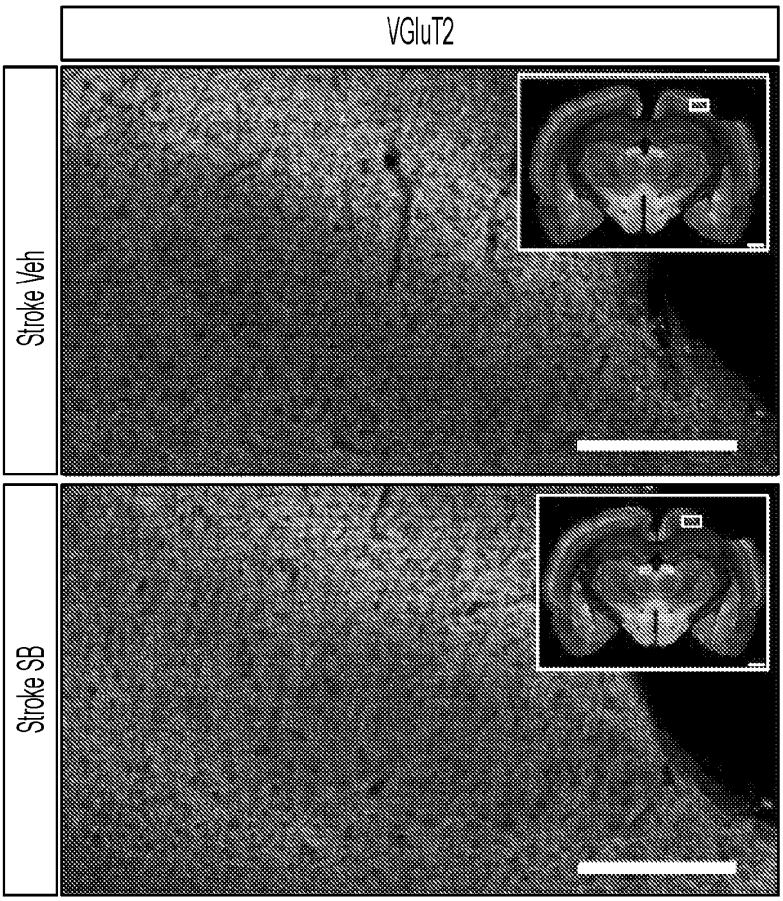


FIG. 12A

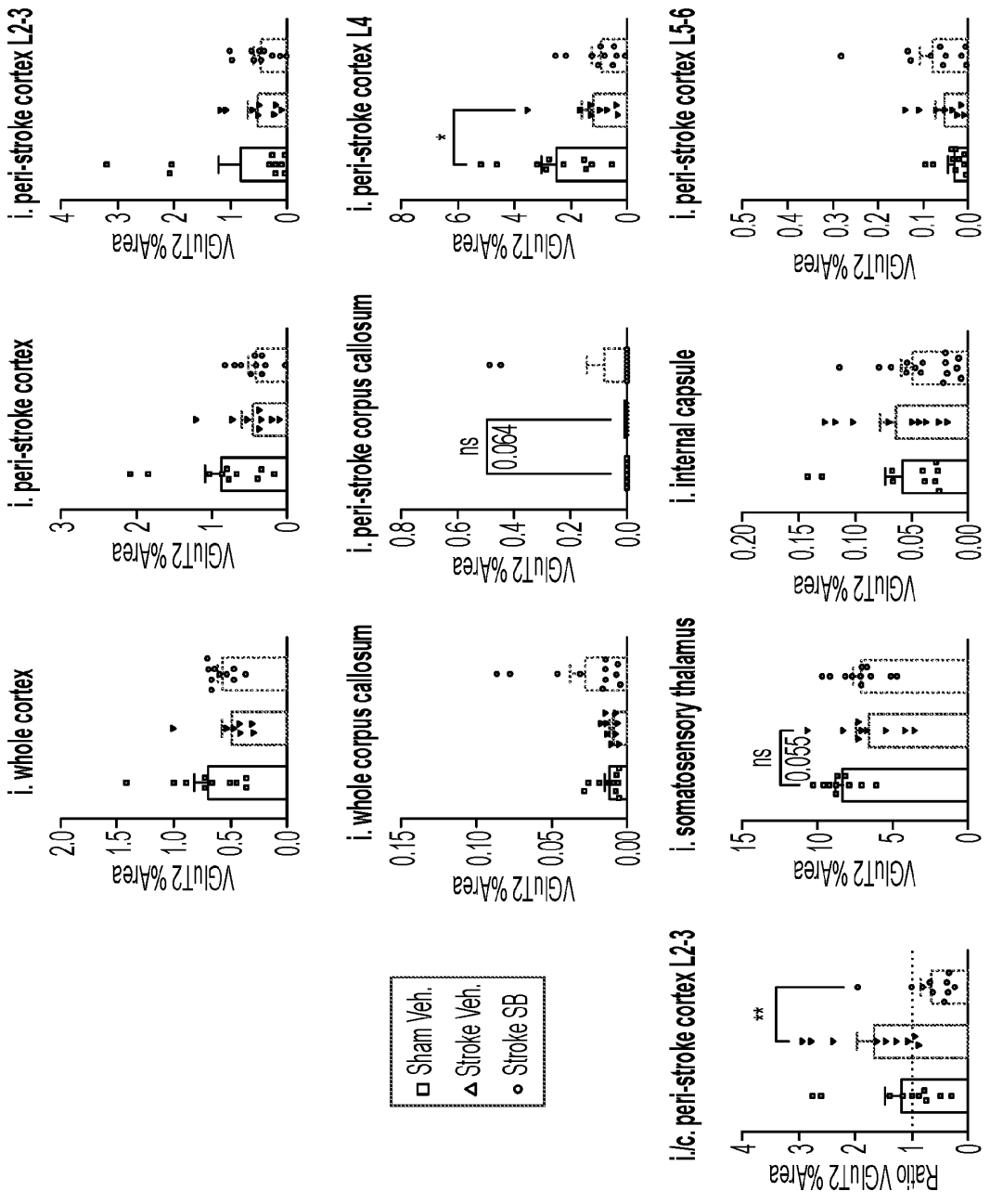

i. whole cortex
i. peri-stroke cortex
i. peri-stroke cortex L2-3
i. whole corpus callosum
i. peri-stroke corpus callosum
i. peri-stroke cortex L4
i. somatosensory thalamus
i. internal capsule
i. peri-stroke cortex L5-6
i./c. peri-stroke cortex L2-3
VGluT2 %Area
Ratio VGluT2 %Area
ns
0.064
0.055
**
*
Sham Veh.
Stroke Veh.
Stroke SB

FIG. 12B

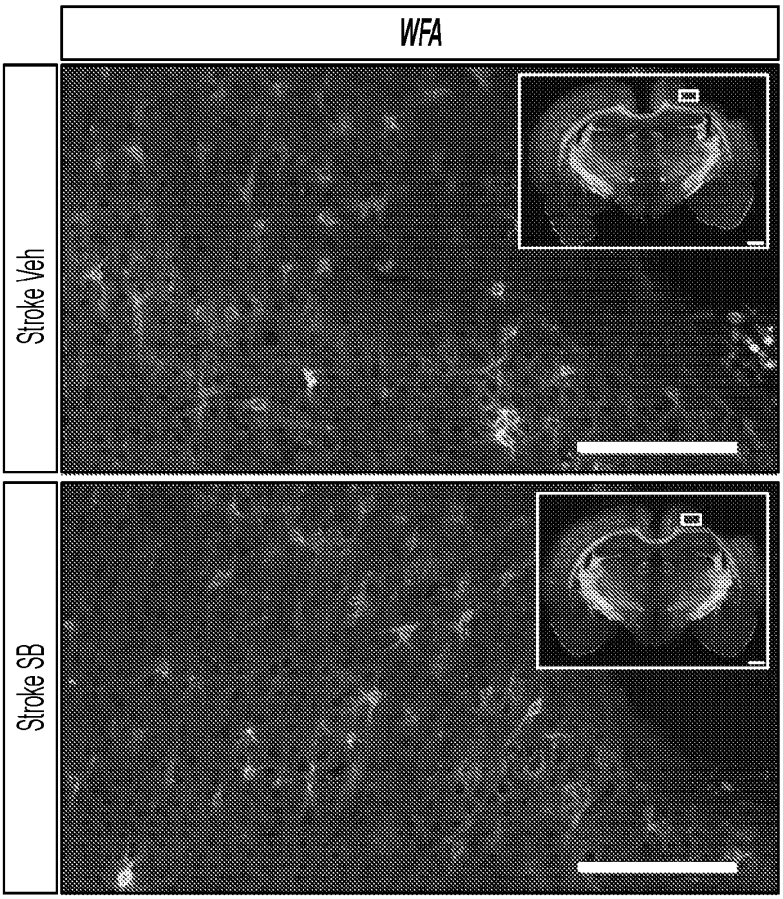


FIG. 12C

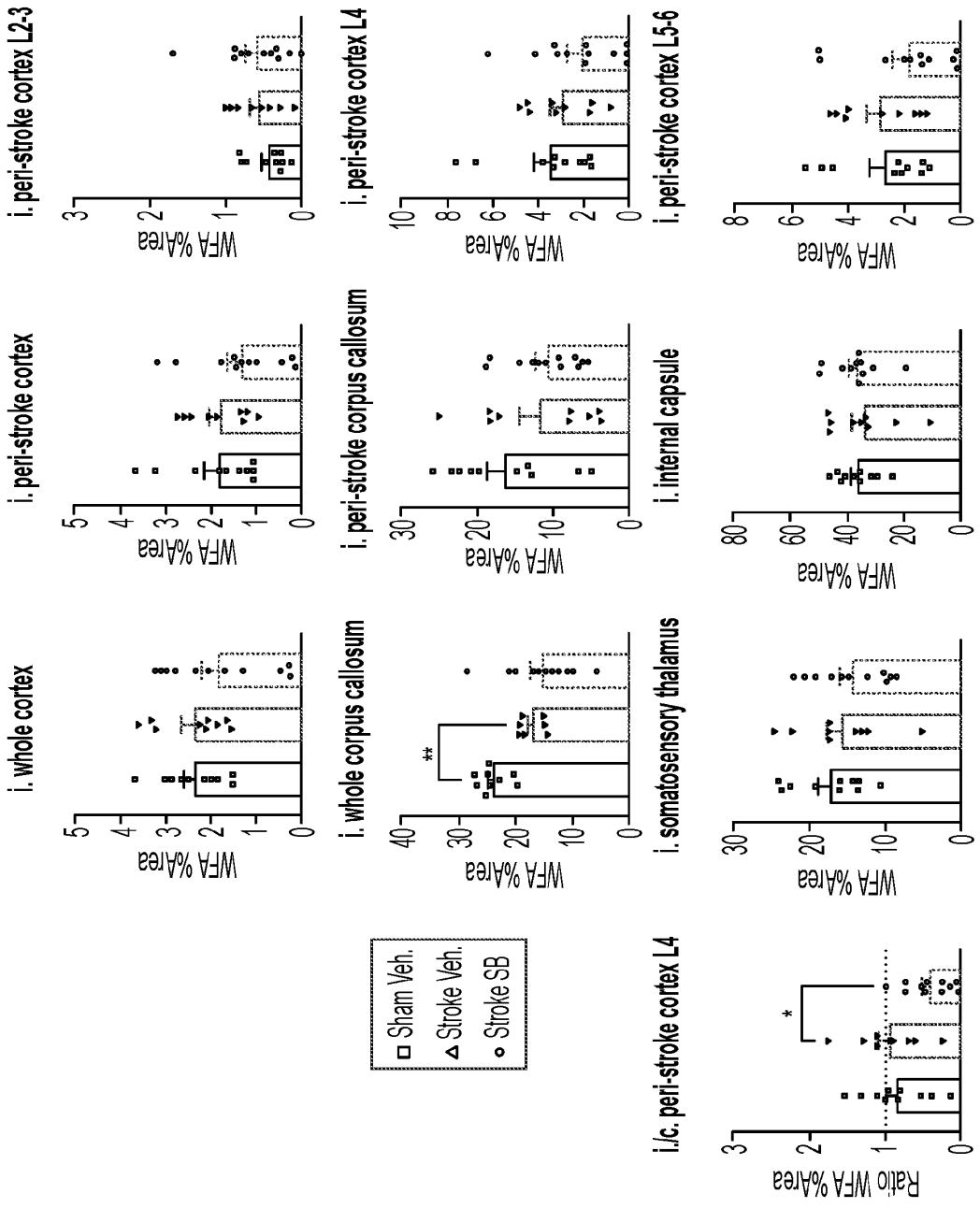

i. whole cortex
i. peri-stroke cortex
i. peri-stroke cortex L2-3
i. whole corpus callosum
i. peri-stroke corpus callosum
i. peri-stroke cortex L4
i. somatosensory thalamus
i. internal capsule
i. peri-stroke cortex L5-6
i./c. peri-stroke cortex L4
WFA %Area
Ratio WFA %Area
Sham Veh.
Stroke Veh.
Stroke SB
*
**

FIG. 12D

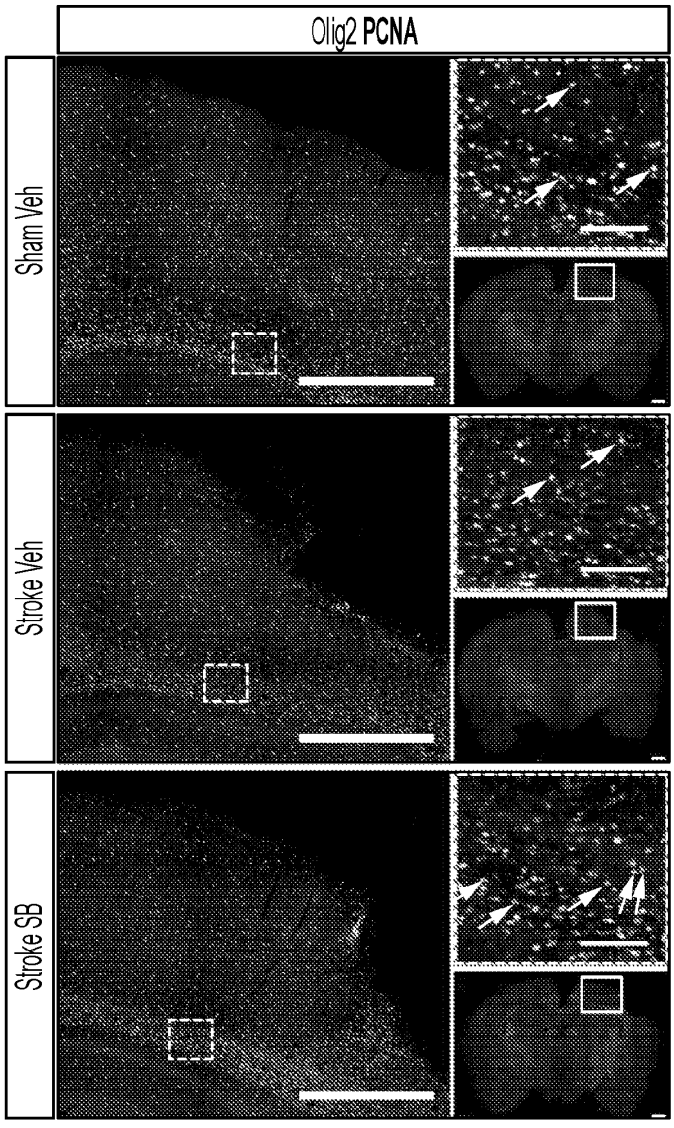


FIG. 13A

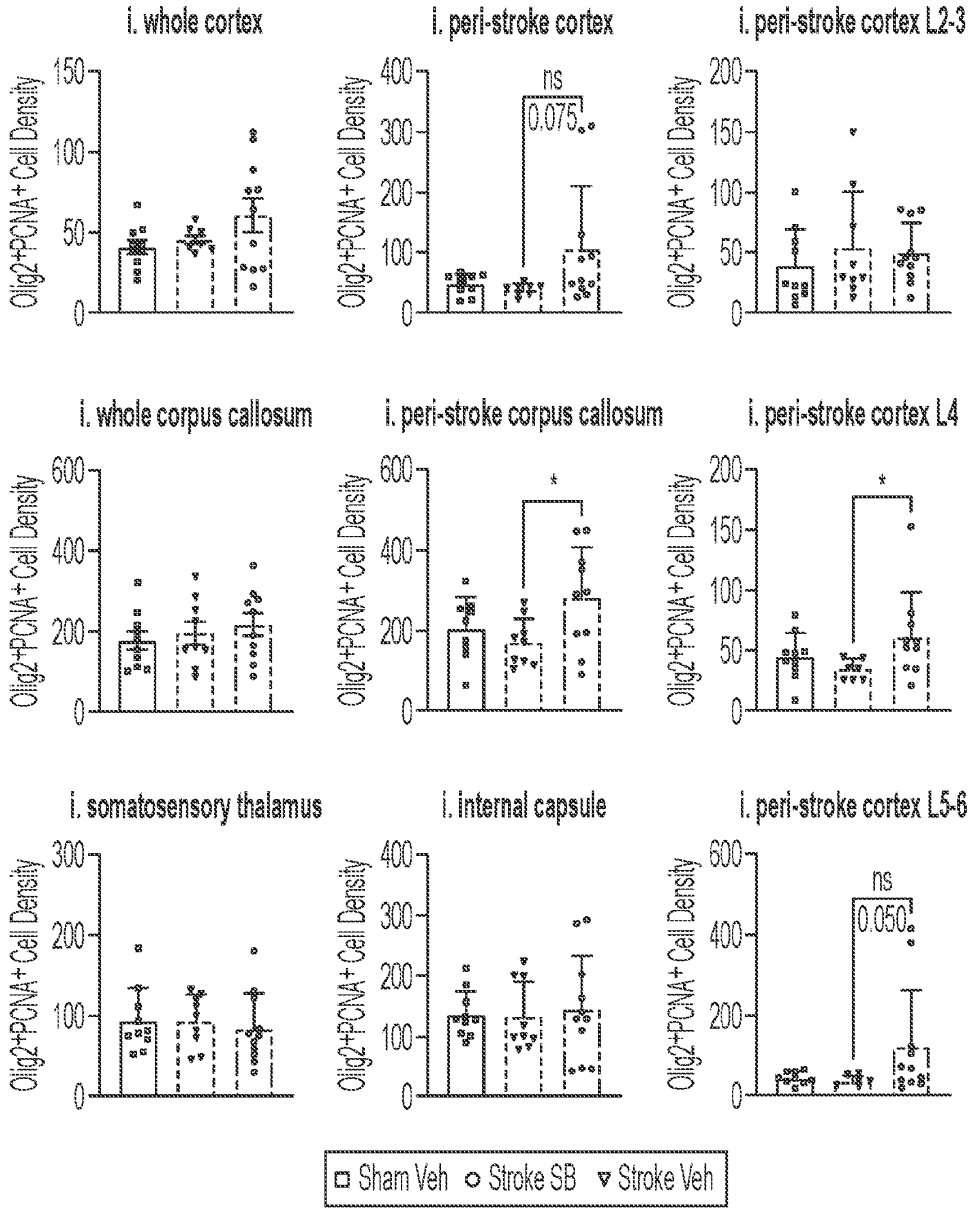

i. whole cortex
i. peri-stroke cortex
i. peri-stroke cortex L2-3
i. whole corpus callosum
i. peri-stroke corpus callosum
i. peri-stroke cortex L4
i. somatosensory thalamus
i. internal capsule
i. peri-stroke cortex L5-6
Olig2+PCNA+ Cell Density
ns
0.075
*
ns
0.050
Sham Veh
Stroke SB
Stroke Veh

FIG. 13B

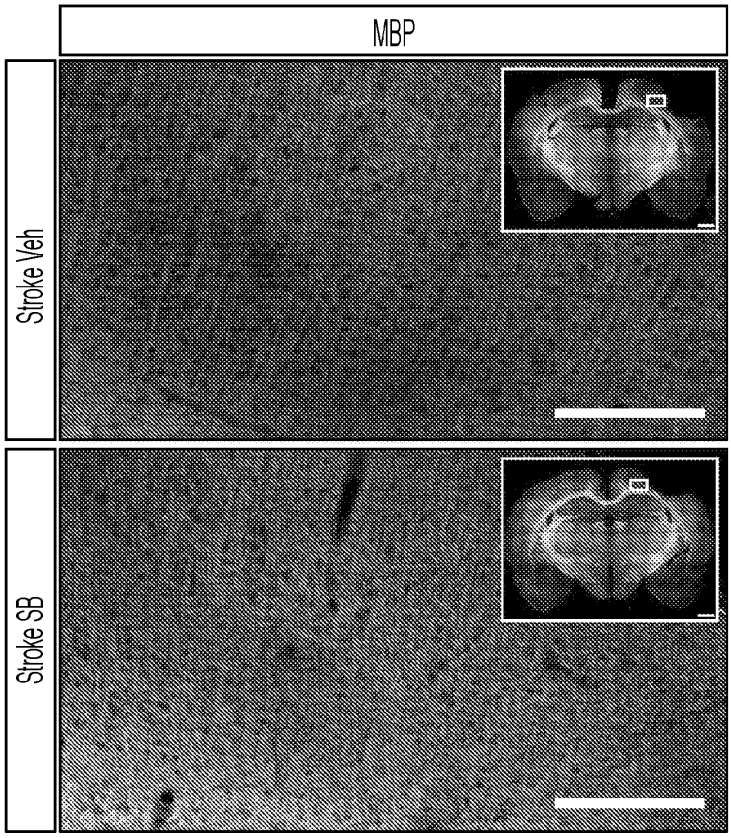


FIG. 13C

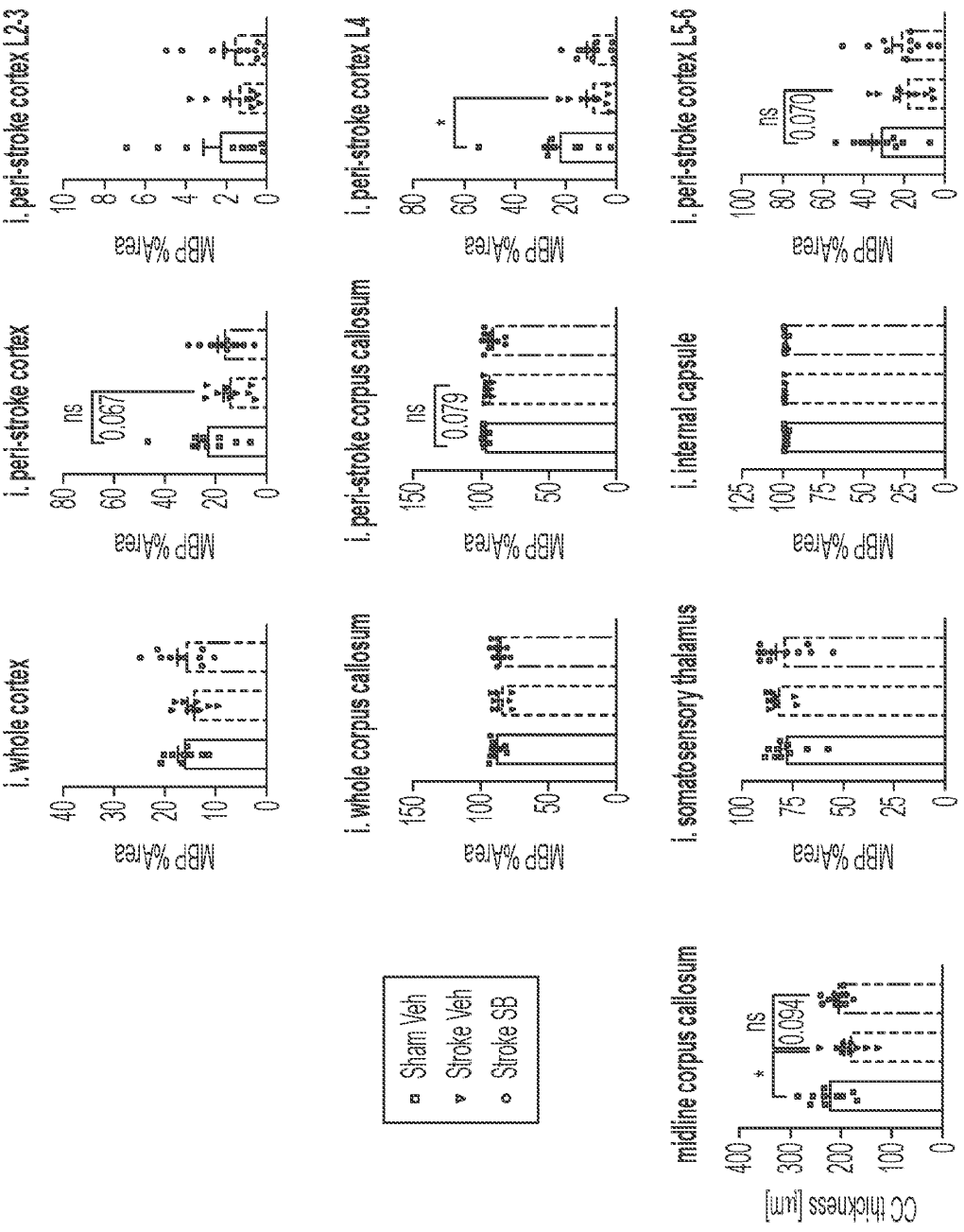

i. whole cortex
i. peri-stroke cortex
i. peri-stroke cortex L2-3
i. whole corpus callosum
i. peri-stroke corpus callosum
i. peri-stroke cortex L4
i. somatosensory thalamus
i. internal capsule
i. peri-stroke cortex L5-6
midline corpus callosum
MBP %Area
CC thickness [µm]
ns
0.067
0.079
0.070
0.094
*
Sham Veh
Stroke Veh
Stroke SB

FIG. 13D

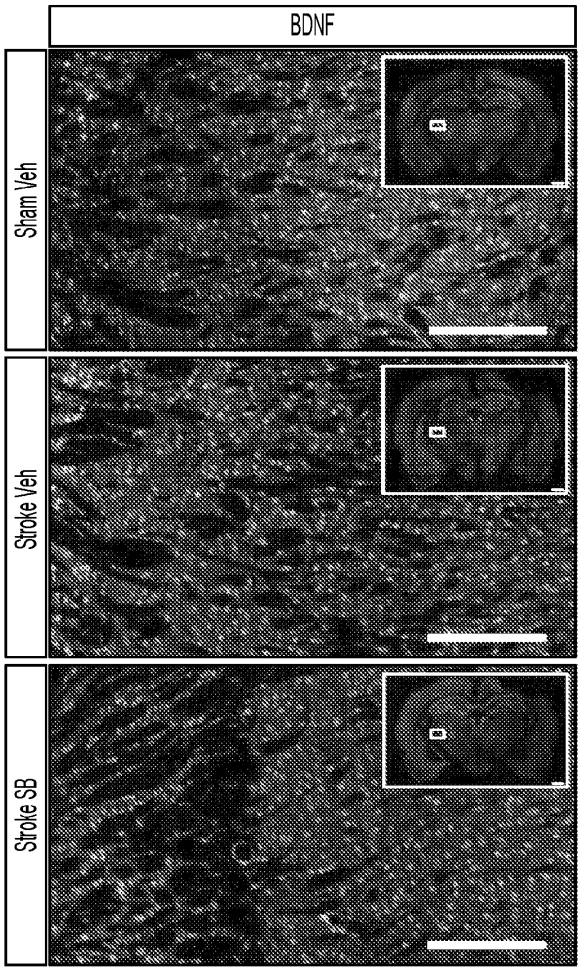


FIG. 14A

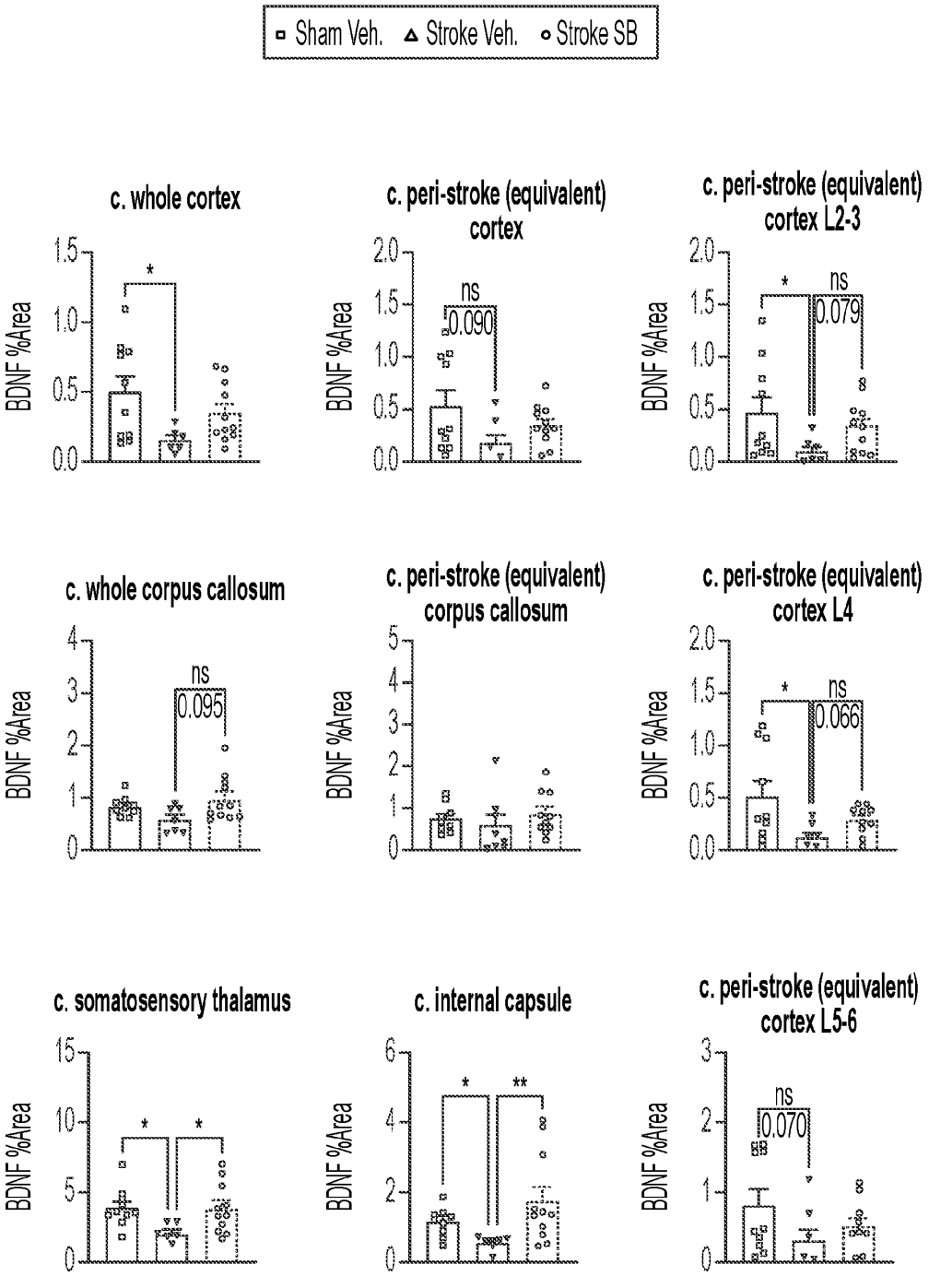

Sham Veh.
Stroke Veh.
Stroke SB
c. whole cortex
c. peri-stroke (equivalent) cortex
c. peri-stroke (equivalent) cortex L2-3
c. whole corpus callosum
c. peri-stroke (equivalent) corpus callosum
c. peri-stroke (equivalent) cortex L4
c. somatosensory thalamus
c. internal capsule
c. peri-stroke (equivalent) cortex L5-6
BDNF %Area
ns
0.090
0.079
0.095
0.066
0.070

FIG. 14B

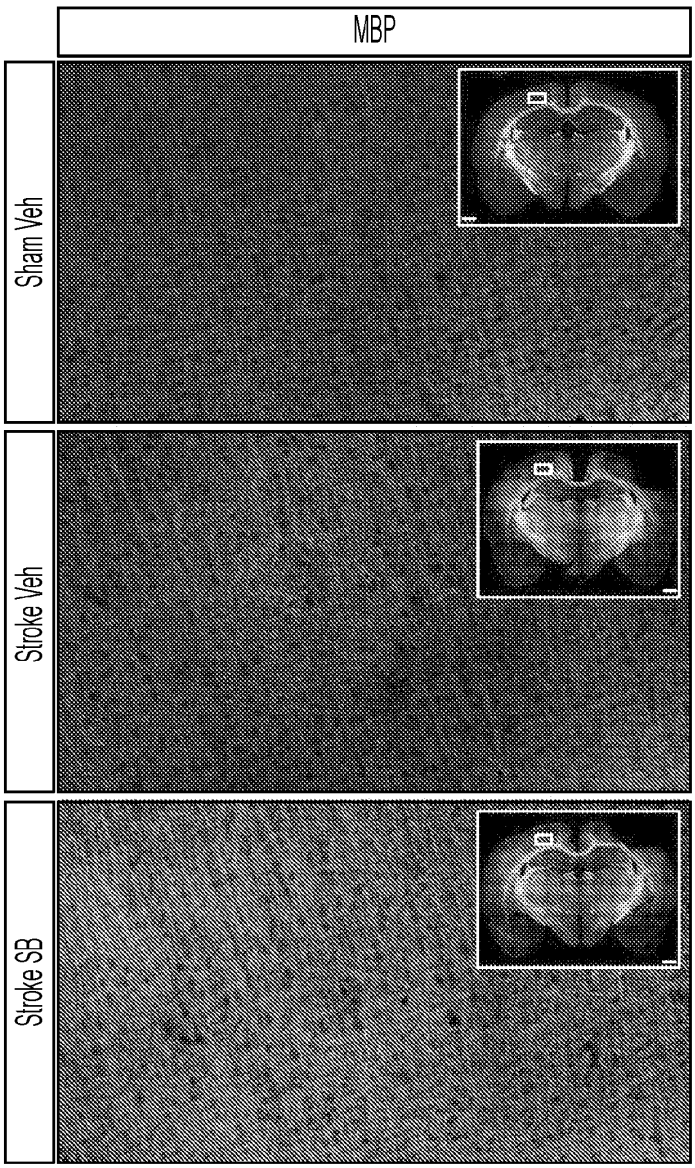


FIG. 14C

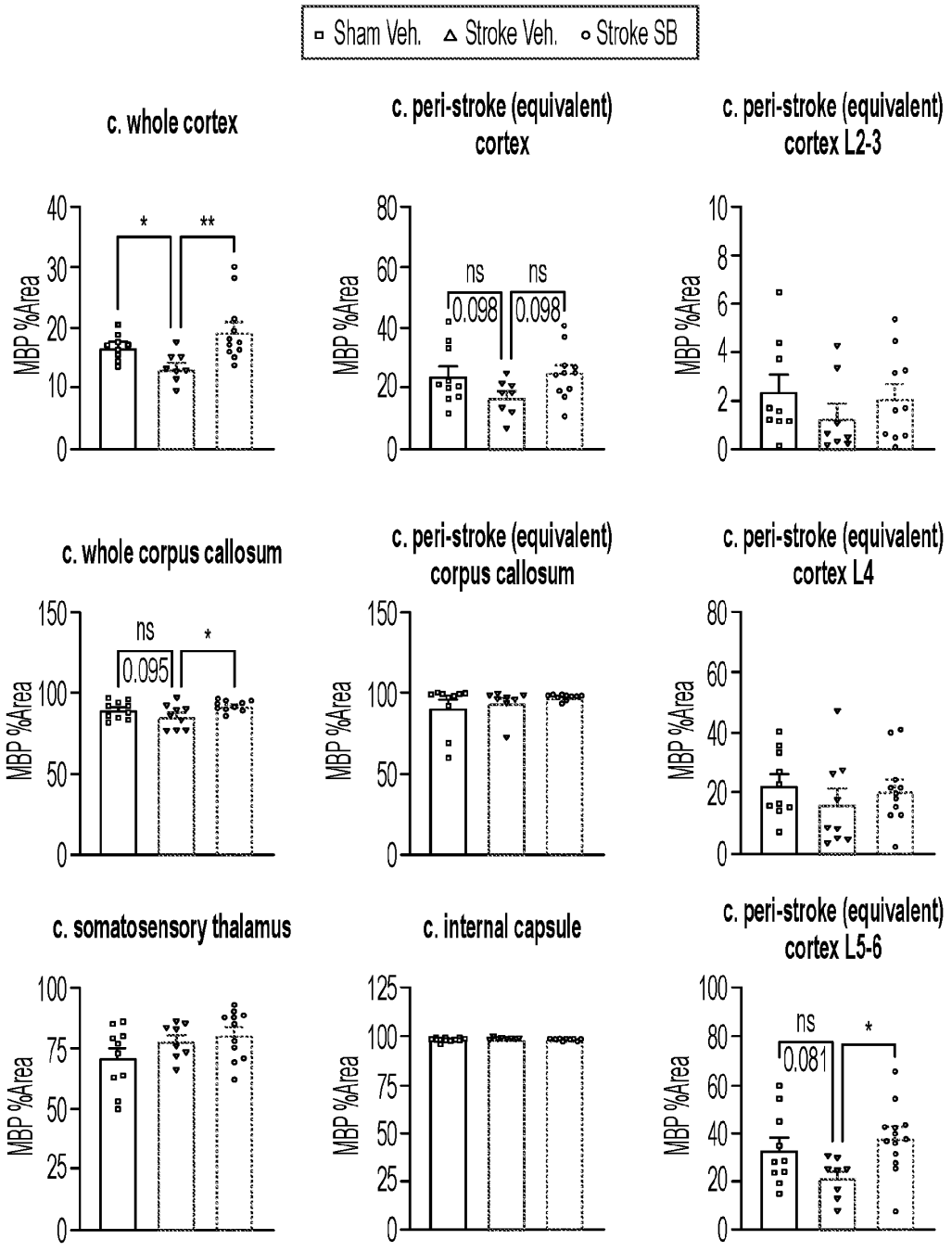

Sham Veh.
Stroke Veh.
Stroke SB
c. whole cortex
c. peri-stroke (equivalent) cortex
c. peri-stroke (equivalent) cortex L2-3
c. whole corpus callosum
c. peri-stroke (equivalent) corpus callosum
c. peri-stroke (equivalent) cortex L4
c. somatosensory thalamus
c. internal capsule
c. peri-stroke (equivalent) cortex L5-6
MBP %Area
ns
0.098
0.095
0.081
*
**

FIG. 14D

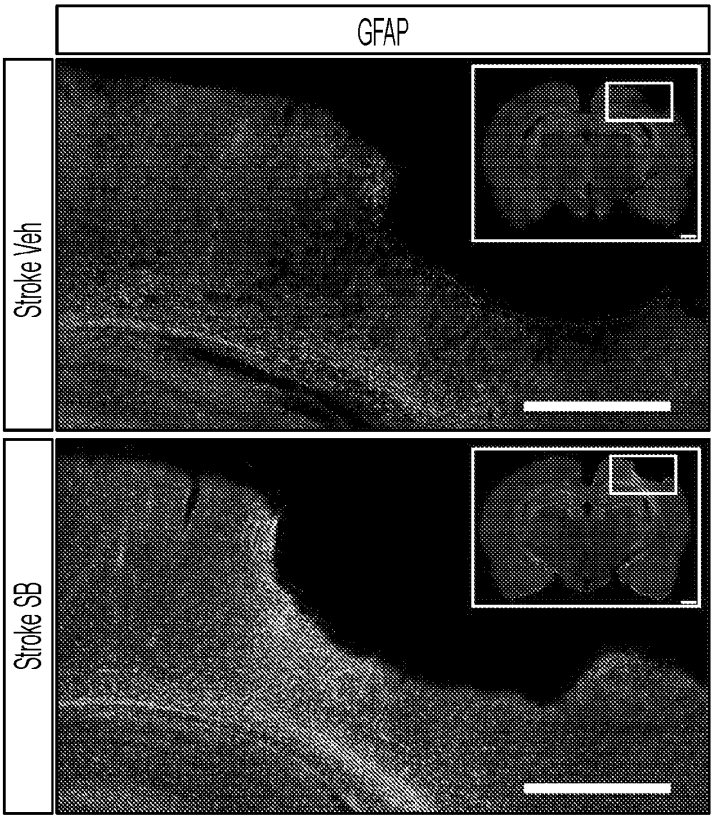


FIG. 15A

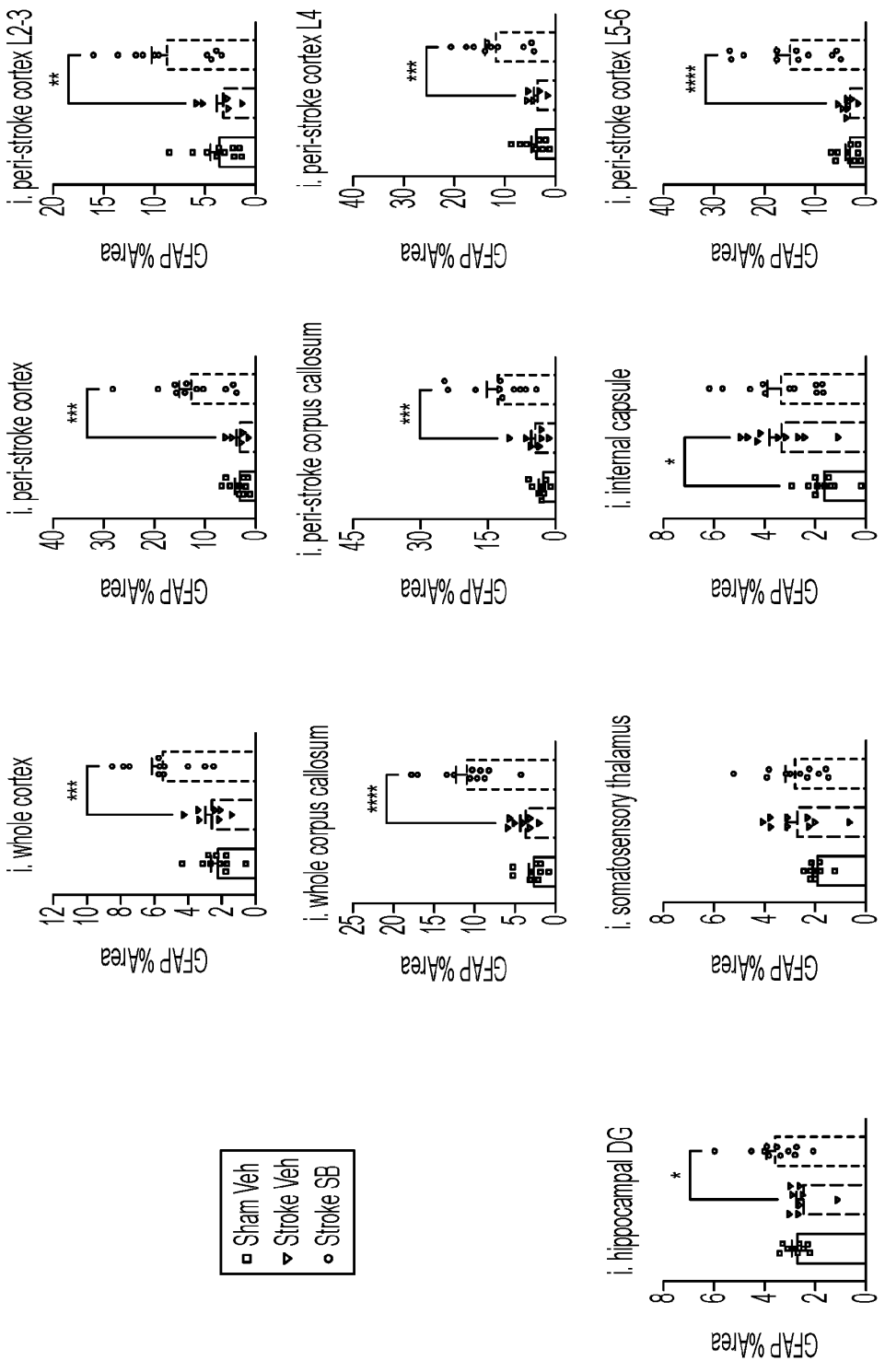

i. peri-stroke cortex L2-3
i. peri-stroke cortex L4
i. peri-stroke cortex L5-6
i. peri-stroke cortex
i. peri-stroke corpus callosum
i. internal capsule
i. whole cortex
i. whole corpus callosum
i. somatosensory thalamus
i. hippocampal DG
GFAP %Area
Sham Veh
Stroke Veh
Stroke SB

FIG. 15B

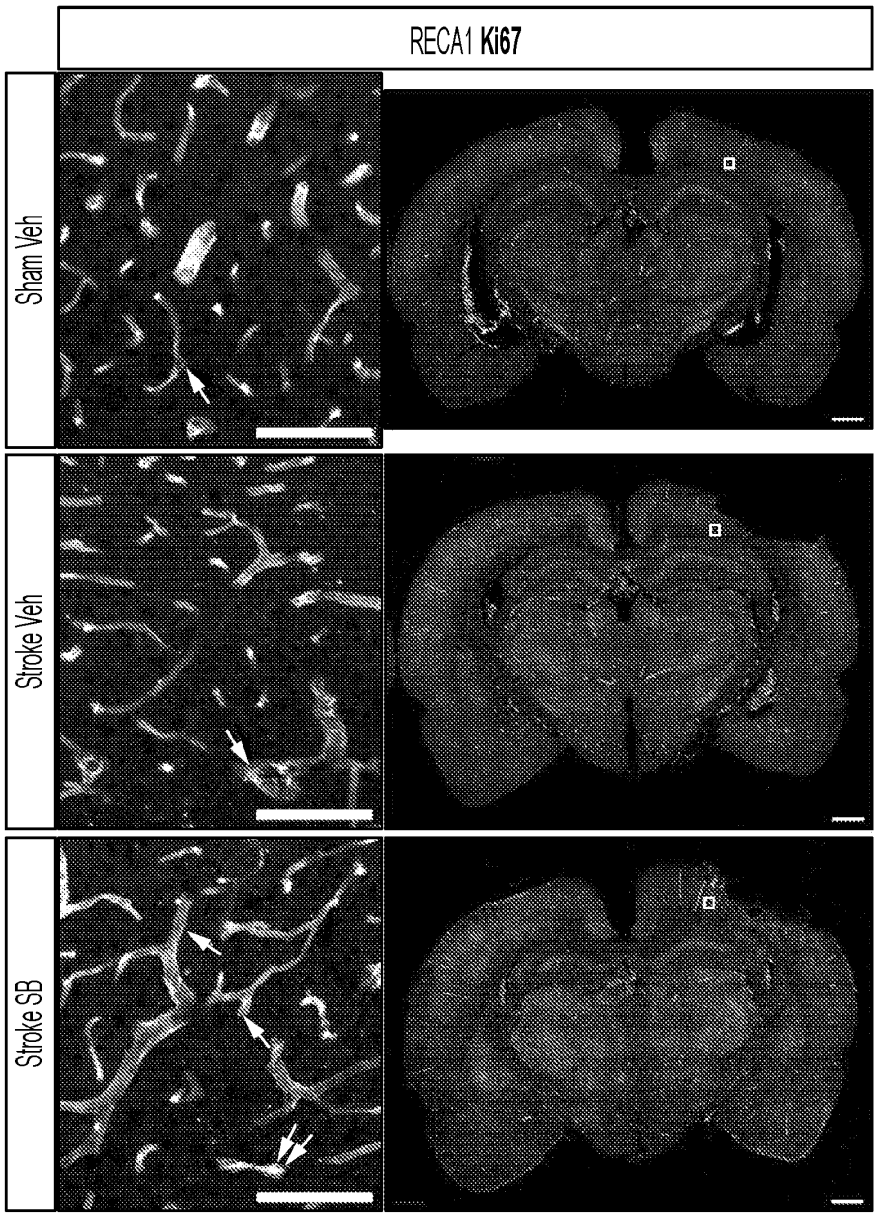


FIG. 15C

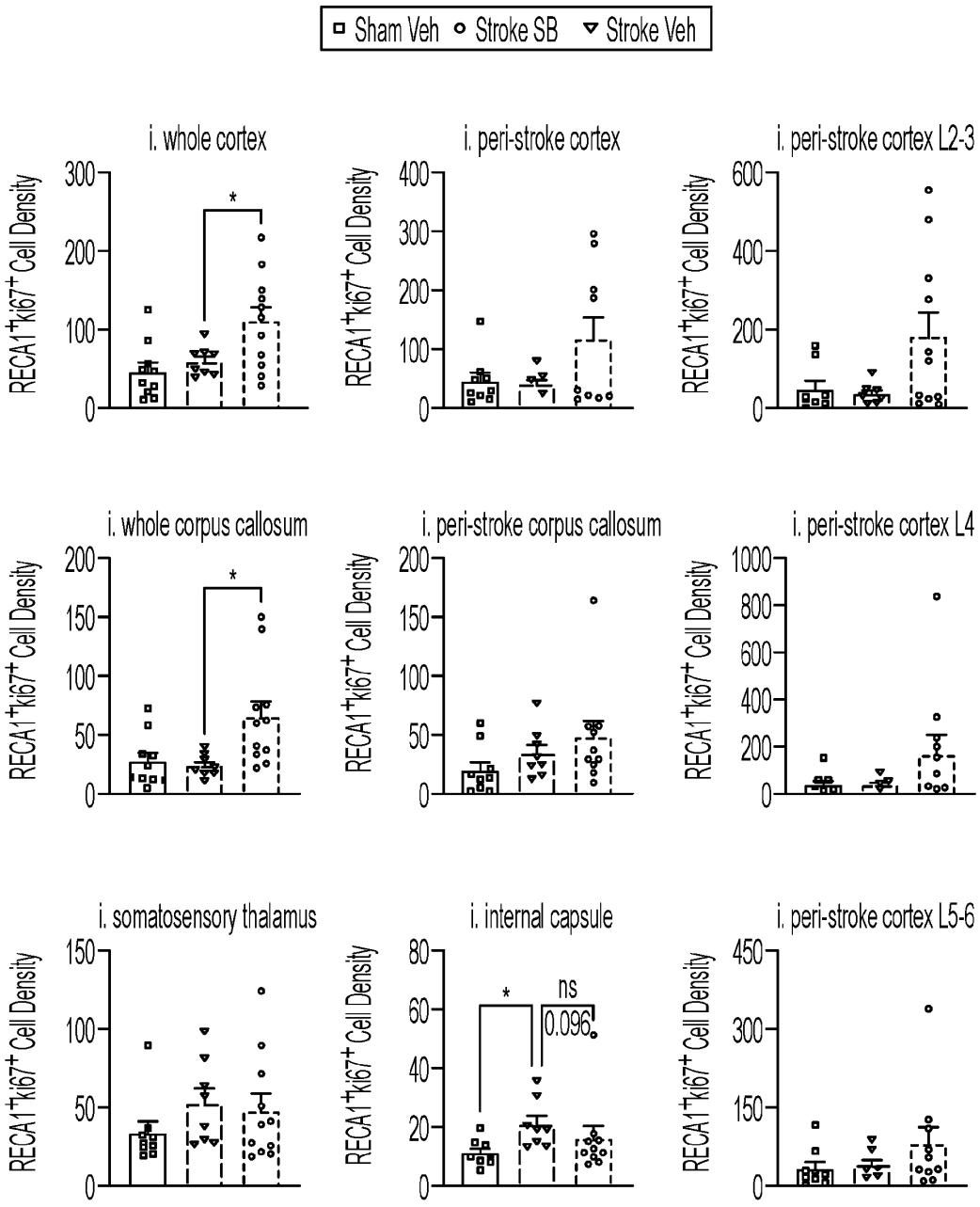

Sham Veh
Stroke SB
Stroke Veh
i. whole cortex
i. peri-stroke cortex
i. peri-stroke cortex L2-3
i. whole corpus callosum
i. peri-stroke corpus callosum
i. peri-stroke cortex L4
i. somatosensory thalamus
i. internal capsule
i. peri-stroke cortex L5-6
RECA1+ki67+ Cell Density
*
ns
0.096

FIG. 15D

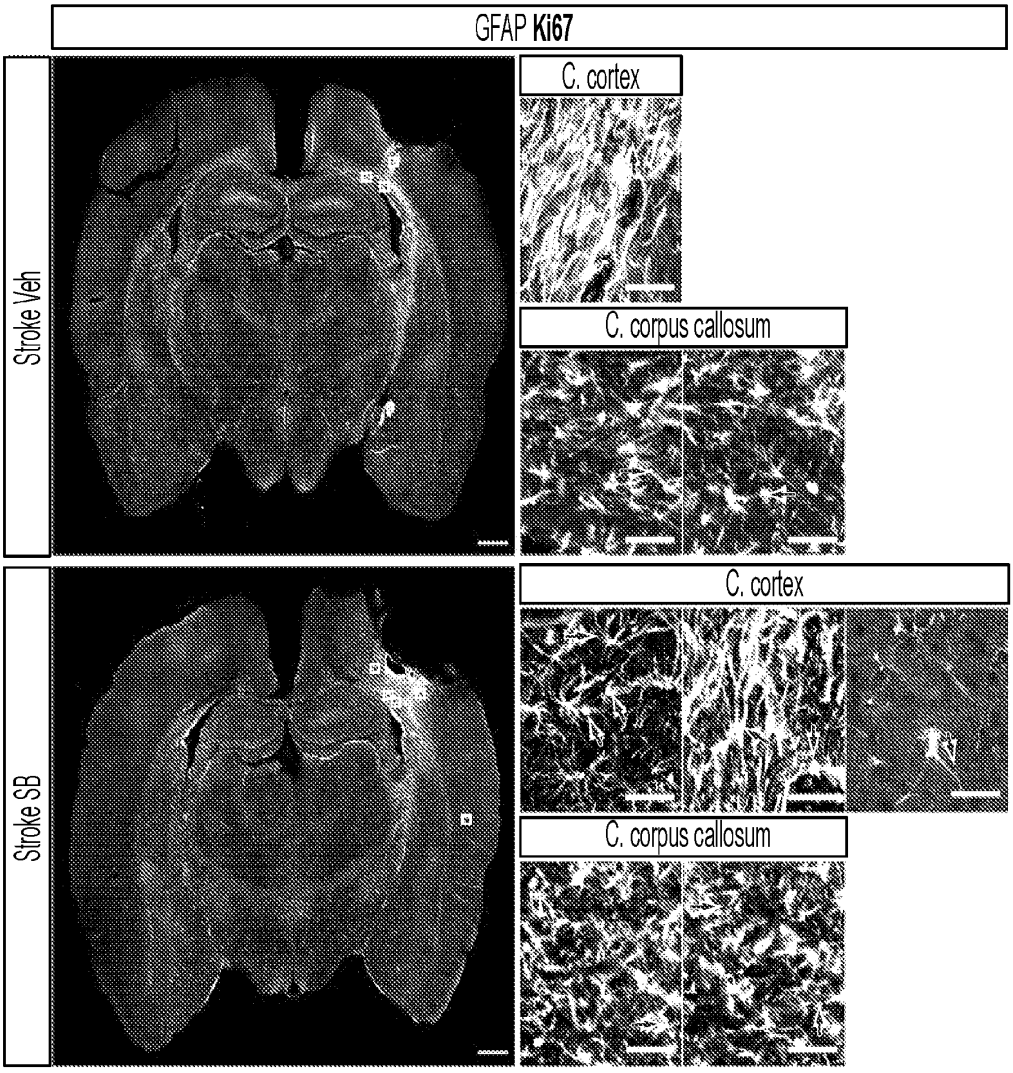

GFAP Ki67
Stroke Veh
C. cortex
C. corpus callosum
Stroke SB
C. cortex
C. corpus callosum

FIG. 16A

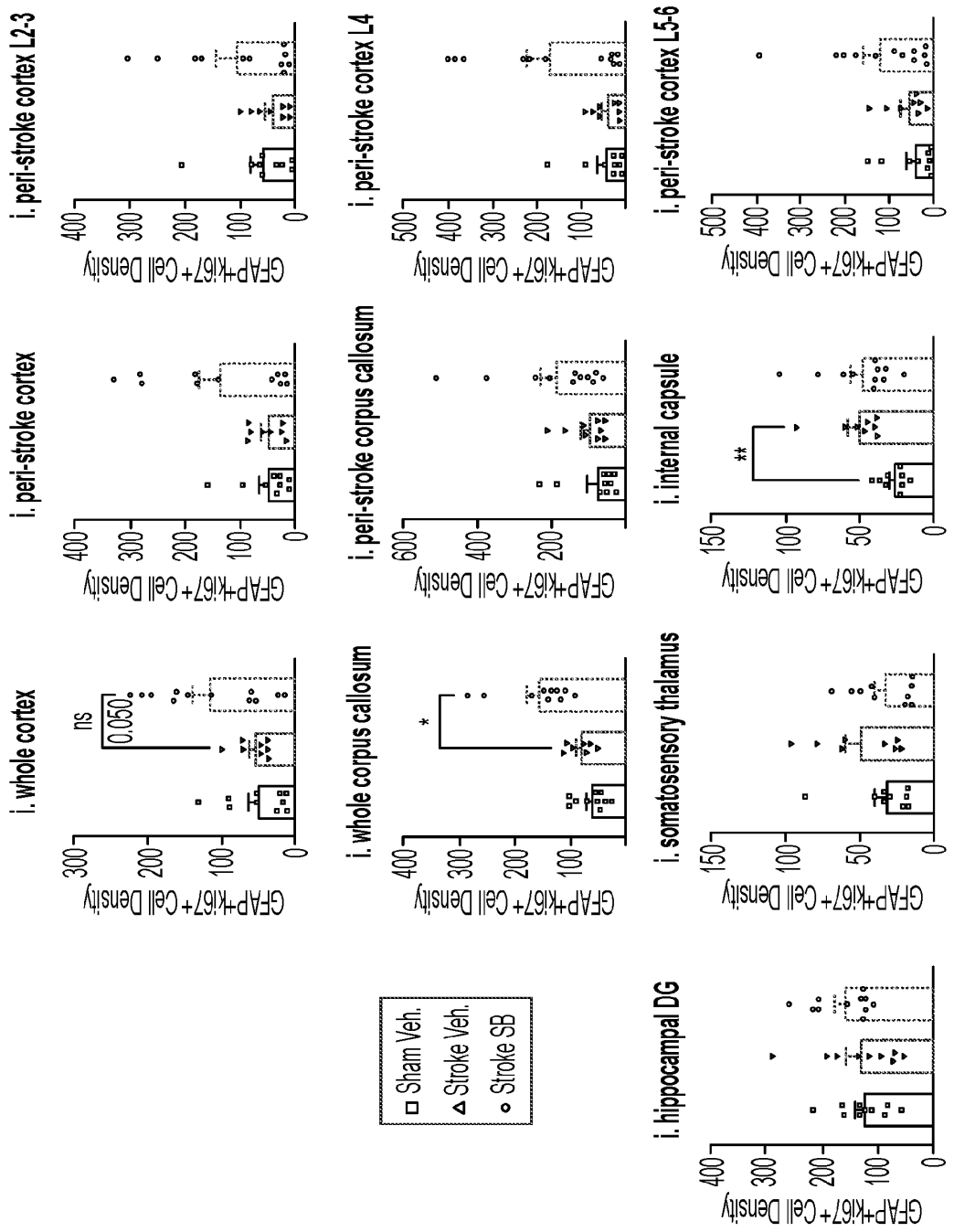

i. whole cortex
ns
0.050
i. peri-stroke cortex
i. peri-stroke cortex L2-3
i. whole corpus callosum
*
i. peri-stroke corpus callosum
i. peri-stroke cortex L4
i. somatosensory thalamus
i. internal capsule
**
i. peri-stroke cortex L5-6
i. hippocampal DG
GFAP+ki67+ Cell Density
Sham Veh.
Stroke Veh.
Stroke SB

FIG. 16B

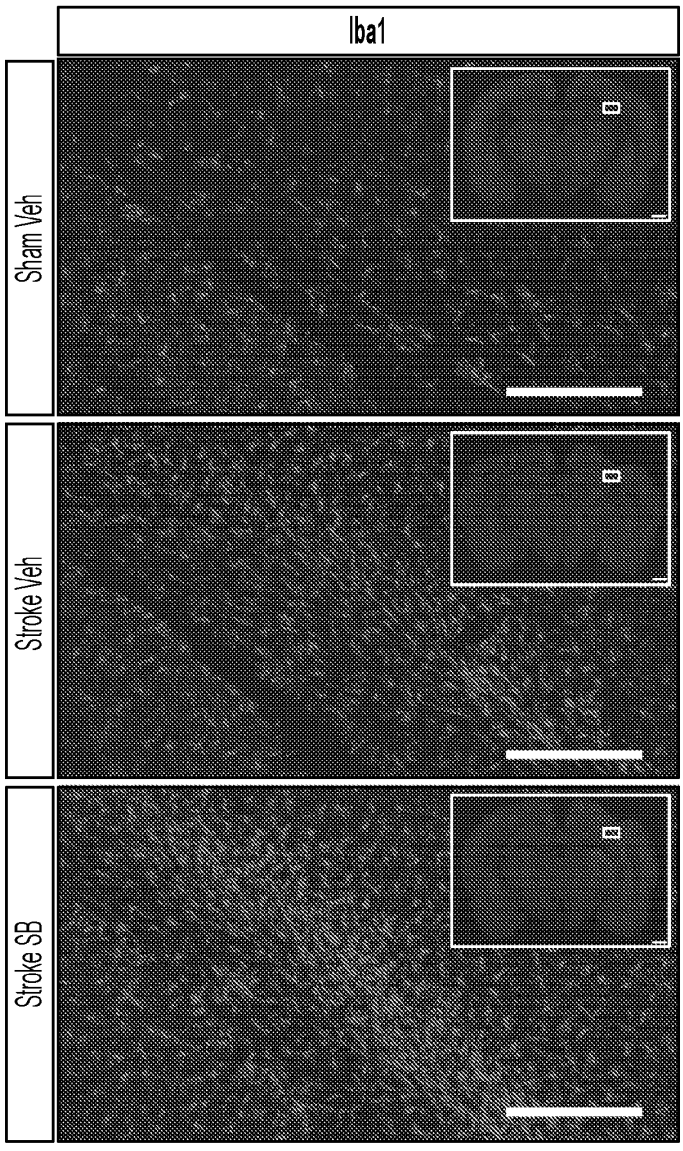


FIG. 16C

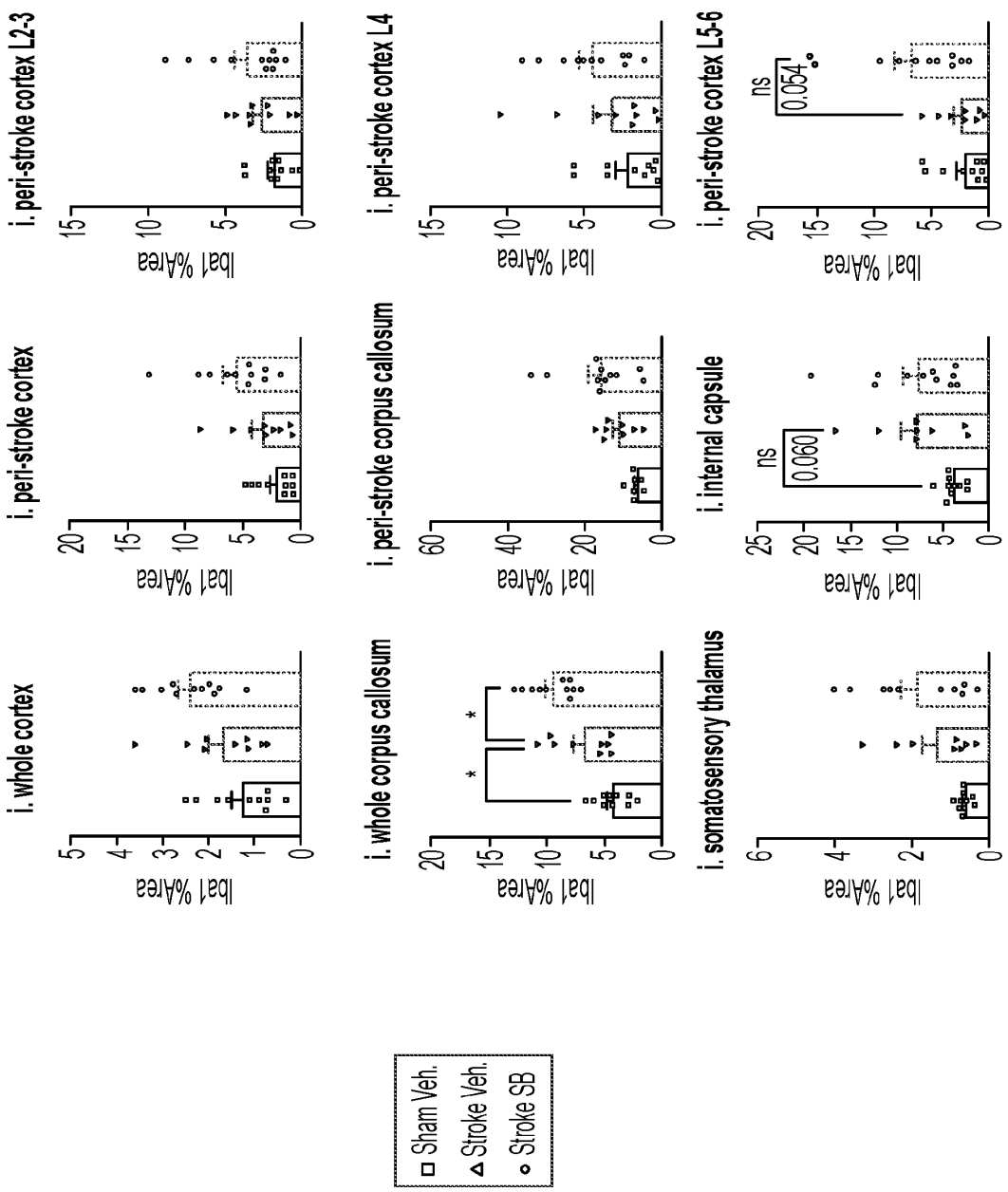

i. whole cortex
i. peri-stroke cortex
i. peri-stroke cortex L2-3
i. whole corpus callosum
i. peri-stroke corpus callosum
i. peri-stroke cortex L4
i. somatosensory thalamus
i. internal capsule
i. peri-stroke cortex L5-6
Iba1 %Area
ns
0.060
0.054
Sham Veh.
Stroke Veh.
Stroke SB

FIG. 16D

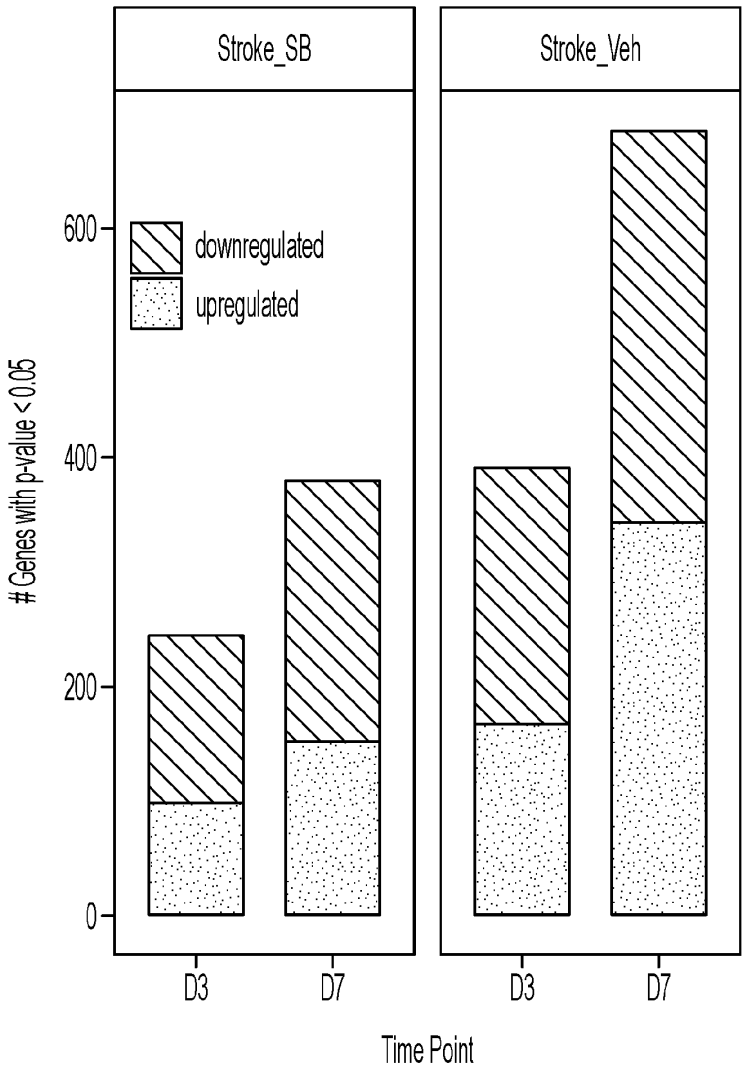

Stroke_SB
Stroke_Veh
downregulated
upregulated
600
400
200
0
Genes with p-value < 0.05
D3
D7
D3
D7
Time Point

FIG. 17A

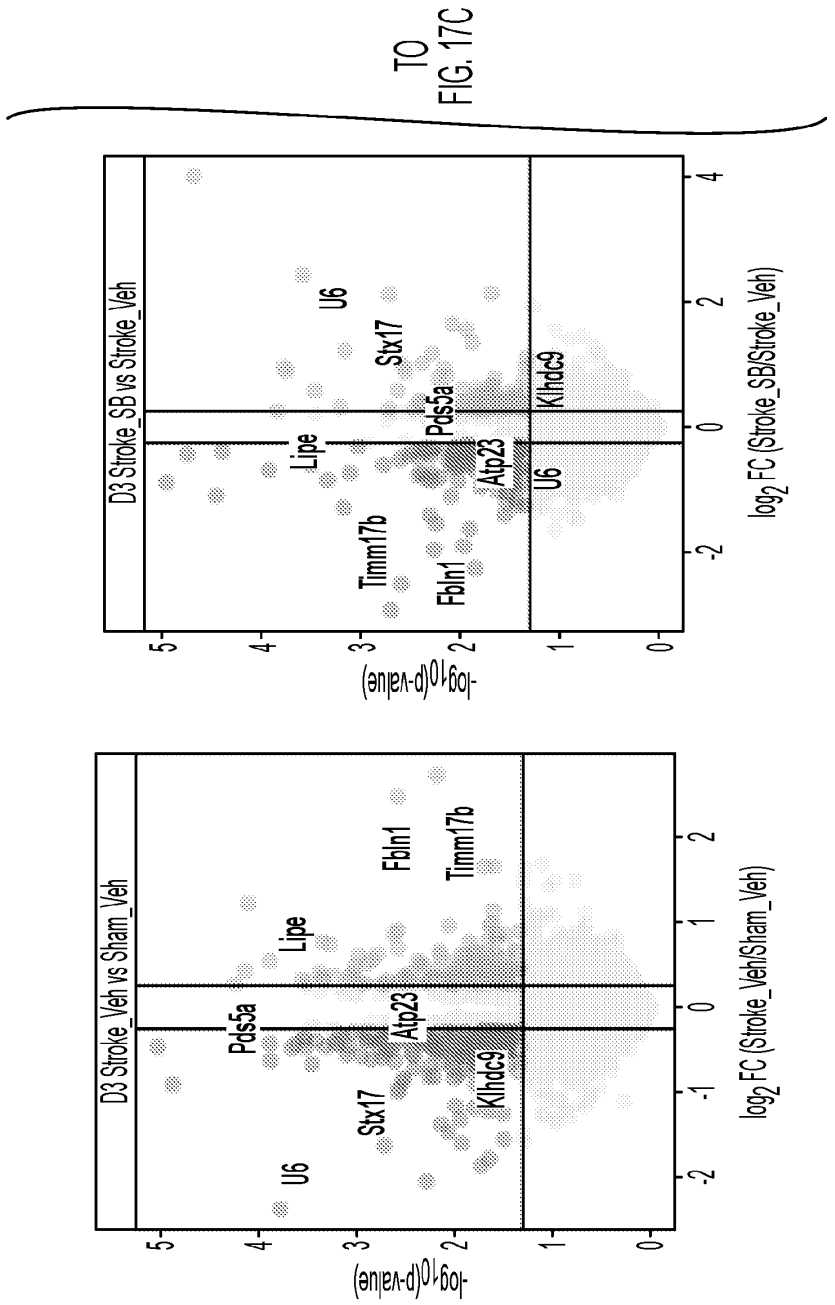

TO
FIG. 17C
D3 Stroke_SB vs Stroke_Veh
D3 Stroke_Veh vs Sham_Veh
-log10(p-value)
log2 FC (Stroke_SB/Stroke_Veh)
log2 FC (Stroke_Veh/Sham_Veh)
U6
Stx17
Pds5a
Lipe
Atp23
Klhdc9
Timm17b
Fbln1

FIG. 17B

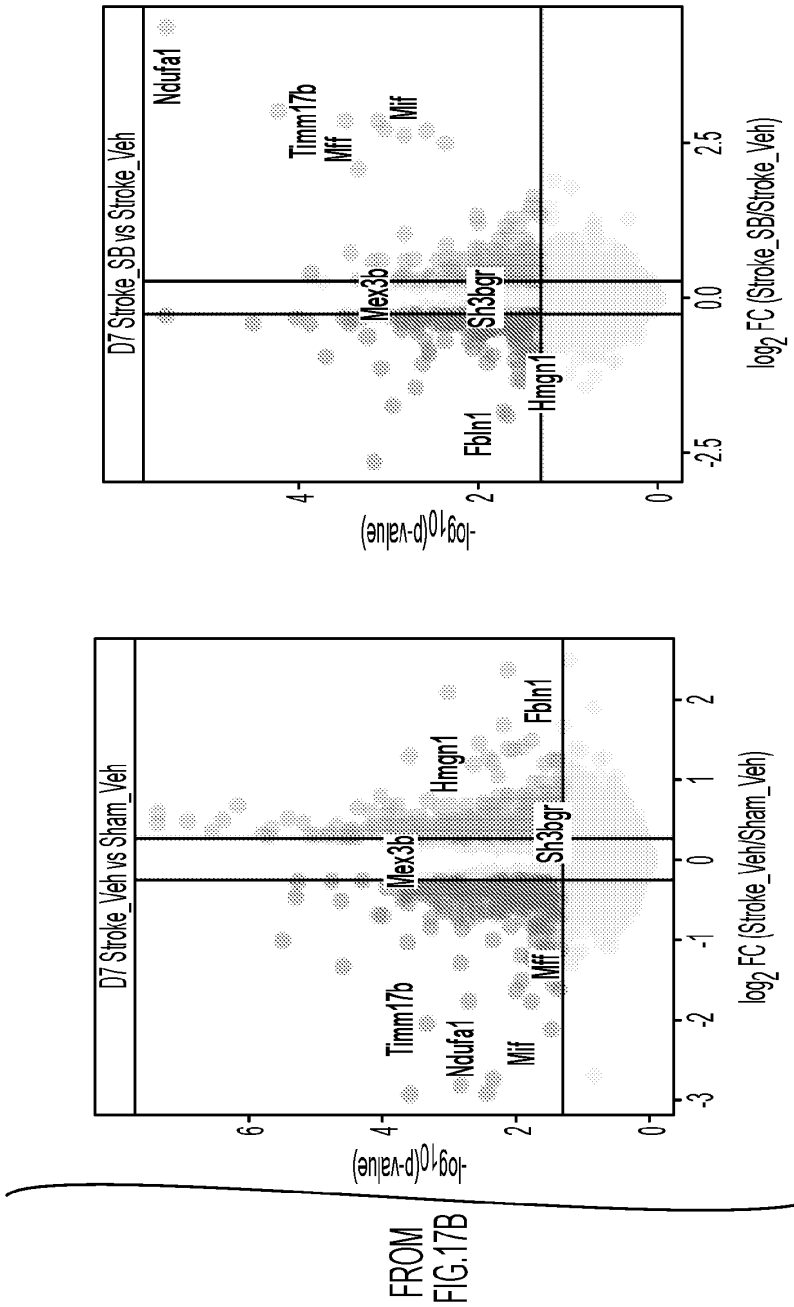

D7 Stroke_SB vs Stroke_Veh
Ndufa1
Timm17b
Miff
Mif
Mex3b
Sh3bgr
Fbln1
Hmgn1
-log10(p-value)
log2 FC (Stroke_SB/Stroke_Veh)
D7 Stroke_Veh vs Sham_Veh
Hmgn1
Fbln1
Mex3b
Sh3bgr
Timm17b
Ndufa1
Mif
Miff
-log10(p-value)
log2 FC (Stroke_Veh/Sham_Veh)
FROM FIG.17B

FIG. 17C

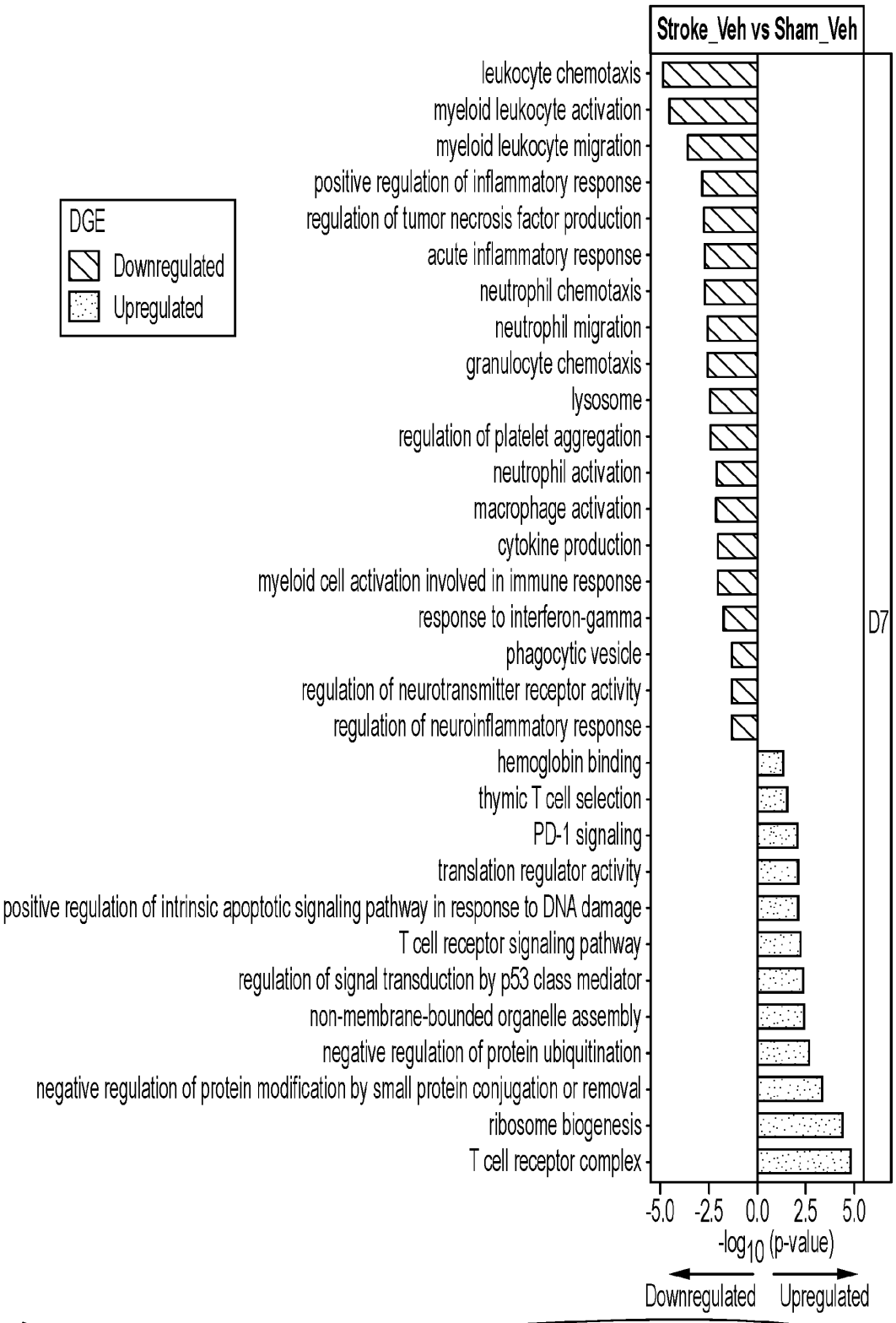


FIG. 17D

TO FIG. 17E

FROM FIG. 17D

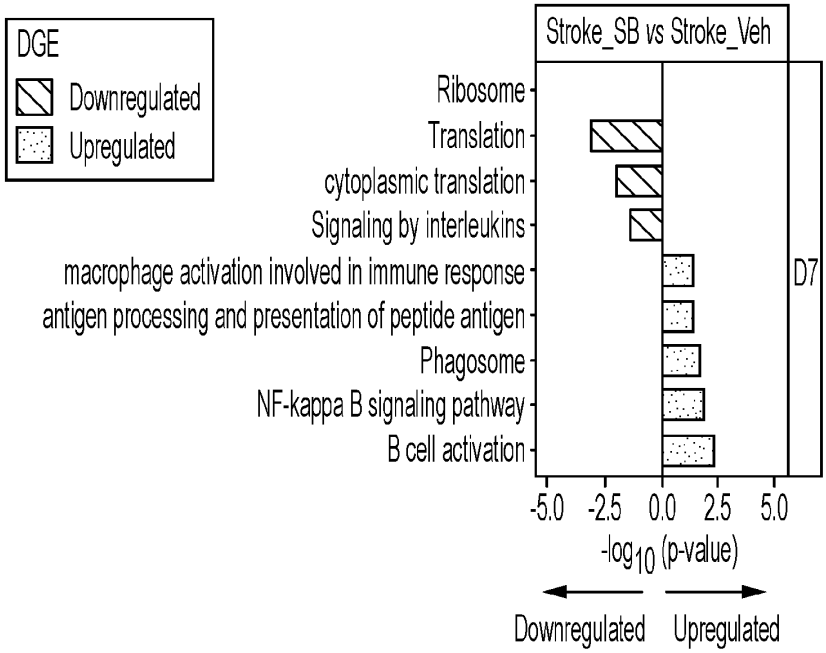


FIG. 17E

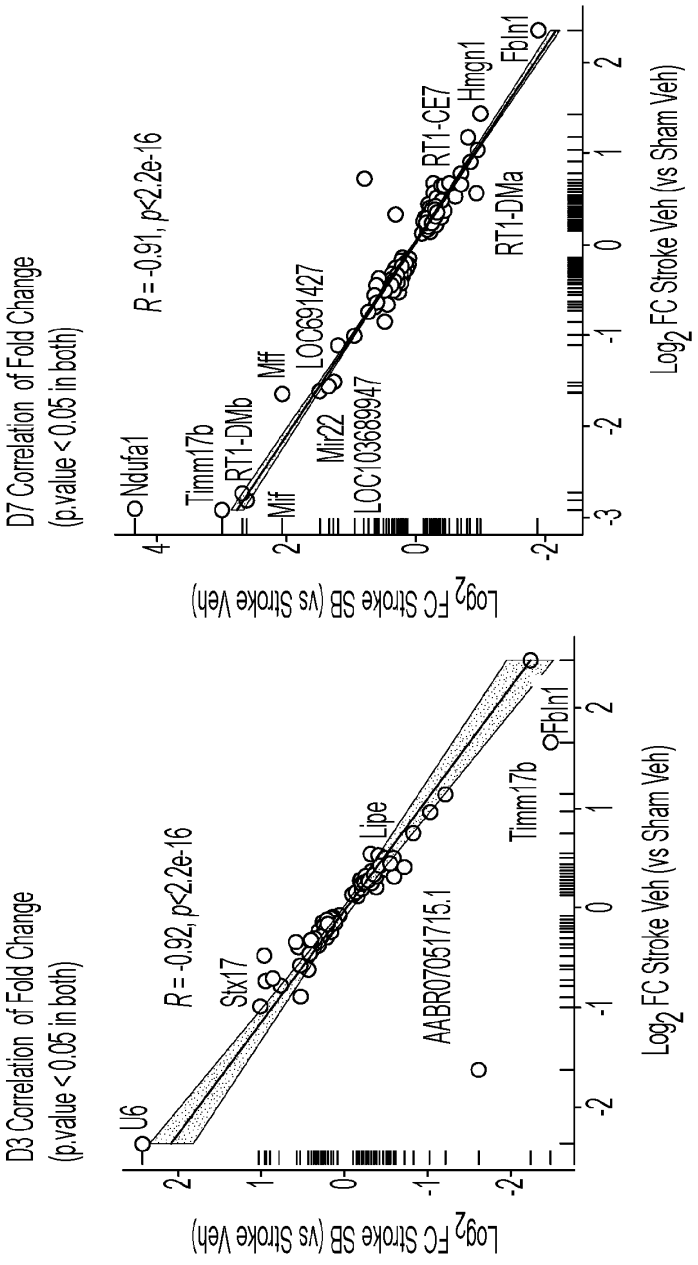

D7 Correlation of Fold Change
(p.value < 0.05 in both)
R = -0.91, p<2.2e-16
Ndufa1
Timm17b
RT1-DMb
Mff
Mff
LOC691427
Mir22
LOC103689947
RT1-CE7
Hmgn1
RT1-DMa
Fbln1
Log2 FC Stroke SB (vs Stroke Veh)
Log2 FC Stroke Veh (vs Sham Veh)
D3 Correlation of Fold Change
(p.value < 0.05 in both)
R = -0.92, p<2.2e-16
U6
Stx17
AABR07051715.1
Lipe
Timm17b
Fbln1
Log2 FC Stroke SB (vs Stroke Veh)
Log2 FC Stroke Veh (vs Sham Veh)

FIG. 17F

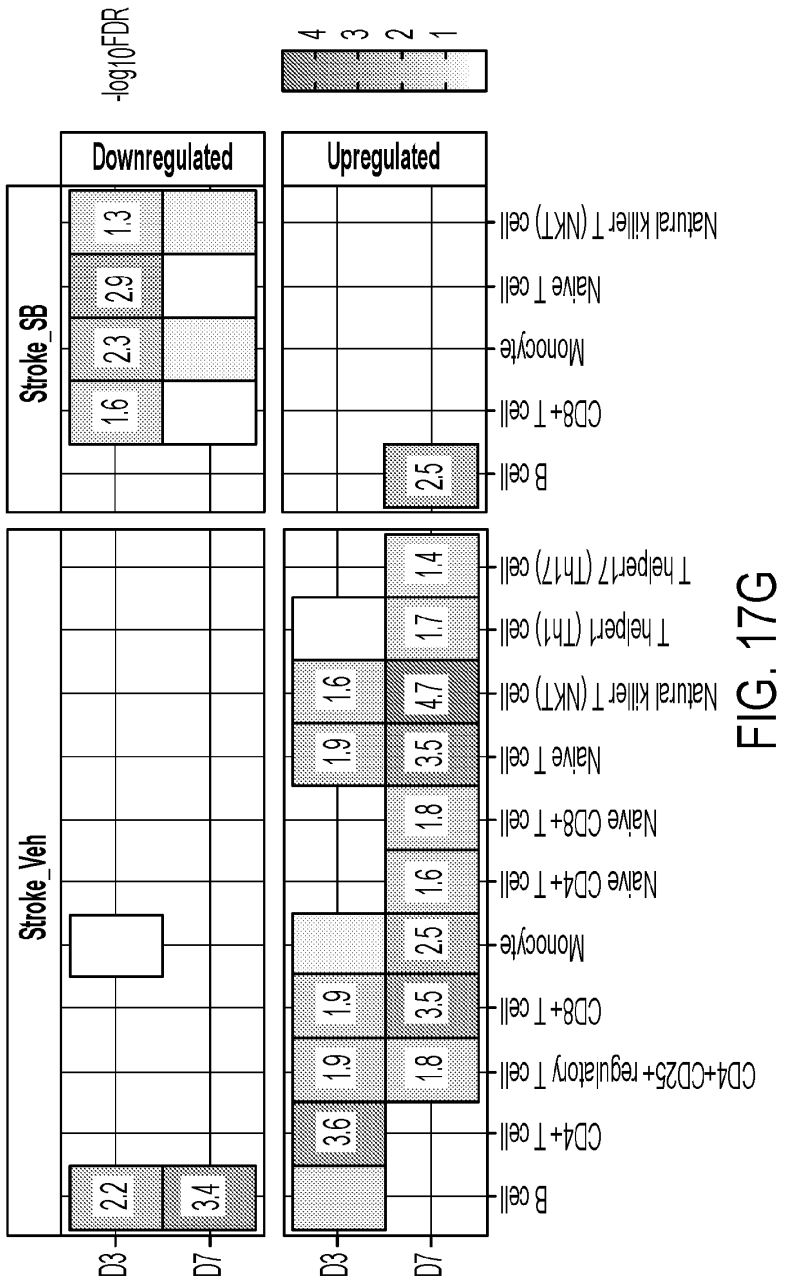

-log10FDR
4
3
2
1
Downregulated
Upregulated
Stroke_SB
Stroke_Veh
1.3
2.9
2.3
1.6
2.5
2.2
3.4
3.6
1.9
1.9
1.9
3.5
3.5
1.8
2.5
1.6
1.8
3.5
4.7
1.6
1.7
1.4
B cell
CD8+ T cell
Monocyte
Naive T cell
Natural killer T (NKT) cell
CD4+ T cell
CD4+CD25+ regulatory T cell
CD8+ T cell
Monocyte
Naive CD4+ T cell
Naive CD8+ T cell
Naive T cell
Natural killer T (NKT) cell
T helper1 (Th1) cell
T helper17 (Th17) cell
D3
D7
D3
D7

FIG. 17G

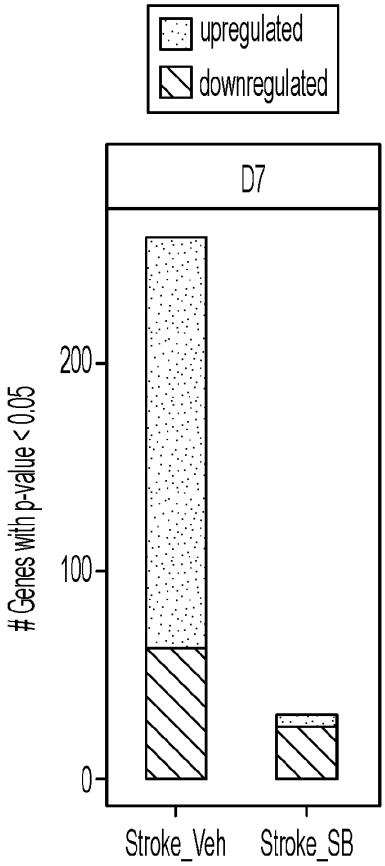

upregulated
downregulated
D7
Genes with p-value < 0.05
200
100
0
Stroke_Veh
Stroke_SB

FIG. 17H

TO
FIG. 17J

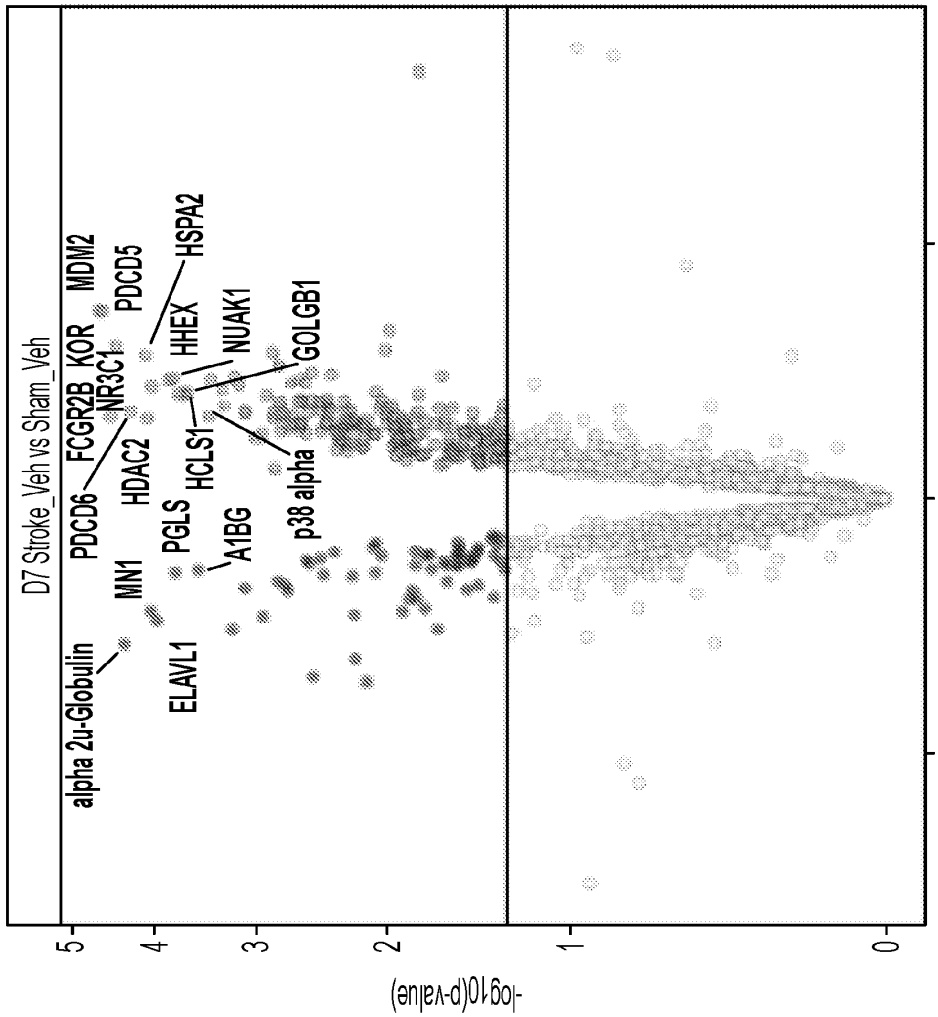


FIG. 17I

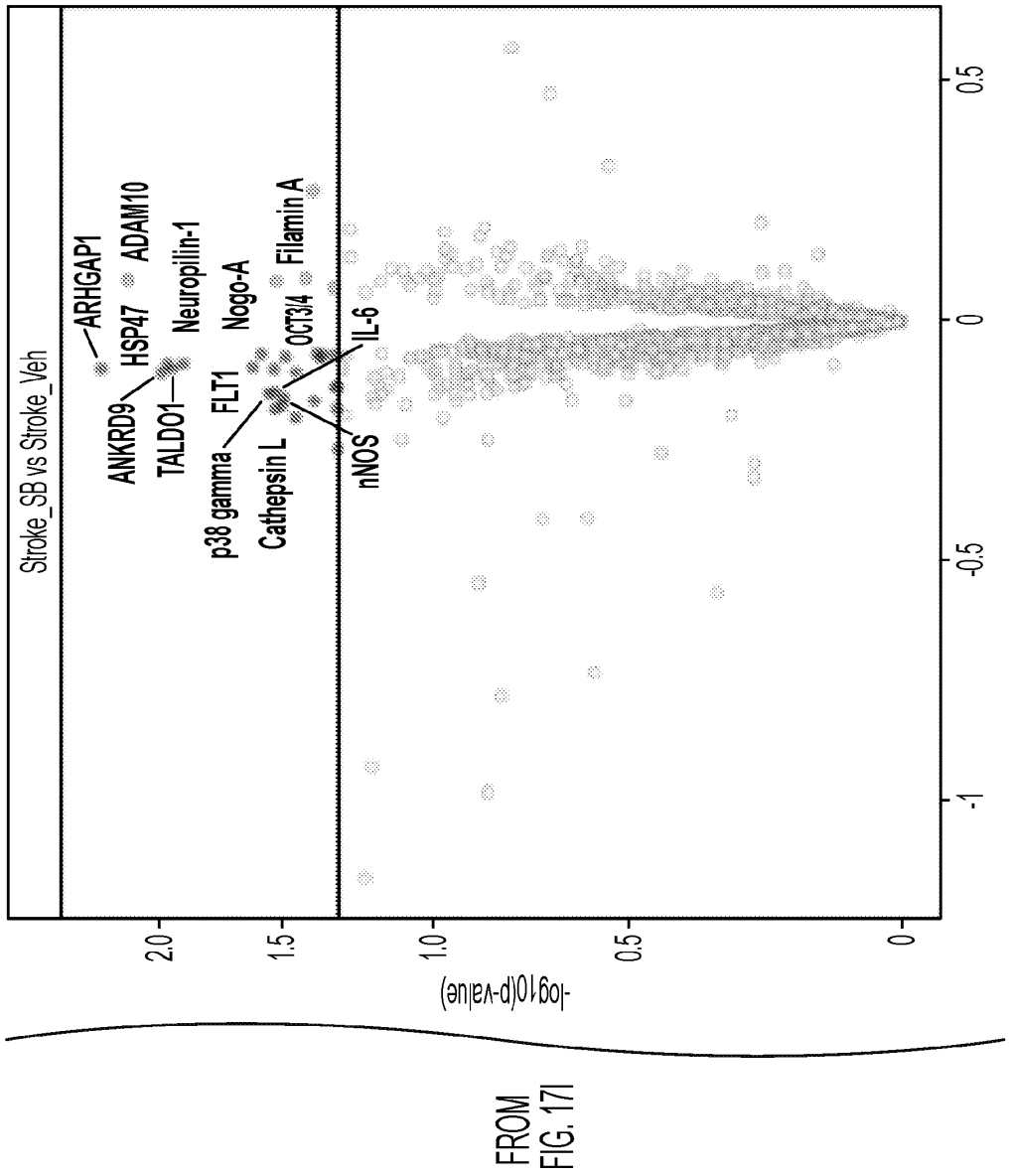

Stroke_SB vs Stroke_Veh
ARHGAP1
HSP47
ADAM10
ANKRD9
TALDO1
Neuropilin-1
p38 gamma
FLT1
Nogo-A
Cathepsin L
OCT3/4
Filamin A
IL-6
nNOS
2.0
1.5
1.0
0.5
0
-log10(p-value)
-1
-0.5
0
0.5
Log2FC (Stroke_SB vs Stroke_Veh)
FROM FIG. 17I

FIG. 17J

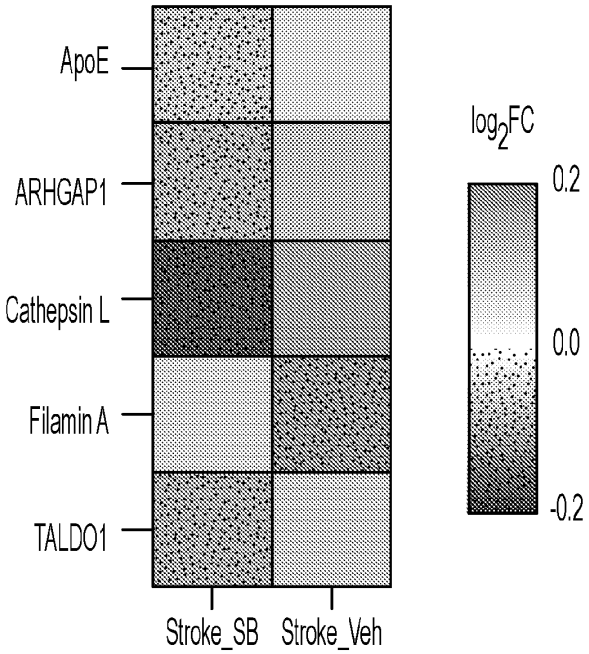

ApoE
ARHGAP1
Cathepsin L
Filamin A
TALDO1
Stroke_SB
Stroke_Veh
log2FC
0.2
0.0
-0.2

FIG. 17K

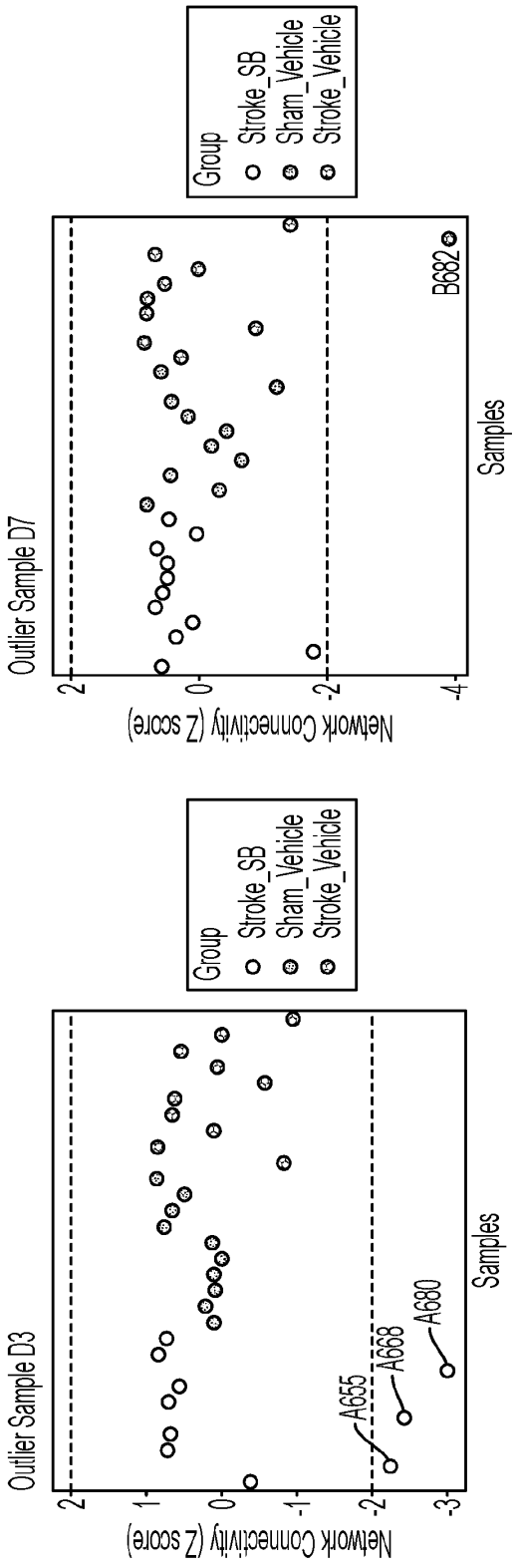

Outlier Sample D7
Network Connectivity (Z score)
2
0
-2
-4
B682
Samples
Group
Stroke_SB
Sham_Vehicle
Stroke_Vehicle
Outlier Sample D3
Network Connectivity (Z score)
2
1
0
-1
-2
-3
A655
A668
A680
Samples
Group
Stroke_SB
Sham_Vehicle
Stroke_Vehicle

FIG. 18A

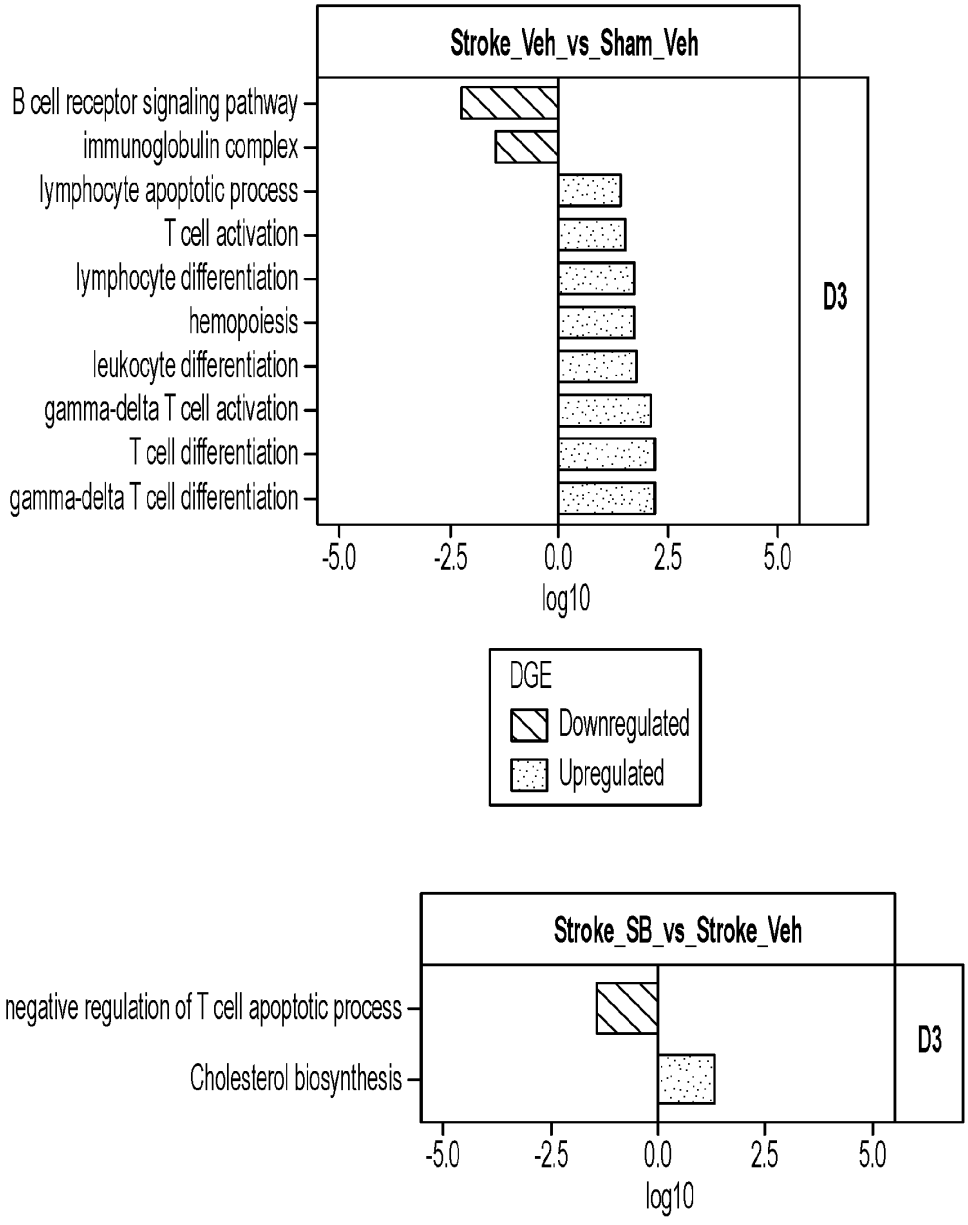

Stroke_Veh_vs_Sham_Veh
B cell receptor signaling pathway
immunoglobulin complex
lymphocyte apoptotic process
T cell activation
lymphocyte differentiation
hemopoiesis
leukocyte differentiation
gamma-delta T cell activation
T cell differentiation
gamma-delta T cell differentiation
D3
-5.0
-2.5
0.0
2.5
5.0
log10
DGE
Downregulated
Upregulated
Stroke_SB_vs_Stroke_Veh
negative regulation of T cell apoptotic process
Cholesterol biosynthesis
D3
-5.0
-2.5
0.0
2.5
5.0
log10

FIG. 18B

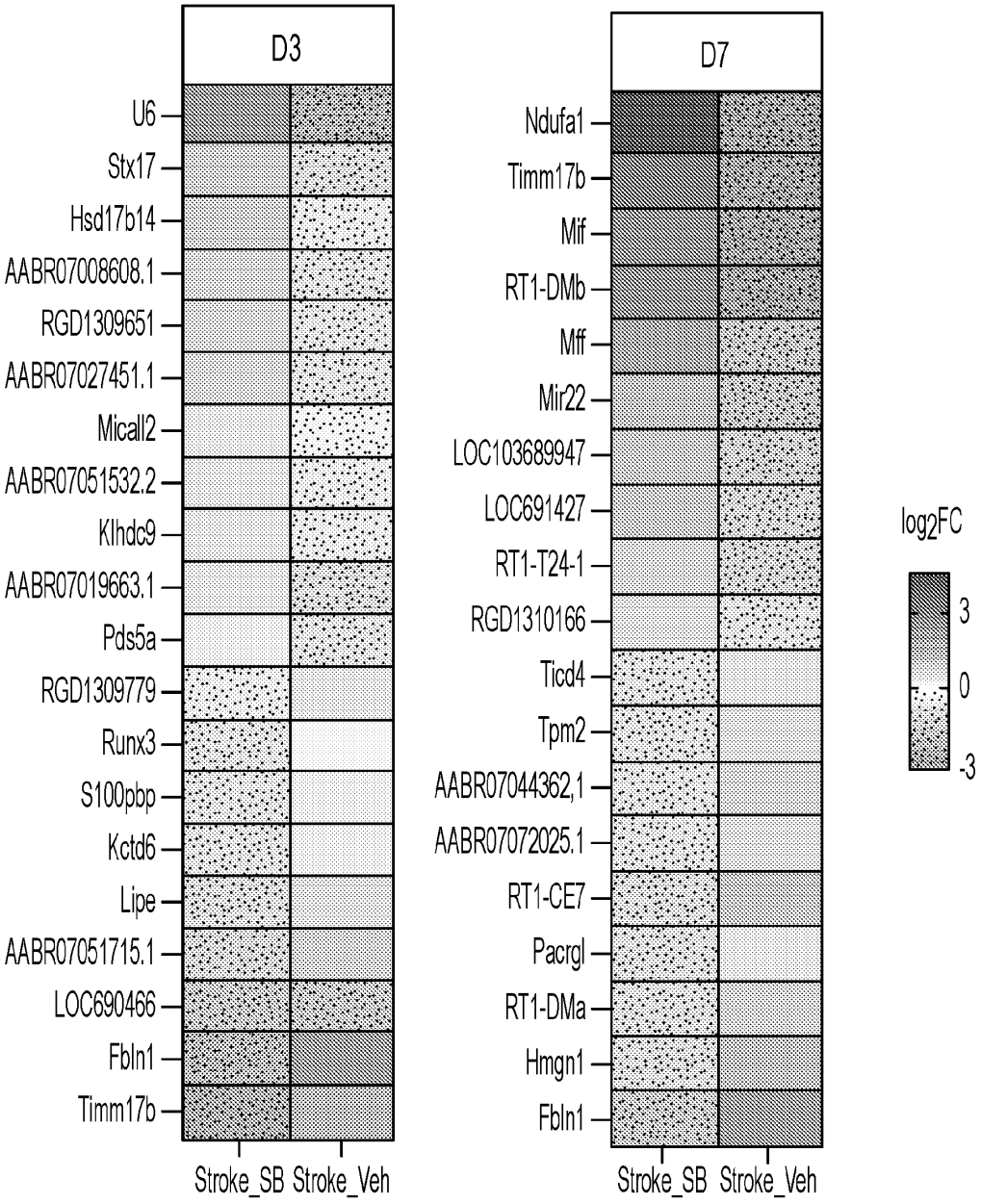

D3
U6
Stx17
Hsd17b14
AABR07008608.1
RGD1309651
AABR07027451.1
Micall2
AABR07051532.2
Klhdc9
AABR07019663.1
Pds5a
RGD1309779
Runx3
S100pbp
Kctd6
Lipe
AABR07051715.1
LOC690466
Fbln1
Timm17b
Stroke_SB
Stroke_Veh
D7
Ndufa1
Timm17b
Mif
RT1-DMb
Mff
Mir22
LOC103689947
LOC691427
RT1-T24-1
RGD1310166
Ticd4
Tpm2
AABR07044362.1
AABR07072025.1
RT1-CE7
Pacrgl
RT1-DMa
Hmgn1
Fbln1
Stroke_SB
Stroke_Veh
log2FC
3
0
-3

FIG. 18C

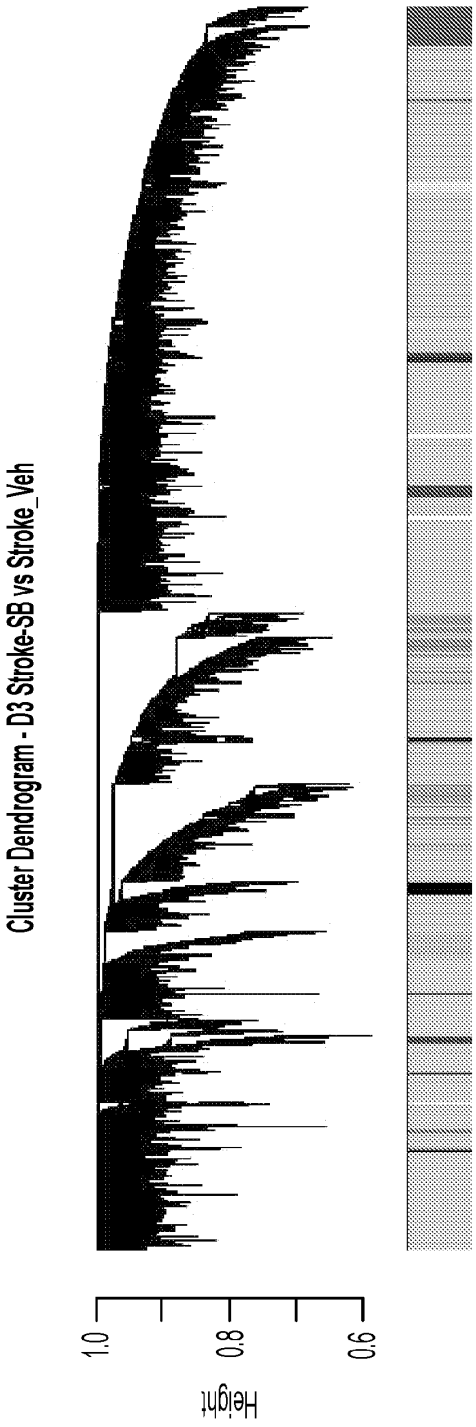

Cluster Dendrogram - D3 Stroke-SB vs Stroke_Veh
1.0
0.8
0.6
Height

FIG. 19A

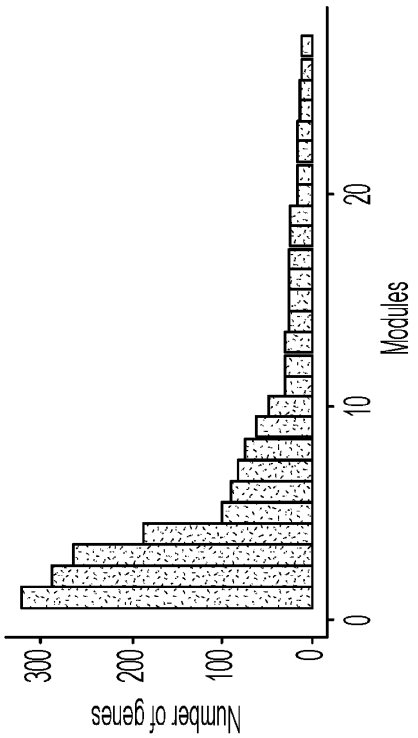


FIG. 19B

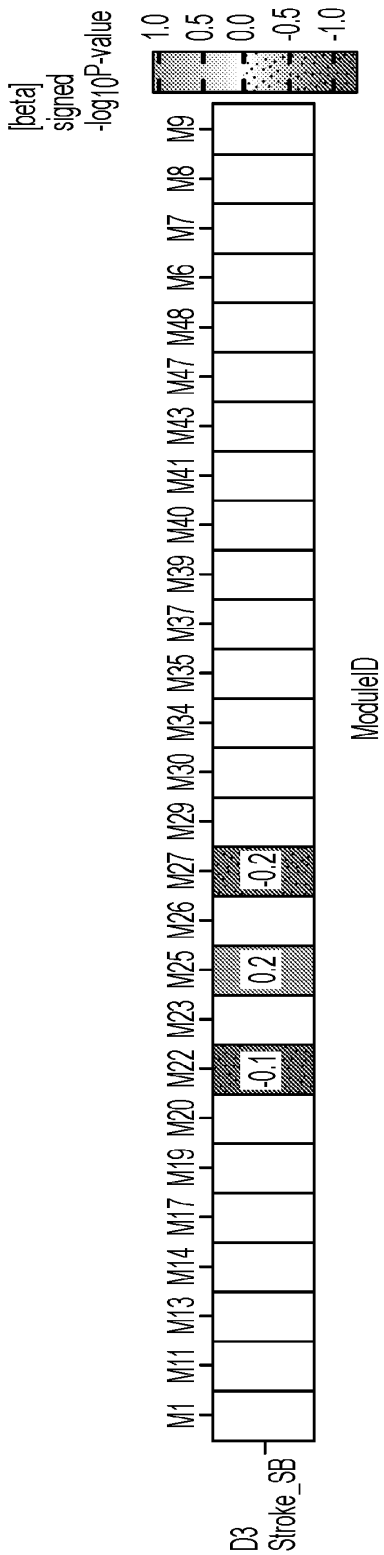

[beta]
signed
-log10P-value
1.0
0.5
0.0
-0.5
-1.0
M9
M8
M7
M6
M48
M47
M43
M41
M40
M39
M37
M35
M34
M30
M29
M27
M26
M25
M23
M22
M20
M19
M17
M14
M13
M11
M1
-0.2
0.2
-0.1
ModuleID
D3
Stroke_SB

FIG. 19C

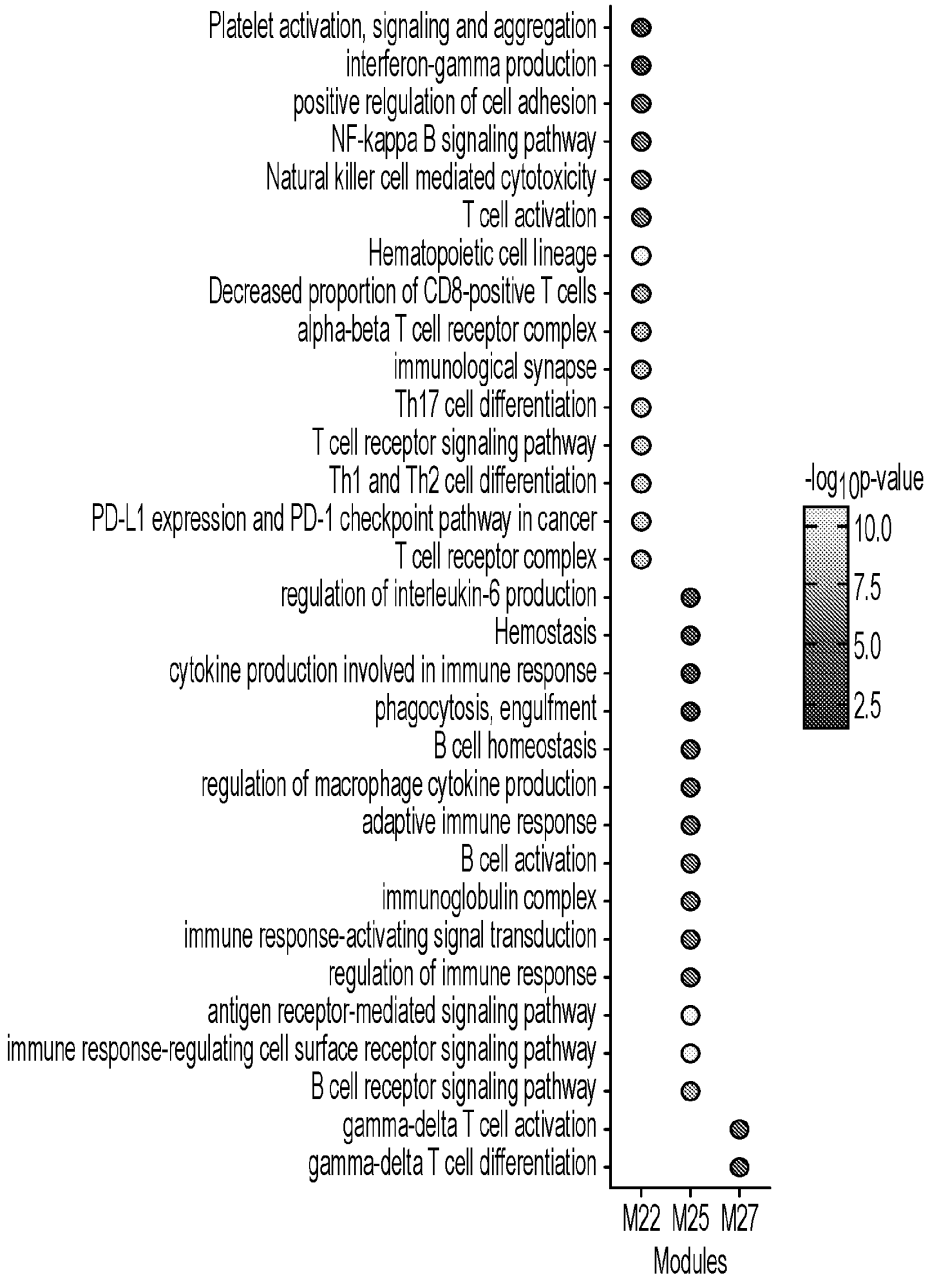

Platelet activation, signaling and aggregation
interferon-gamma production
positive relgulation of cell adhesion
NF-kappa B signaling pathway
Natural killer cell mediated cytotoxicity
T cell activation
Hematopoietic cell lineage
Decreased proportion of CD8-positive T cells
alpha-beta T cell receptor complex
immunological synapse
Th17 cell differentiation
T cell receptor signaling pathway
Th1 and Th2 cell differentiation
PD-L1 expression and PD-1 checkpoint pathway in cancer
T cell receptor complex
regulation of interleukin-6 production
Hemostasis
cytokine production involved in immune response
phagocytosis, engulfment
B cell homeostasis
regulation of macrophage cytokine production
adaptive immune response
B cell activation
immunoglobulin complex
immune response-activating signal transduction
regulation of immune response
antigen receptor-mediated signaling pathway
immune response-regulating cell surface receptor signaling pathway
B cell receptor signaling pathway
gamma-delta T cell activation
gamma-delta T cell differentiation
M22 M25 M27
Modules
-log10p-value
10.0
7.5
5.0
2.5

FIG. 19D

M22

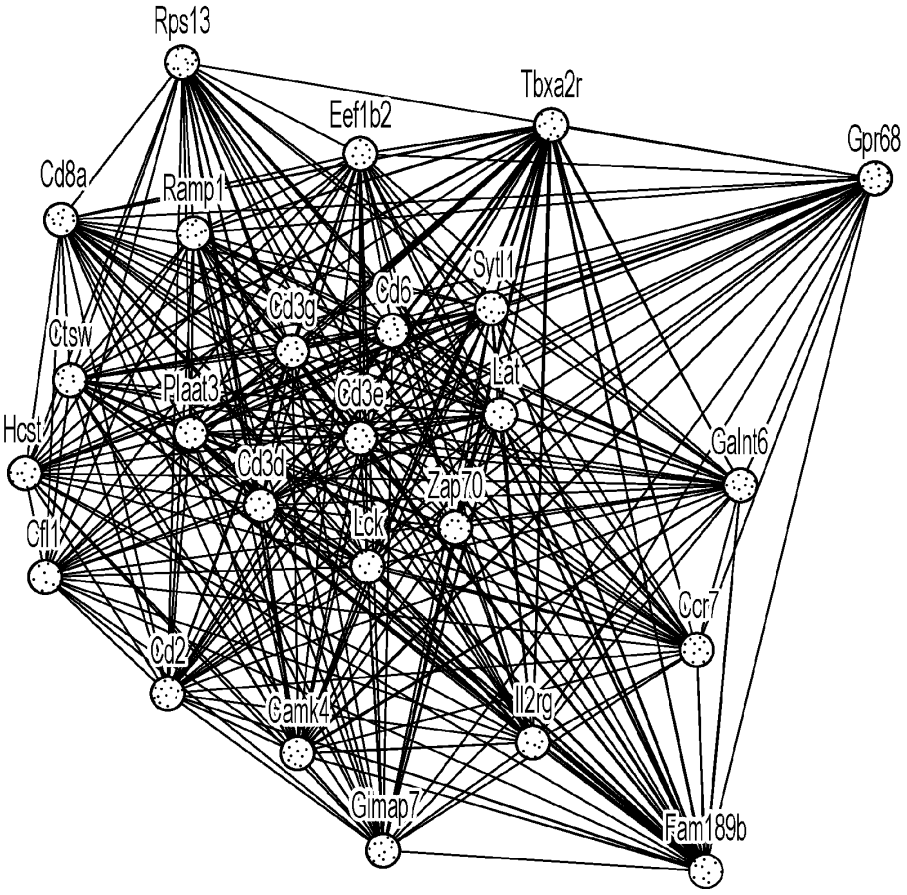

Rps13
Tbxa2r
Eef1b2
Gpr68
Cd8a
Ramp1
Sytl1
Cd6
Cd3g
Ctsw
Lat
Plaat3
Cd3e
Hcst
Galnt6
Cd3d
Zap70
Lck
Cfl1
Ccr7
Cd2
Il2rg
Gamk4
Gimap7
Fam189b

FIG. 19E

M25

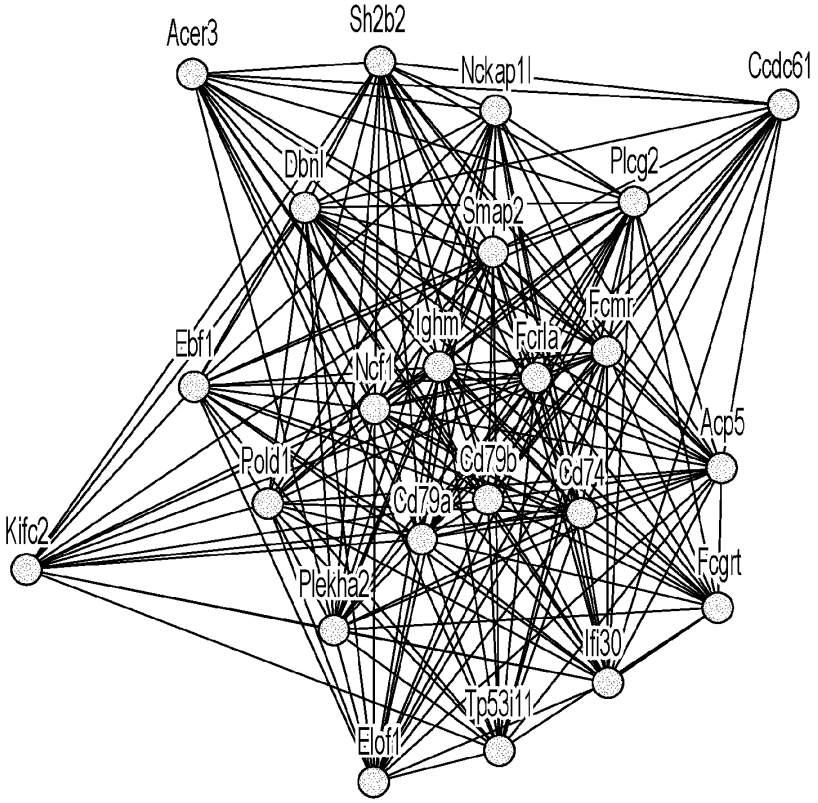

Acer3
Sh2b2
Nckap1l
Ccdc61
Dbnl
Plcg2
Smap2
Ebf1
Ighm
Fcmr
Fcrla
Ncf1
Acp5
Pold1
Cd79b
Cd74
Cd79a
Kifc2
Fcgrt
Plekha2
Ifi30
Tp53i11
Elof1

FIG. 19F

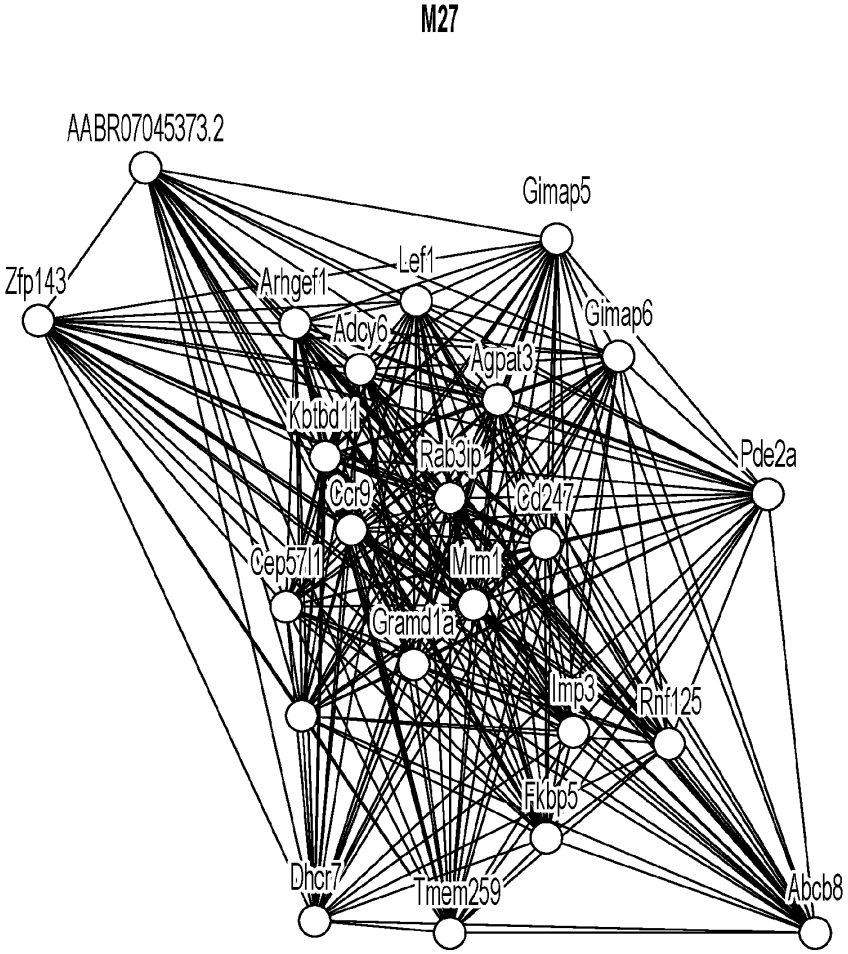

M27
AABR07045373.2
Gimap5
Zfp143
Arhgef1
Lef1
Adcy6
Gimap6
Agpat3
Kbtbd11
Rab3ip
Pde2a
Ccr9
Cd247
Cep57l1
Mrm1
Gramd1a
Imp3
Rnf125
Fkbp5
Dhcr7
Tmem259
Abcb8

FIG. 19G

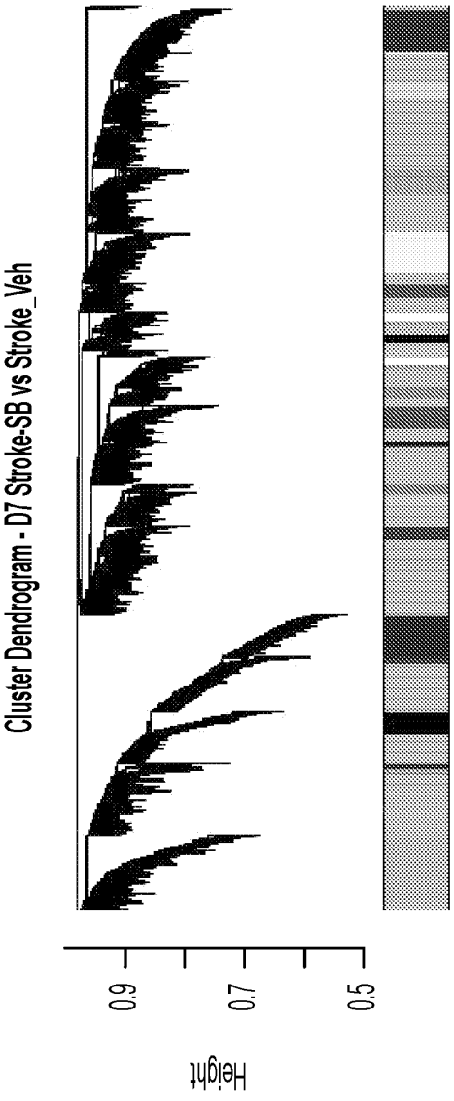

Cluster Dendrogram - D7 Stroke-SB vs Stroke_Veh
0.9
0.7
0.5
Height

FIG. 20A

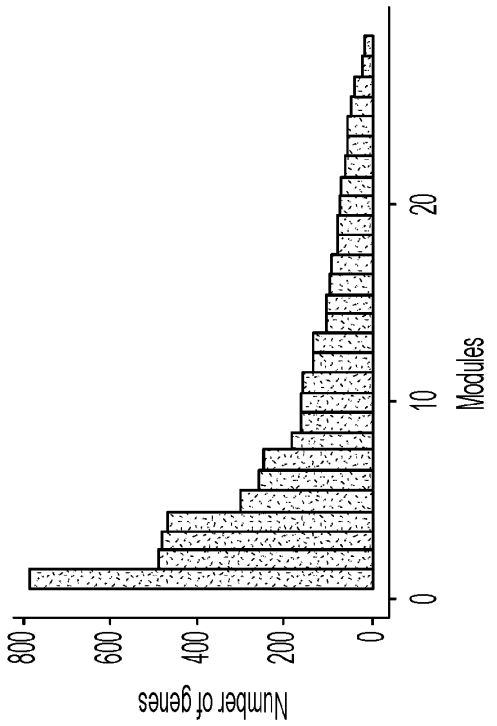


FIG. 20B

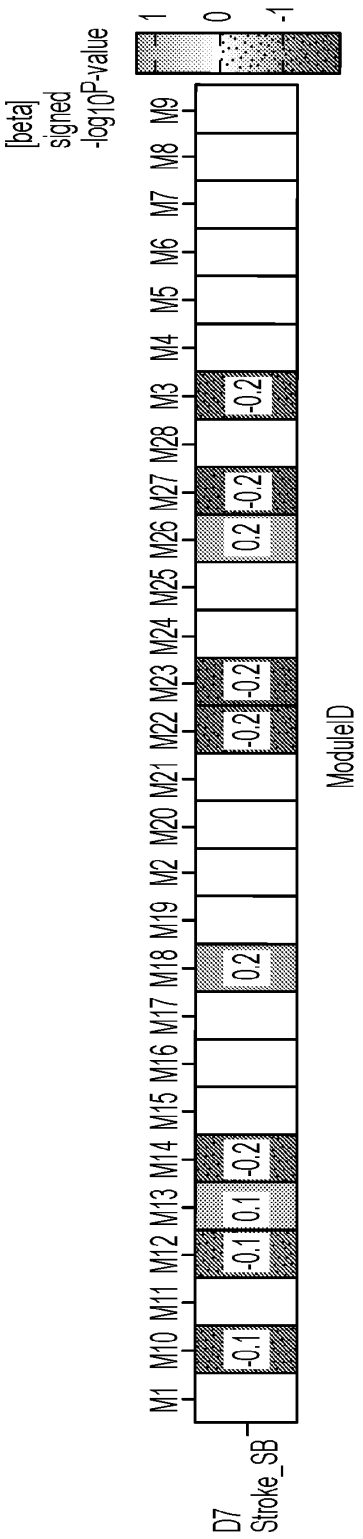

[beta]
signed
-log10P-value
1
0
-1
M9
M8
M7
M6
M5
M4
M3
M28
M27
M26
M25
M24
M23
M22
M21
M20
M2
M19
M18
M17
M16
M15
M14
M13
M12
M11
M10
M1
-0.2
-0.2
0.2
-0.2
-0.2
0.2
-0.2
0.1
-0.1
-0.1
ModuleID
D7
Stroke_SB

FIG. 20C

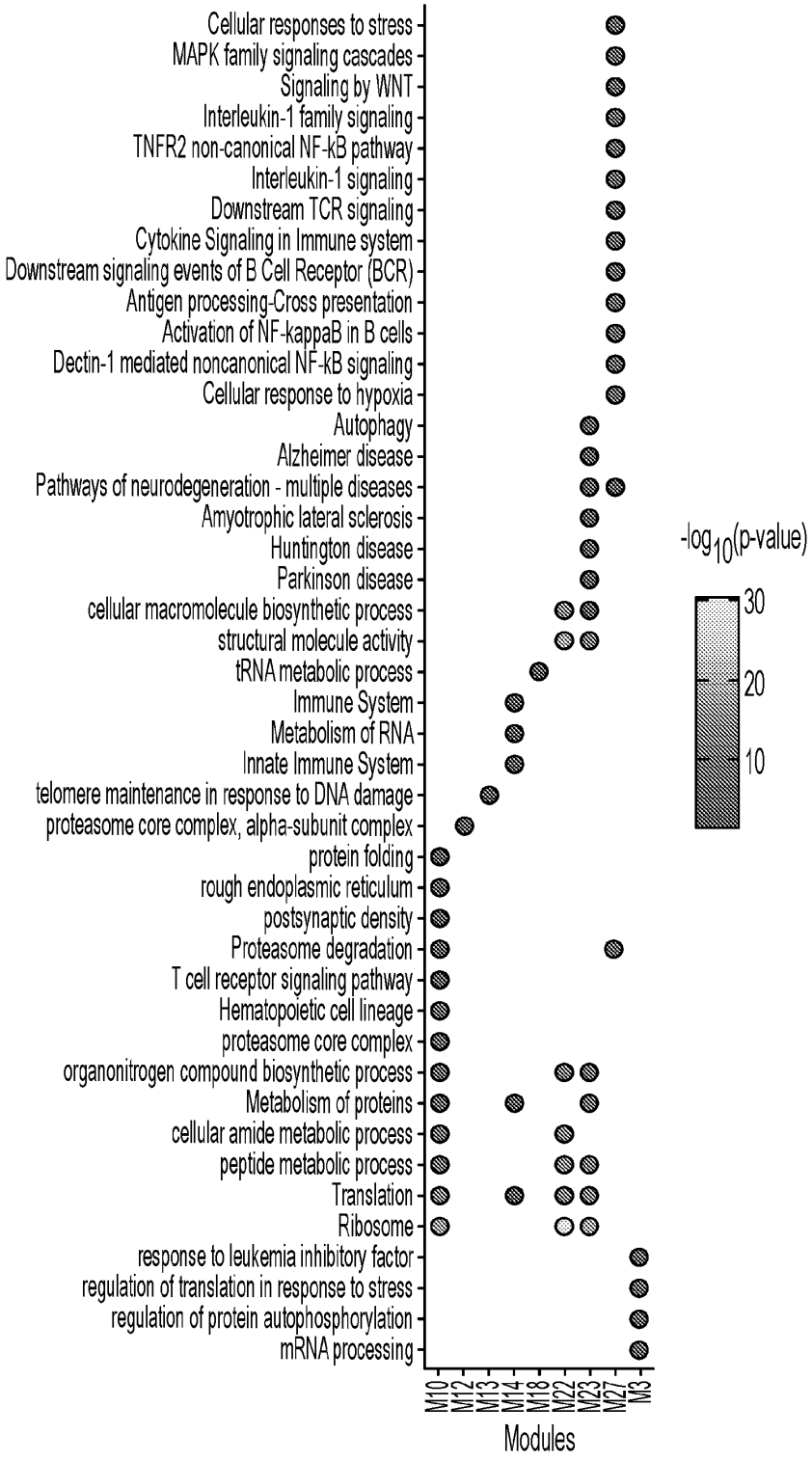

Cellular responses to stress
MAPK family signaling cascades
Signaling by WNT
Interleukin-1 family signaling
TNFR2 non-canonical NF-kB pathway
Interleukin-1 signaling
Downstream TCR signaling
Cytokine Signaling in Immune system
Downstream signaling events of B Cell Receptor (BCR)
Antigen processing-Cross presentation
Activation of NF-kappaB in B cells
Dectin-1 mediated noncanonical NF-kB signaling
Cellular response to hypoxia
Autophagy
Alzheimer disease
Pathways of neurodegeneration - multiple diseases
Amyotrophic lateral sclerosis
Huntington disease
Parkinson disease
cellular macromolecule biosynthetic process
structural molecule activity
tRNA metabolic process
Immune System
Metabolism of RNA
Innate Immune System
telomere maintenance in response to DNA damage
proteasome core complex, alpha-subunit complex
protein folding
rough endoplasmic reticulum
postsynaptic density
Proteasome degradation
T cell receptor signaling pathway
Hematopoietic cell lineage
proteasome core complex
organonitrogen compound biosynthetic process
Metabolism of proteins
cellular amide metabolic process
peptide metabolic process
Translation
Ribosome
response to leukemia inhibitory factor
regulation of translation in response to stress
regulation of protein autophosphorylation
mRNA processing
M10
M12
M13
M14
M18
M22
M23
M27
M3
Modules
-log10(p-value)
30
20
10

FIG. 20D

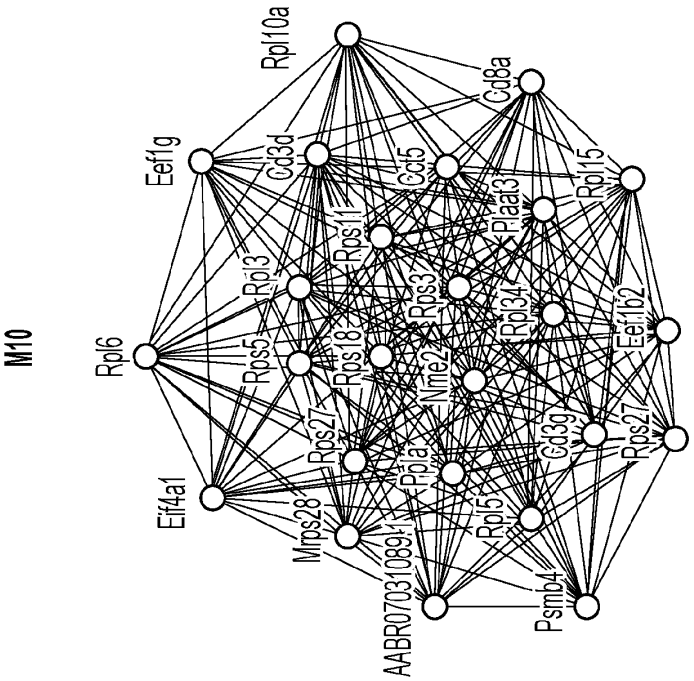


FIG. 20F

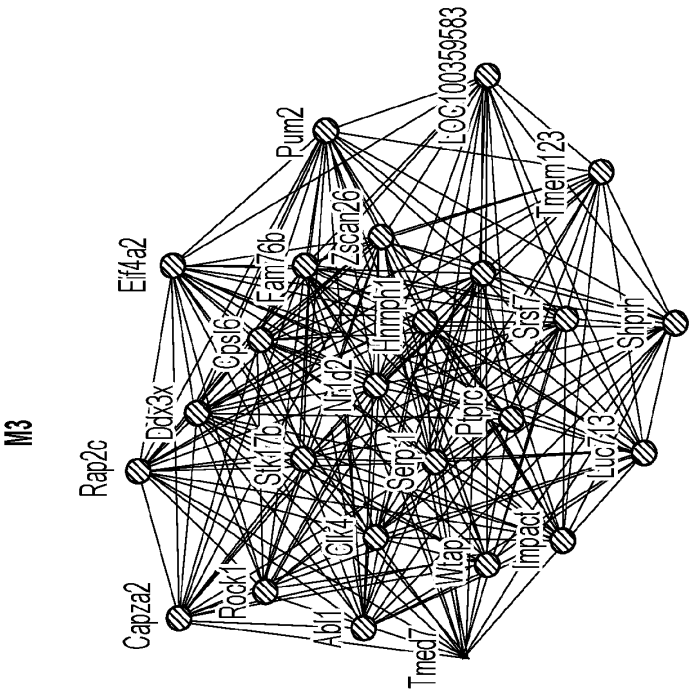


FIG. 20E

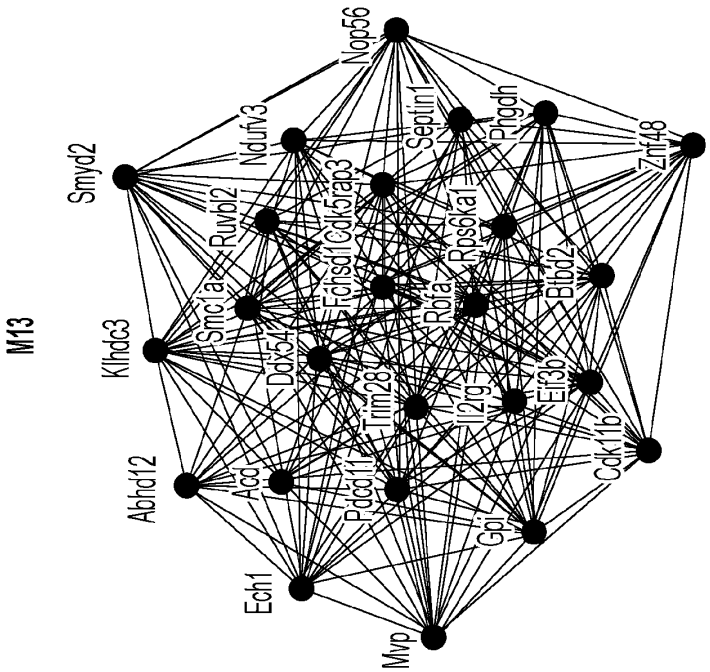


FIG. 20H

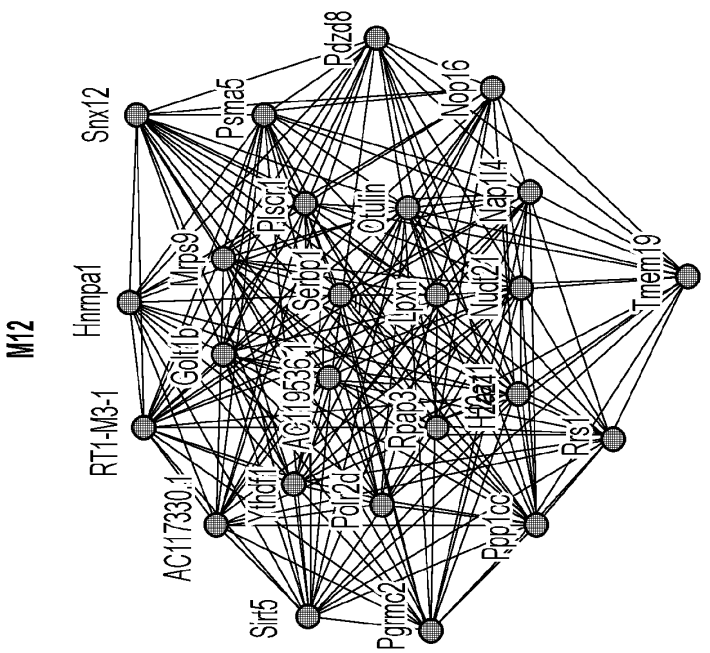


FIG. 20G

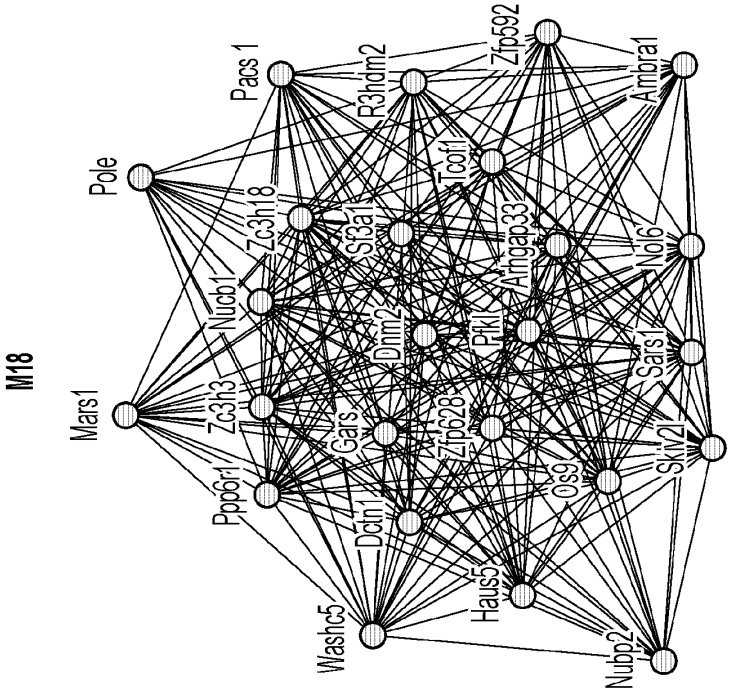


FIG. 20J

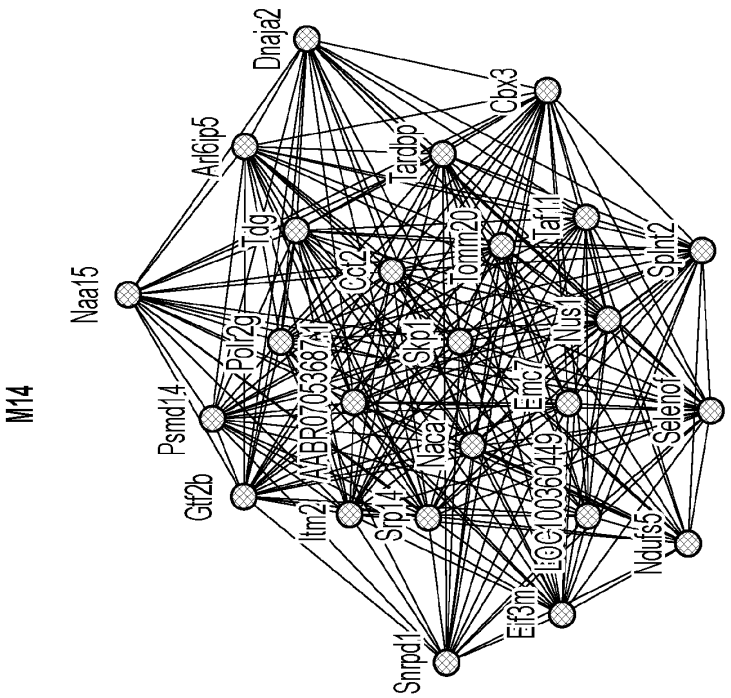


FIG. 20I

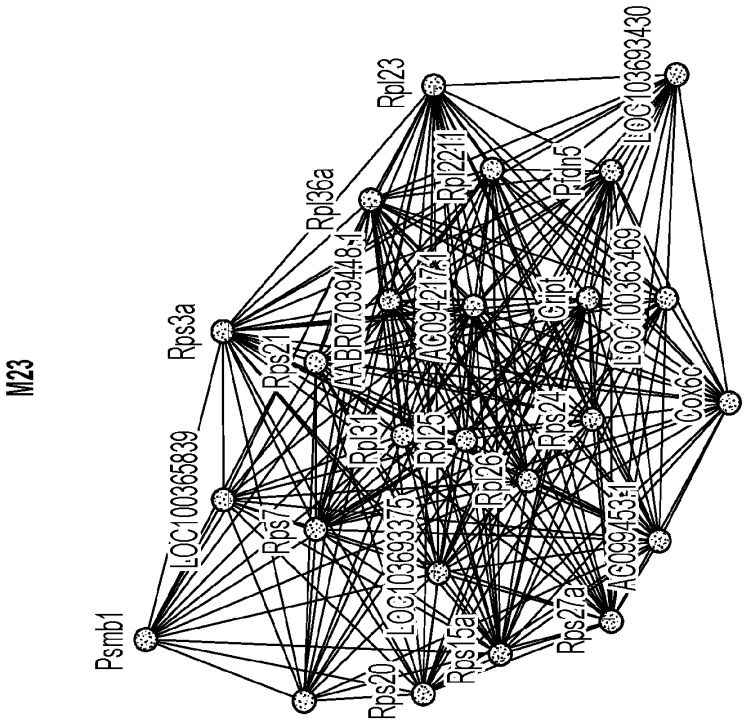


FIG. 20L

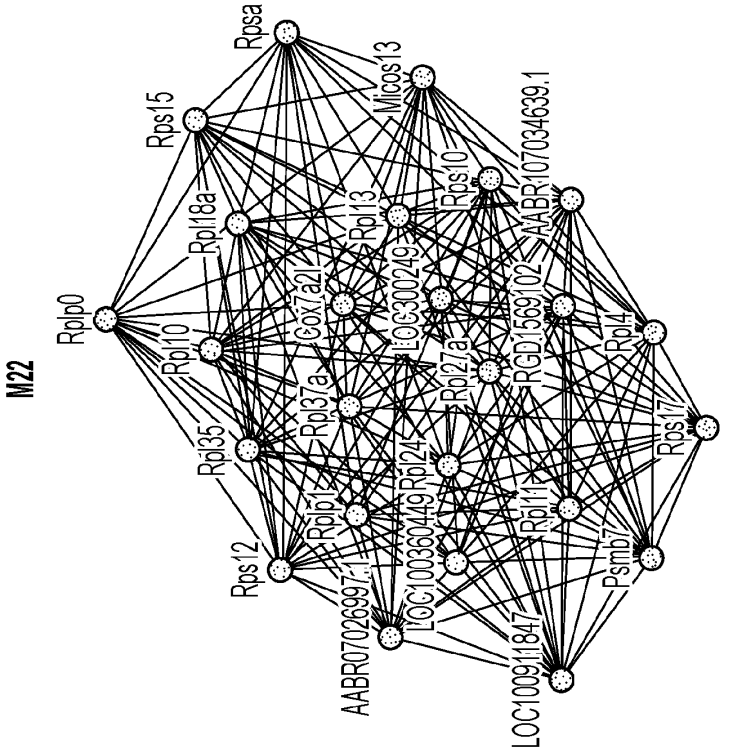


FIG. 20K

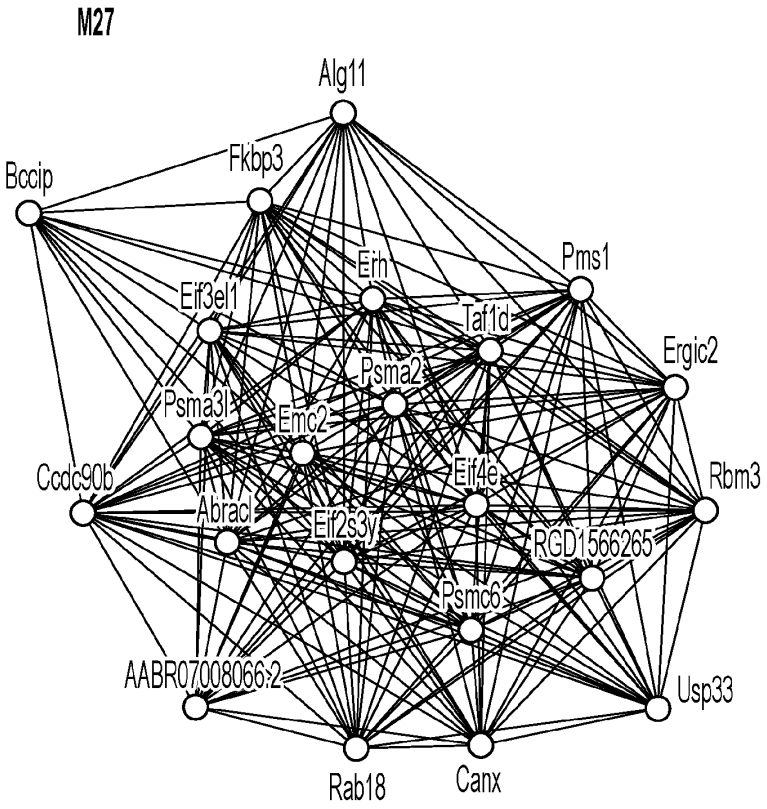

M27
Alg11
Fkbp3
Bccip
Eirh
Pms1
Eif3el1
Taf1d
Ergic2
Psma2
Psma3l
Emc2
Ccdc90b
Eif4e
Rbm3
Abraci
Eif2s3y
RGD1566265
Psmc6
AABR07008066.2
Usp33
Rab18
Canx

FIG. 20M

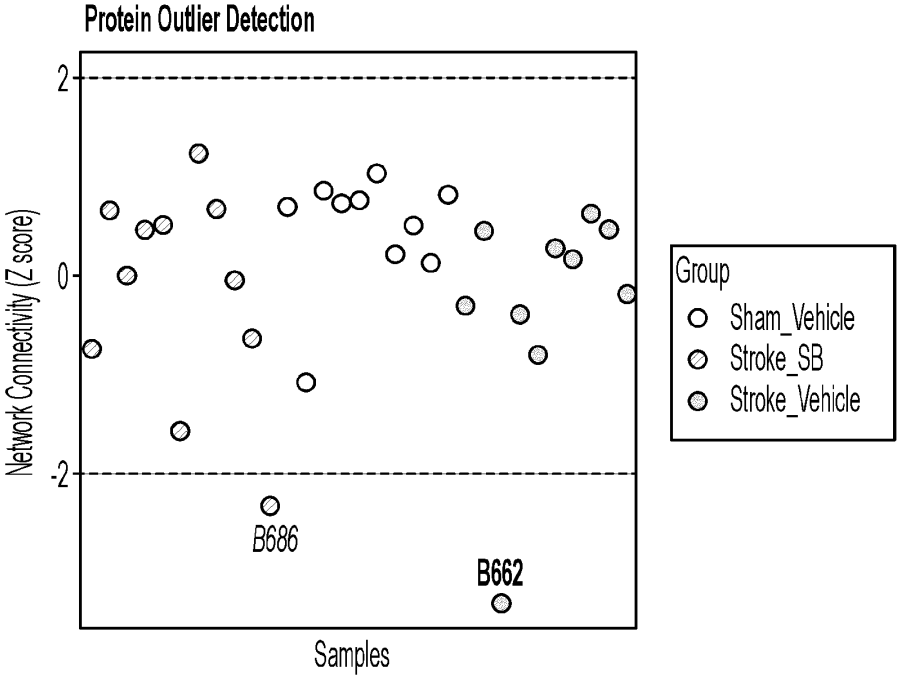

Protein Outlier Detection
2
0
-2
Network Connectivity (Z score)
B686
B662
Samples
Group
Sham_Vehicle
Stroke_SB
Stroke_Vehicle

FIG. 21A

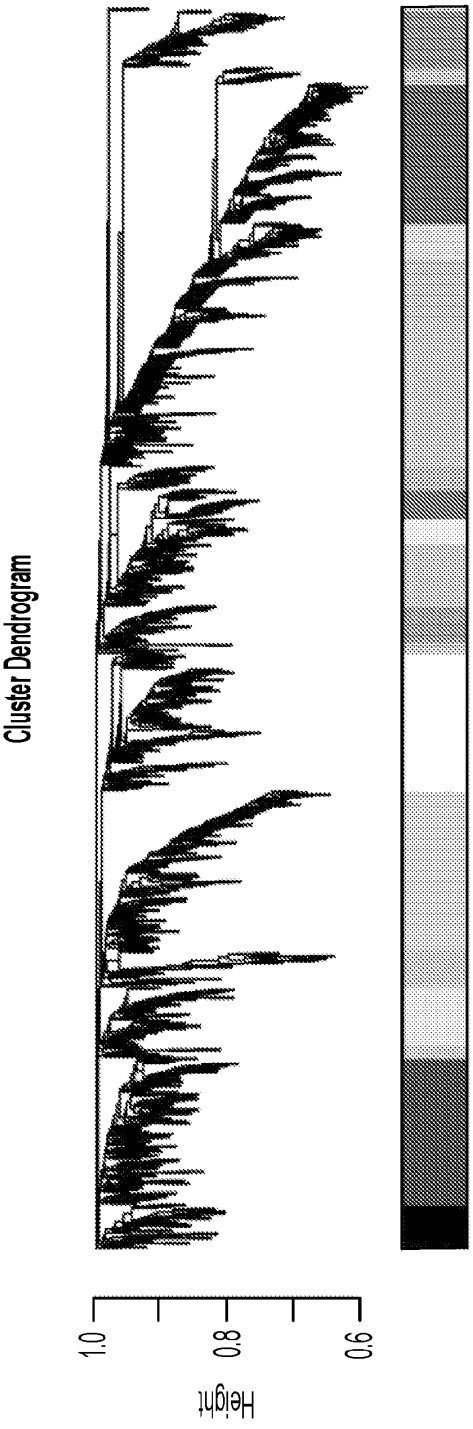


FIG. 21B

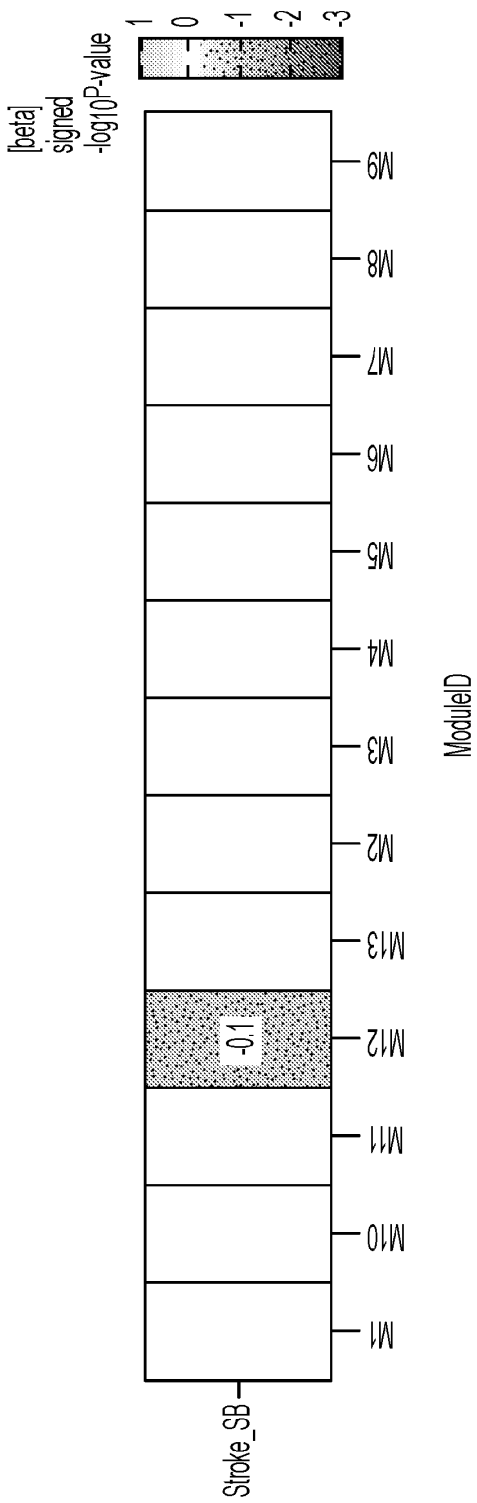

[beta]
signed
-log10^P-value
1
0
-1
-2
-3
M9
M8
M7
M6
M5
M4
M3
M2
M13
M12
-0.1
M11
M10
M1
ModuleID
Stroke_SB

FIG. 21C

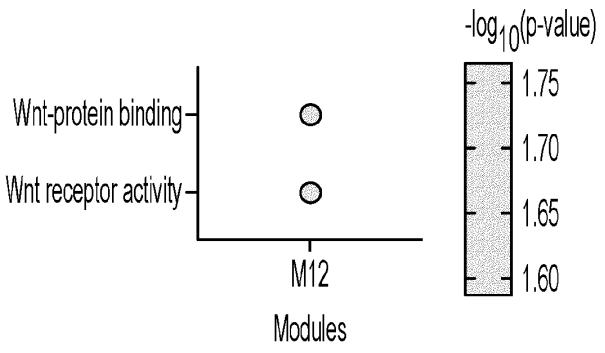

-log10(p-value)
1.75
1.70
1.65
1.60
Wnt-protein binding
Wnt receptor activity
M12
Modules

FIG. 21D

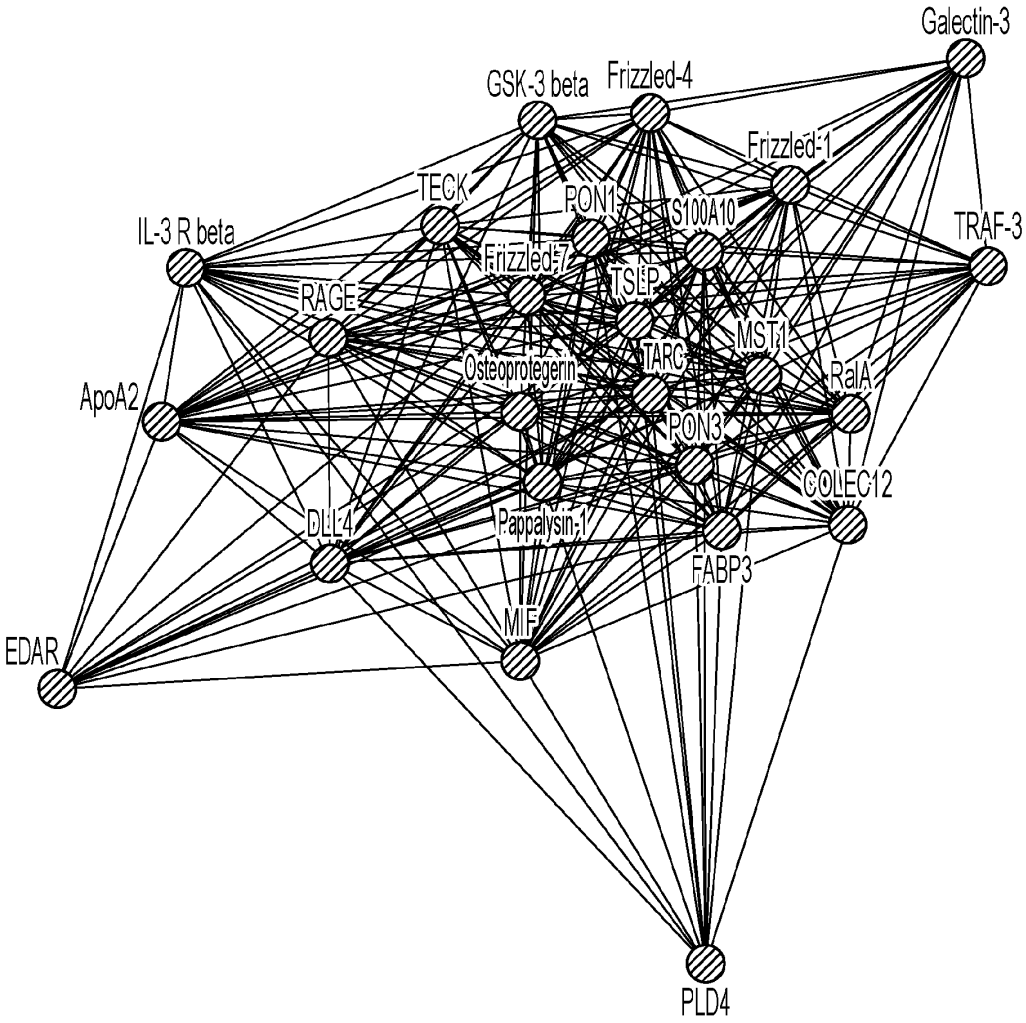

Galectin-3
GSK-3 beta
Frizzled-4
Frizzled-1
TECK
PON1
S100A10
IL-3 R beta
TRAF-3
Frizzled-7
TSLP
RAGE
MST1
TARC
Osteoprotegerin
RalA
ApoA2
PON3
COLEC12
DLL4
Pappalysin-1
FABP3
MIF
EDAR
PLD4

FIG. 21E

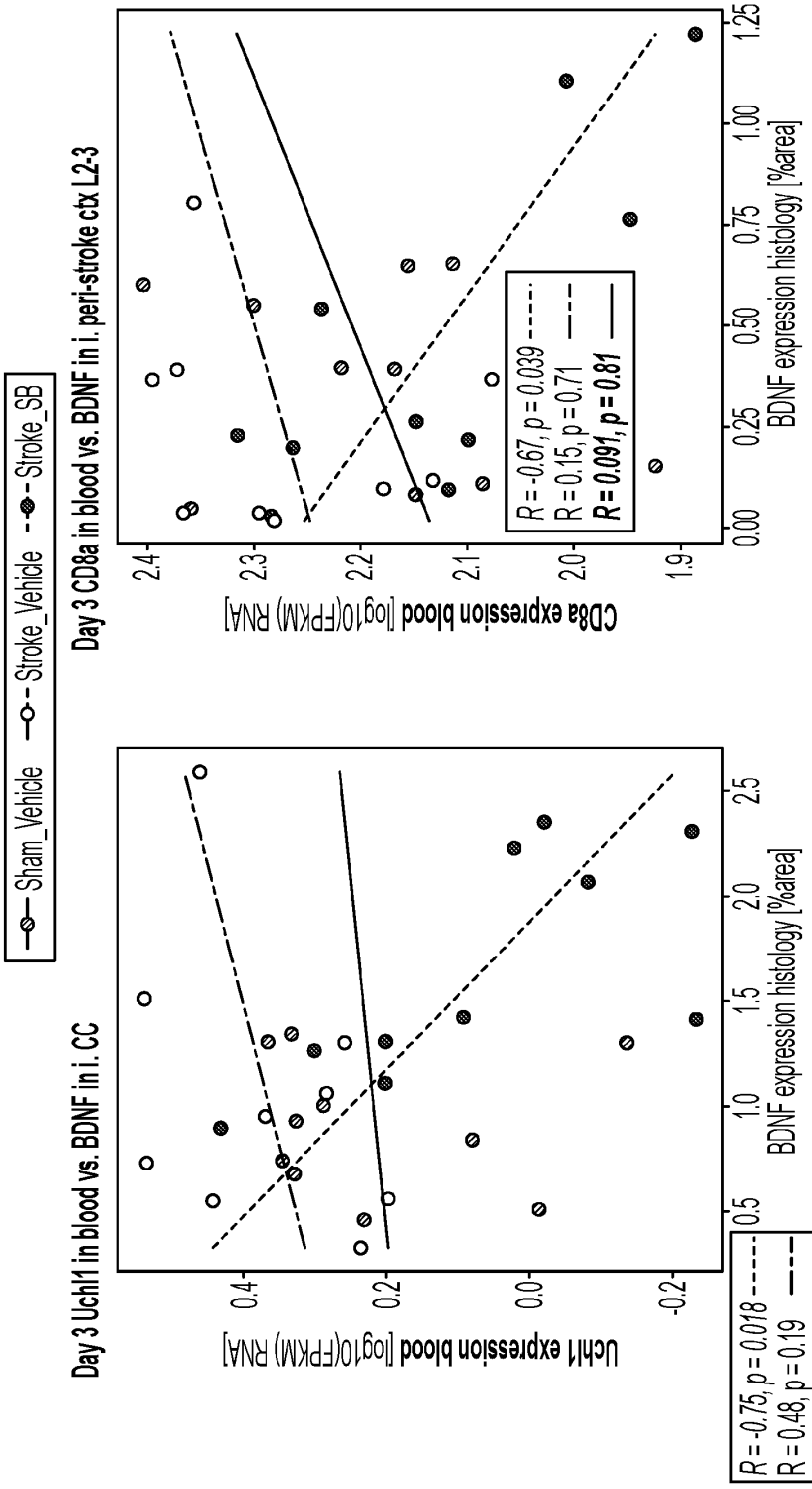

Sham_Vehicle
Stroke_Vehicle
Stroke_SB
Day 3 Uchl1 in blood vs. BDNF in i. CC
Uchl1 expression blood [log10(FPKM) RNA]
BDNF expression histology [%area]
R = -0.75, p = 0.018
R = 0.48, p = 0.19
R = 0.32, p = 0.37
Day 3 CD8a in blood vs. BDNF in i. peri-stroke ctx L2-3
CD8a expression blood [log10(FPKM) RNA]
BDNF expression histology [%area]
R = -0.67, p = 0.039
R = 0.15, p = 0.71
R = 0.091, p = 0.81

FIG. 22A

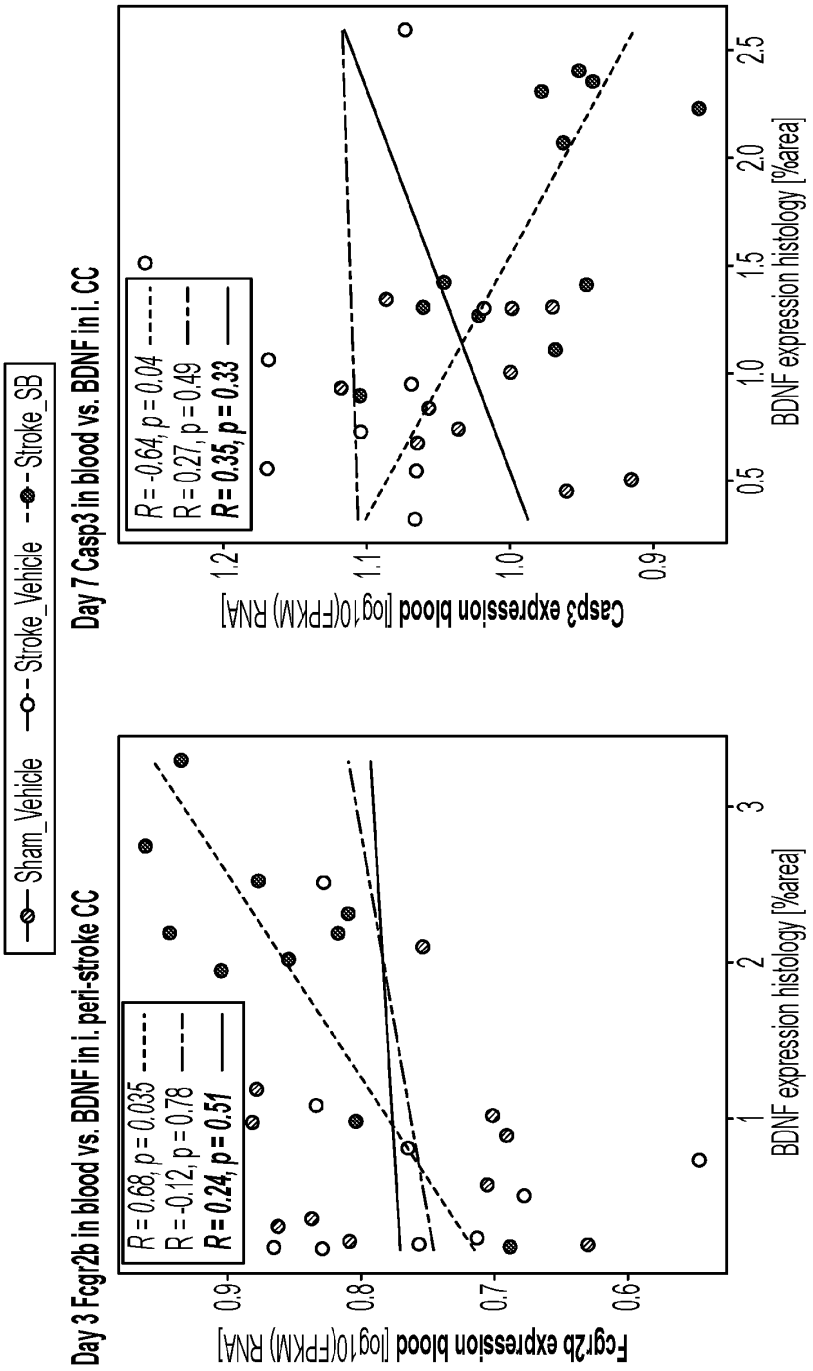

Sham_Vehicle
Stroke_Vehicle
Stroke_SB
Day 3 Fcgr2b in blood vs. BDNF in i. peri-stroke CC
R = 0.68, p = 0.035
R = -0.12, p = 0.78
R = 0.24, p = 0.51
Fcgr2b expression blood [log10(FPKM) RNA]
BDNF expression histology [%area]
Day 7 Casp3 in blood vs. BDNF in i. CC
R = -0.64, p = 0.04
R = 0.27, p = 0.49
R = 0.35, p = 0.33
Casp3 expression blood [log10(FPKM) RNA]
BDNF expression histology [%area]

FIG. 22B

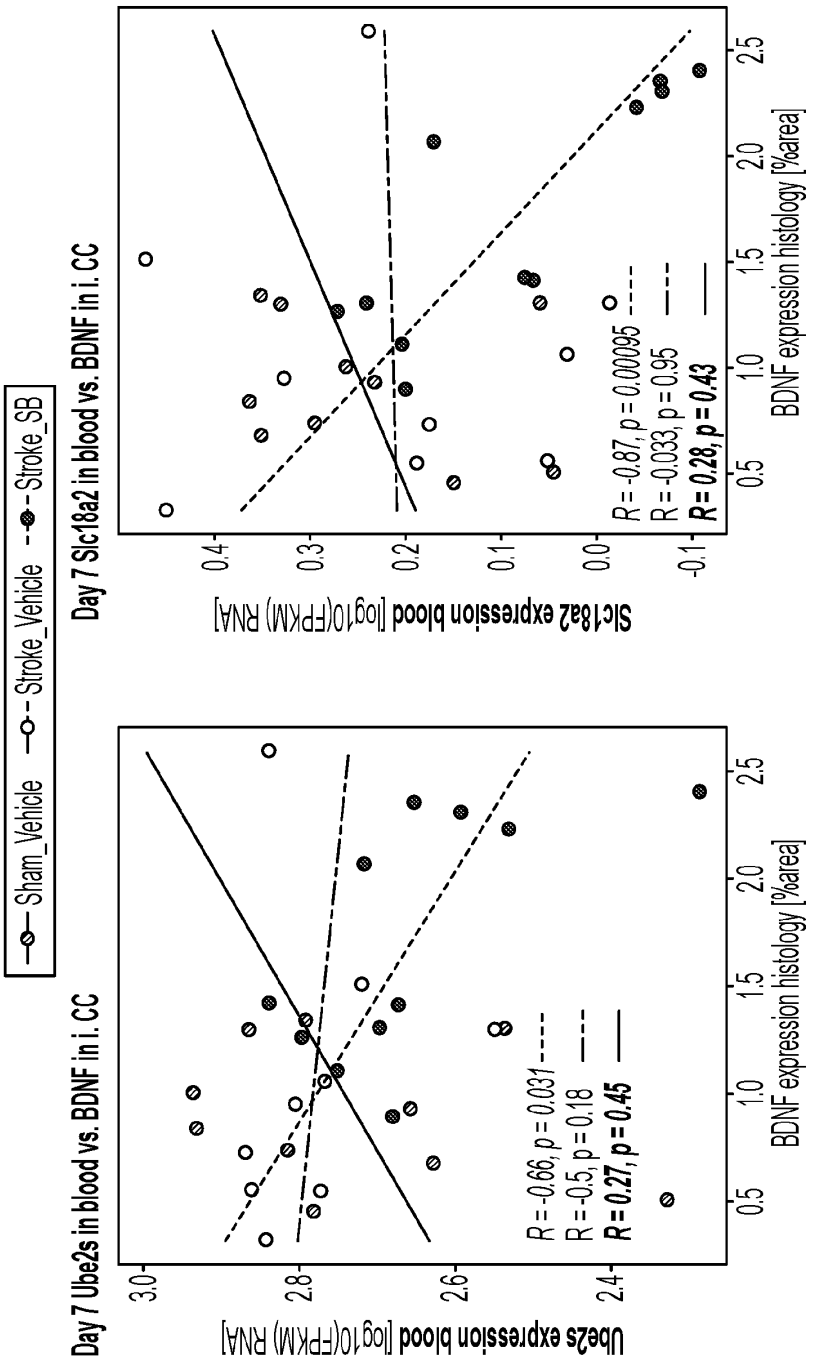

Sham_Vehicle
Stroke_Vehicle
Stroke_SB
Day 7 Ube2s in blood vs. BDNF in i. CC
Ube2s expression blood [log10(FPKM) RNA]
BDNF expression histology [%area]
R = -0.66, p = 0.031
R = -0.5, p = 0.18
R = 0.27, p = 0.45
Day 7 Slc18a2 in blood vs. BDNF in i. CC
Slc18a2 expression blood [log10(FPKM) RNA]
BDNF expression histology [%area]
R = -0.87, p = 0.00095
R = -0.033, p = 0.95
R = 0.28, p = 0.43

FIG. 22C

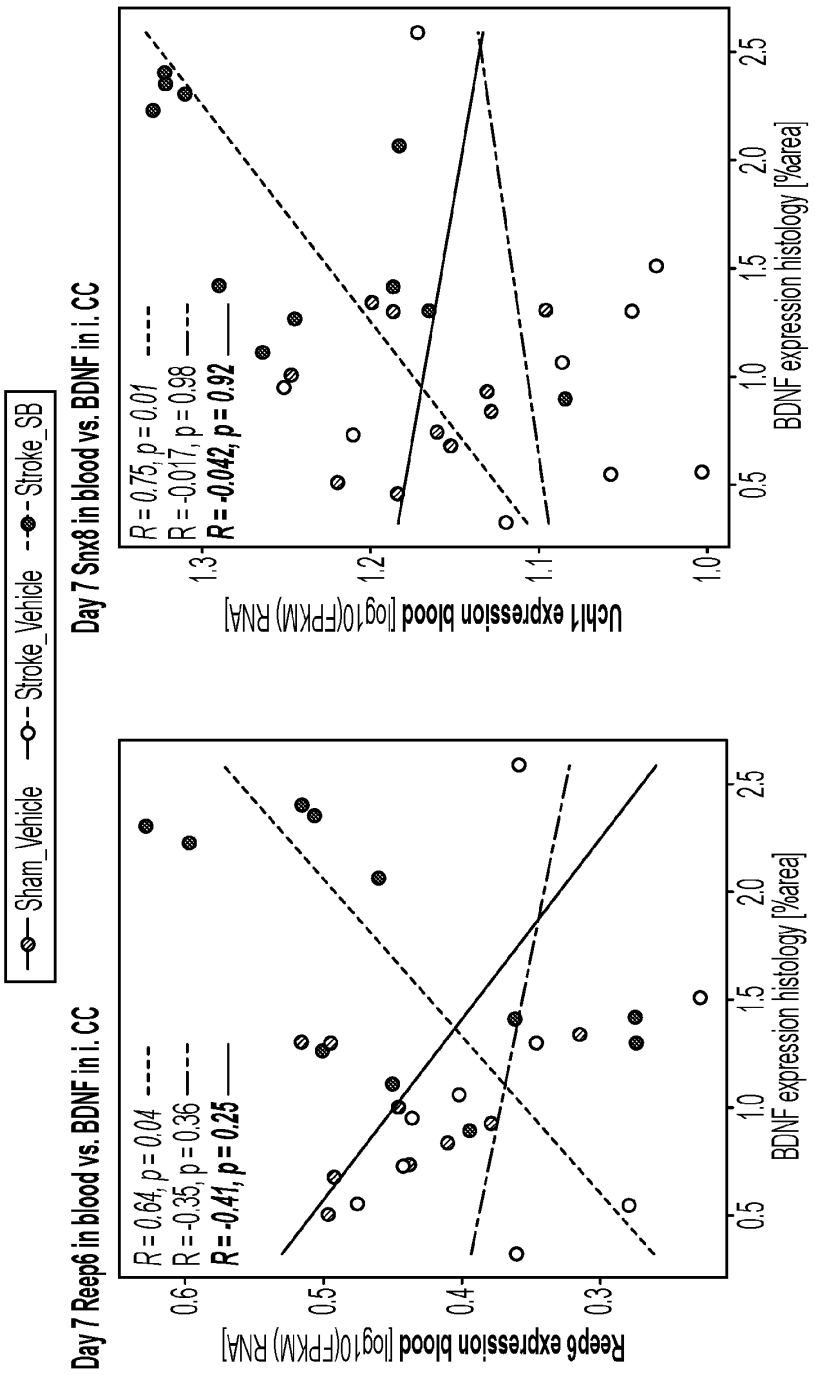

Sham_Vehicle
Stroke_Vehicle
Stroke_SB
Day 7 Reep6 in blood vs. BDNF in i. CC
R = 0.64, p = 0.04
R = -0.35, p = 0.36
R = -0.41, p = 0.25
Reep6 expression blood [log10(FPKM) RNA]
BDNF expression histology [%area]
Day 7 Snx8 in blood vs. BDNF in i. CC
R = 0.75, p = 0.01
R = -0.017, p = 0.98
R = -0.042, p = 0.92
Uchl1 expression blood [log10(FPKM) RNA]
BDNF expression histology [%area]

FIG. 22D

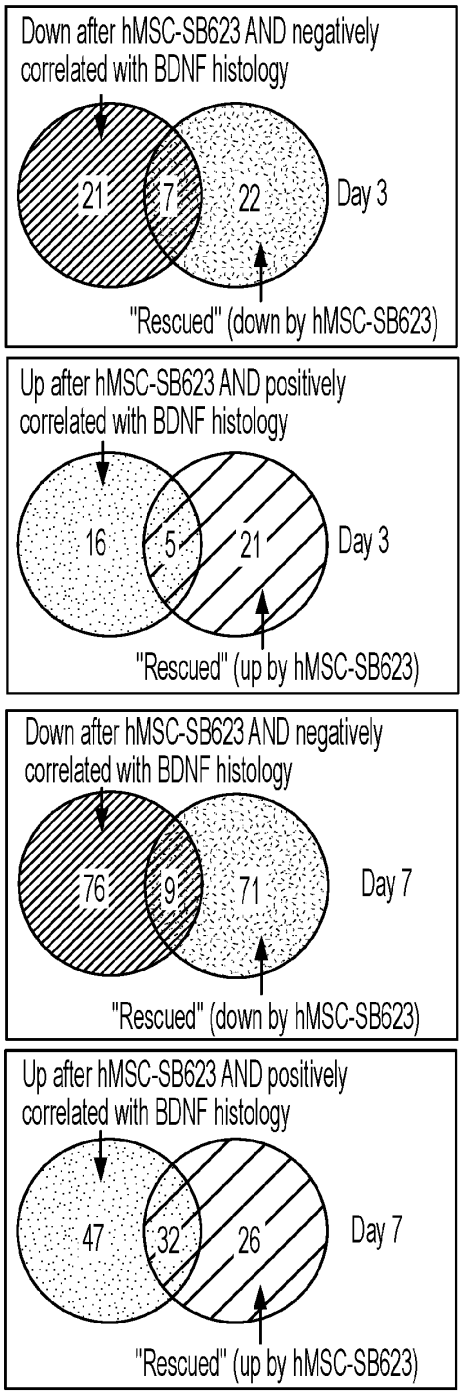

Down after hMSC-SB623 AND negatively correlated with BDNF histology
21
7
22
Day 3
"Rescued" (down by hMSC-SB623)
Up after hMSC-SB623 AND positively correlated with BDNF histology
16
5
21
Day 3
"Rescued" (up by hMSC-SB623)
Down after hMSC-SB623 AND negatively correlated with BDNF histology
76
9
71
Day 7
"Rescued" (down by hMSC-SB623)
Up after hMSC-SB623 AND positively correlated with BDNF histology
47
32
26
Day 7
"Rescued" (up by hMSC-SB623)

FIG. 22E