FIG.1

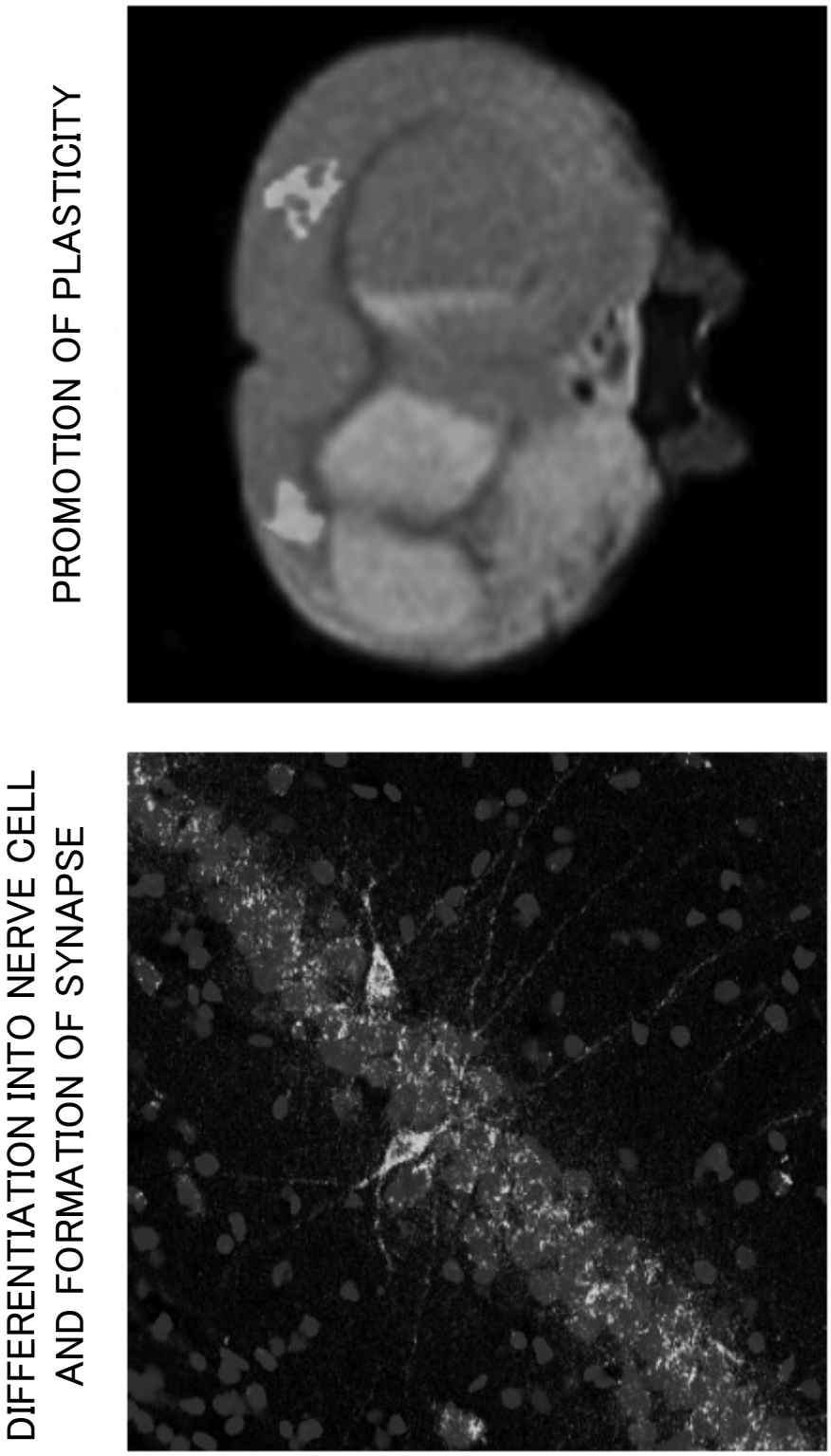

DIFFERENTIATION INTO NERVE CELL
AND FORMATION OF SYNAPSE
PROMOTION OF PLASTICITY

FIG.2

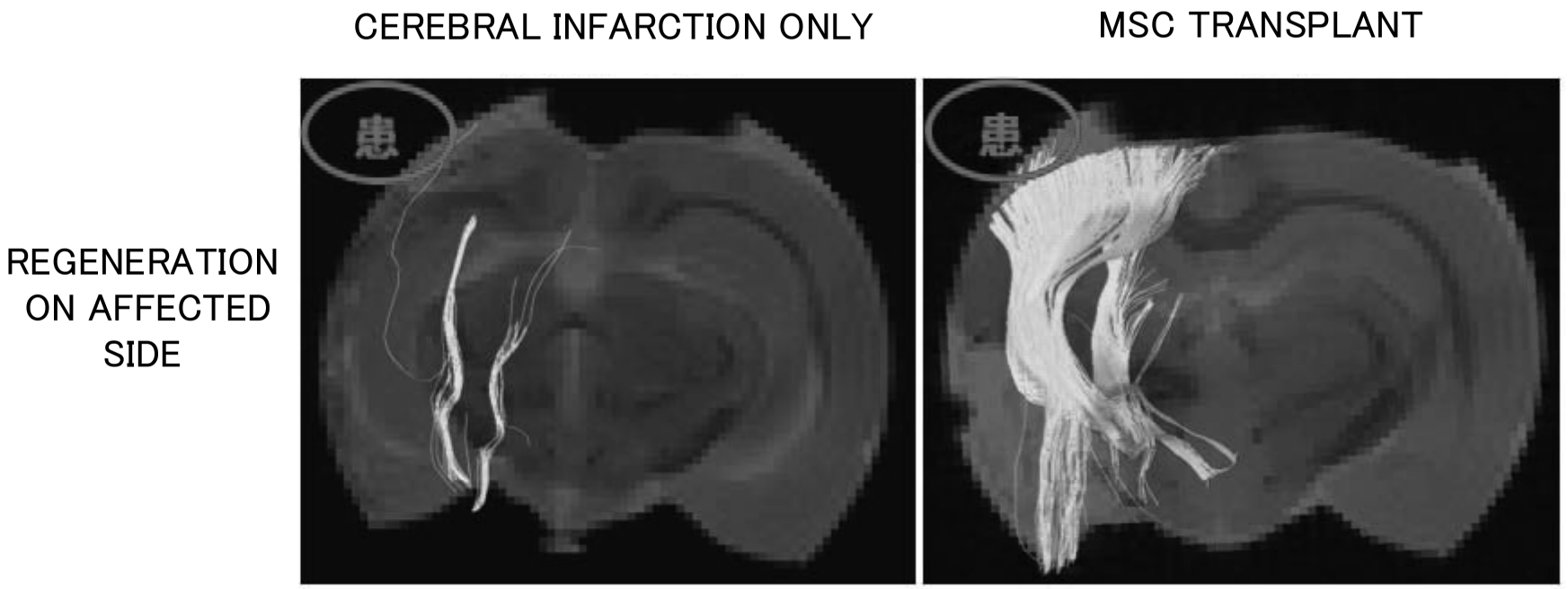

CEREBRAL INFARCTION ONLY
MSC TRANSPLANT
REGENERATION ON AFFECTED SIDE
患
患

FIG.3

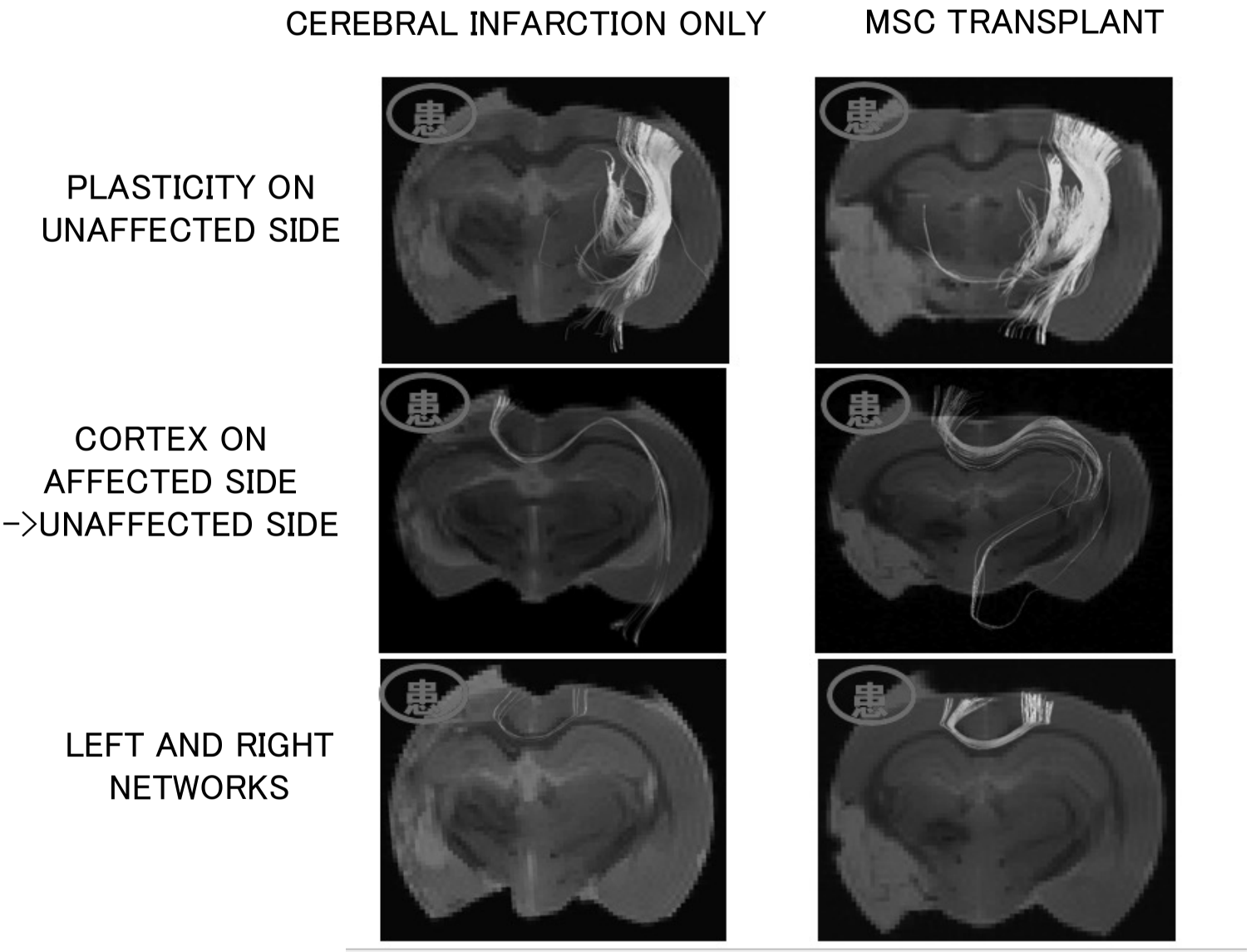

CEREBRAL INFARCTION ONLY
MSC TRANSPLANT
PLASTICITY ON UNAFFECTED SIDE
CORTEX ON AFFECTED SIDE ->UNAFFECTED SIDE
LEFT AND RIGHT NETWORKS
患

FIG.4

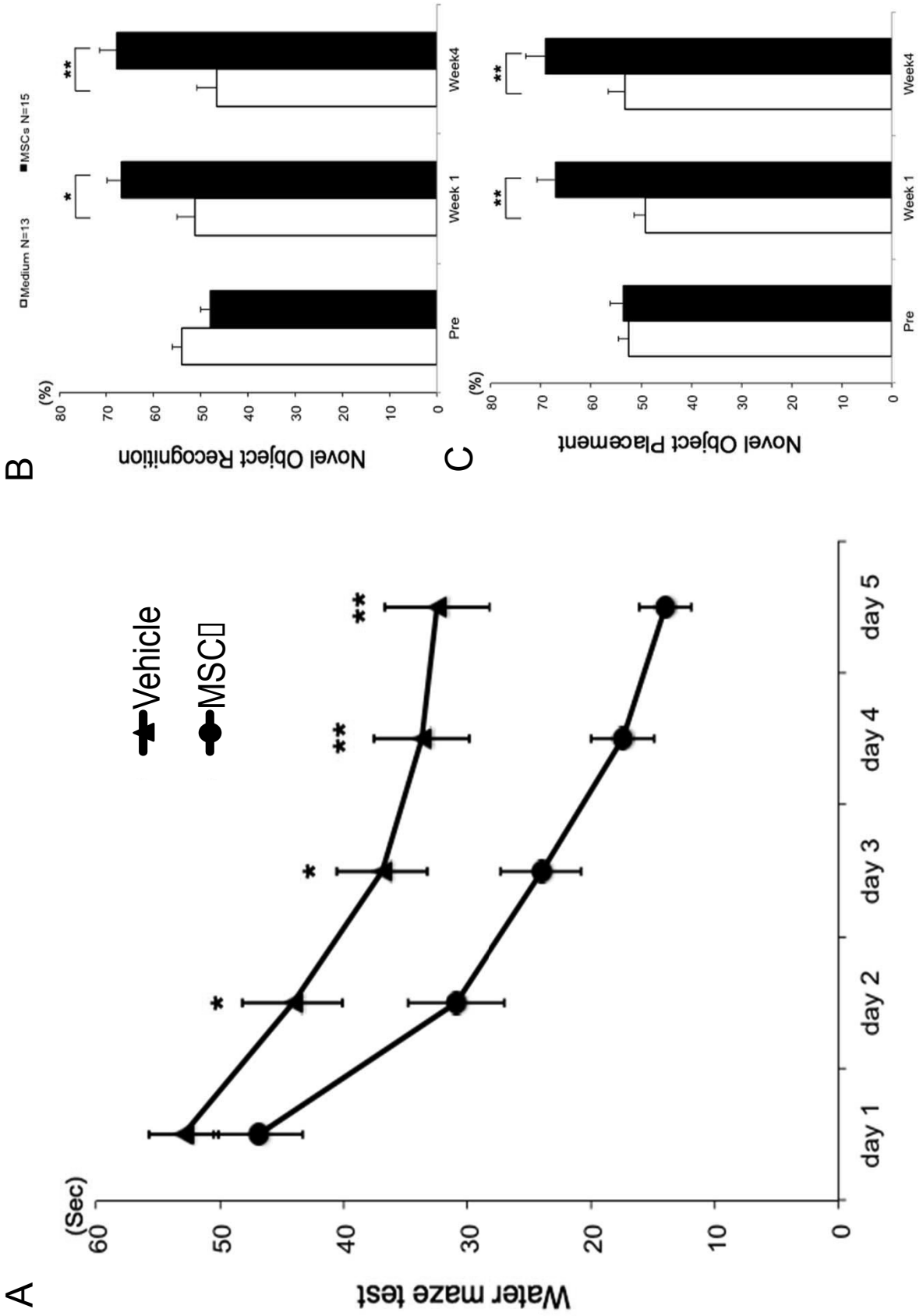

A
Water maze test
(Sec)
60
50
40
30
20
10
0
day 1
day 2
day 3
day 4
day 5
Vehicle
MSC
*
*
**
**
B
Novel Object Recognition
(%)
80
70
60
50
40
30
20
10
0
Medium N=13
MSCs N=15
Pre
Week 1
Week4
*
**
C
Novel Object Placement
(%)
80
70
60
50
40
30
20
10
0
Pre
Week 1
Week4
**
**

FIG.5

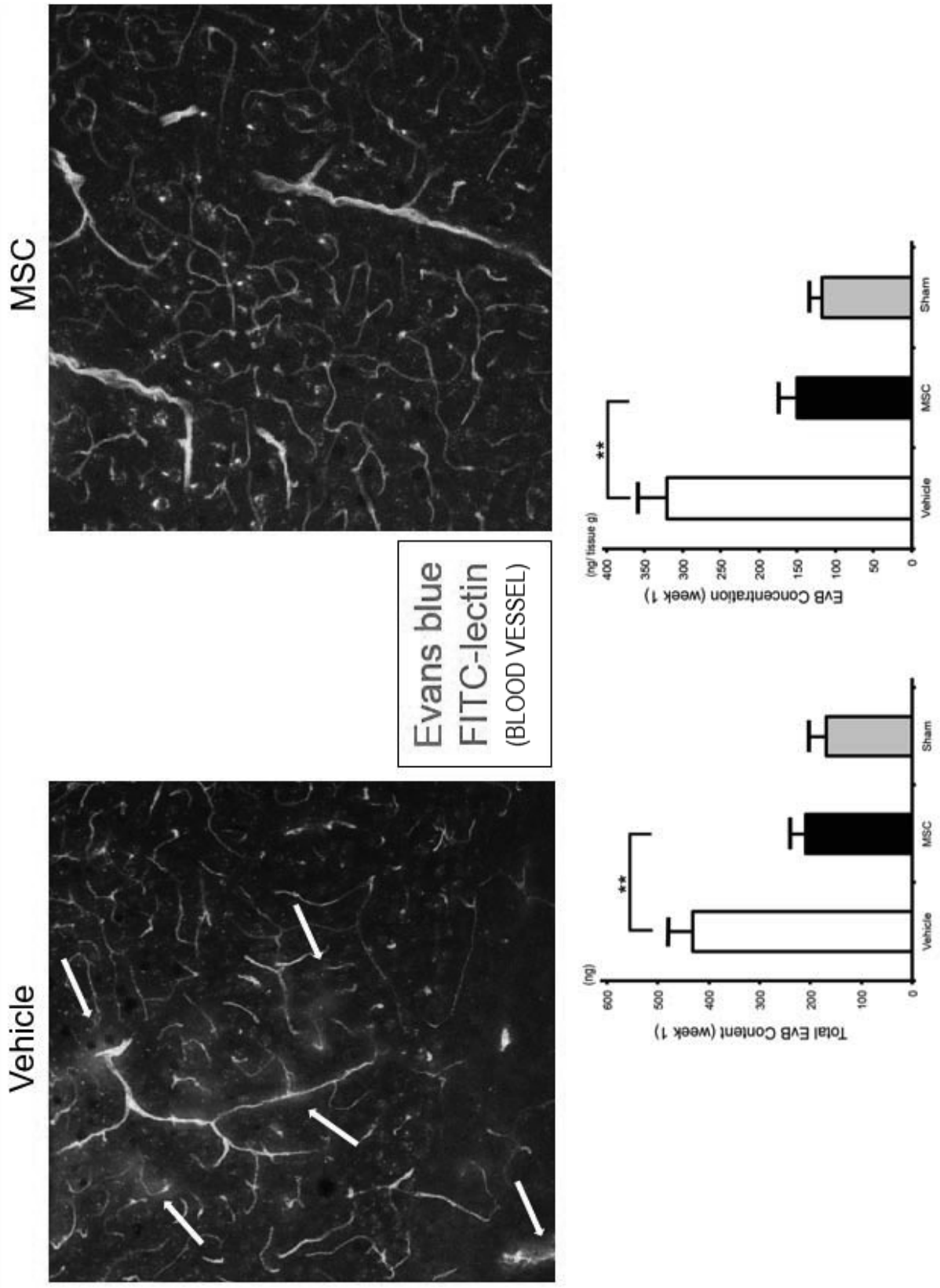

MSC
Vehicle
Evans blue
FITC-lectin
(BLOOD VESSEL)
EVB Concentration (week 1)
(ng/ tissue g)
400
350
300
250
200
150
100
50
0
**
Vehicle
MSC
Sham
Total EVB Content (week 1)
(ng)
600
500
400
300
200
100
0
**
Vehicle
MSC
Sham

FIG.6

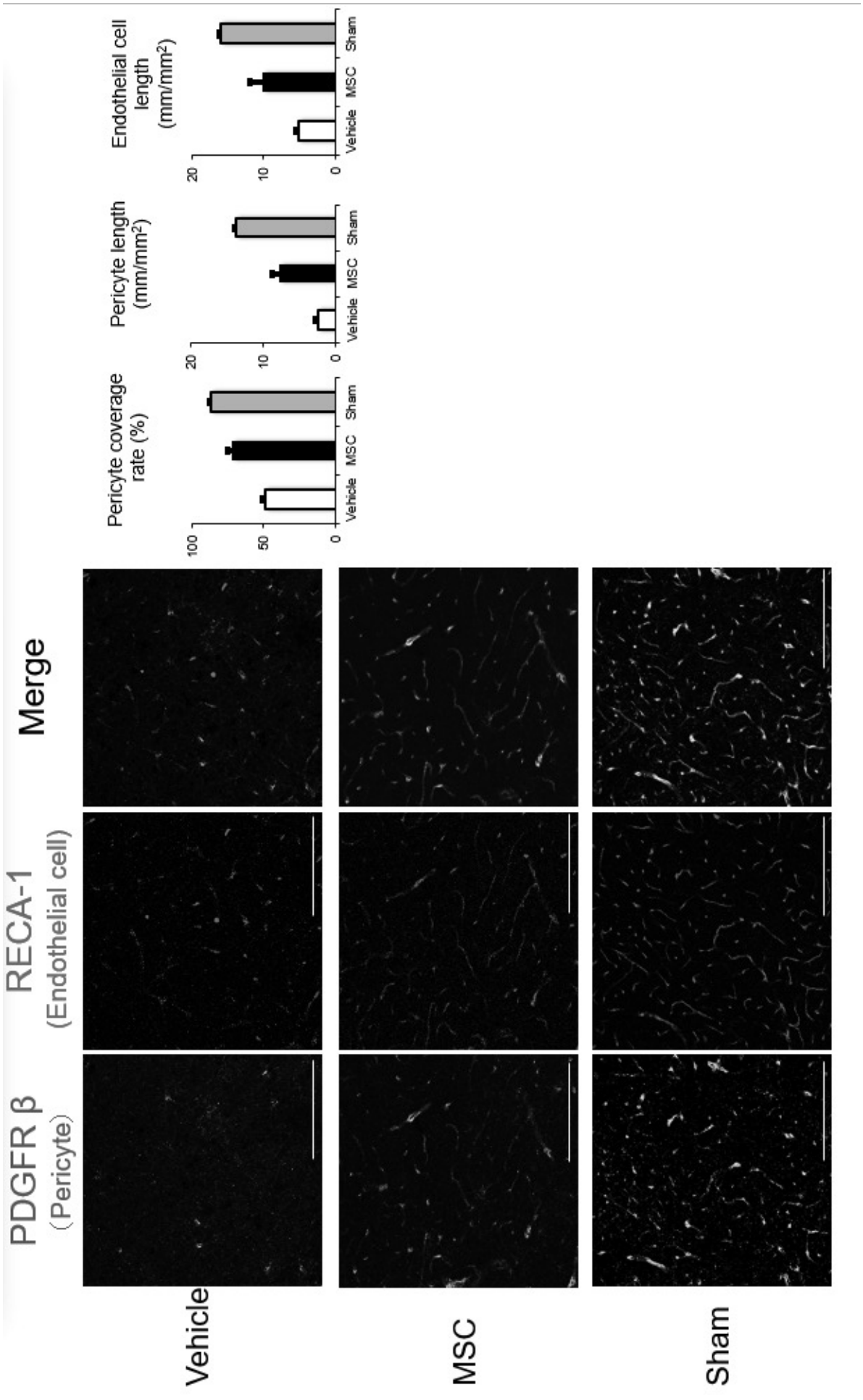

PDGFR β
(Pericyte)
RECA-1
(Endothelial cell)
Merge
Vehicle
MSC
Sham
Pericyte coverage rate (%)
Pericyte length (mm/mm²)
Endothelial cell length (mm/mm²)
Vehicle
MSC
Sham
0
50
100
10
20

FIG.7

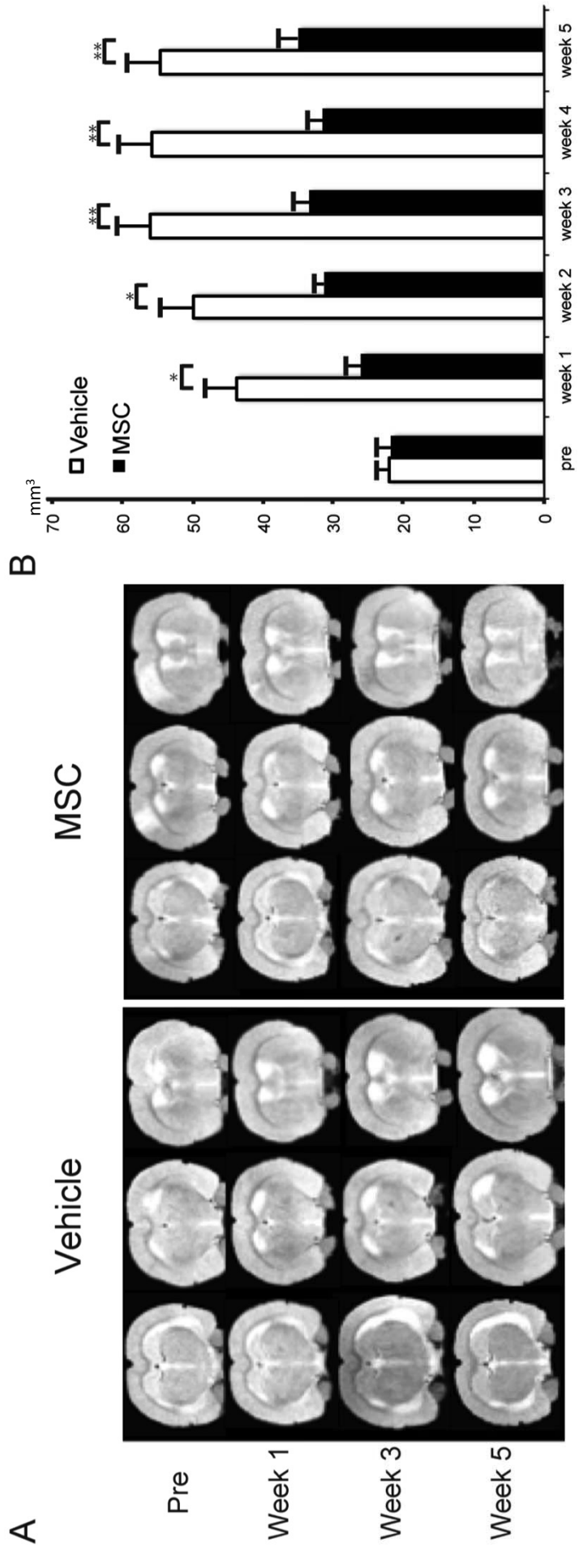

A
Vehicle
MSC
Pre
Week 1
Week 3
Week 5
B
mm3
70
60
50
40
30
20
10
0
Vehicle
MSC
pre
week 1
week 2
week 3
week 4
week 5
*
*
**
**
**

FIG.8

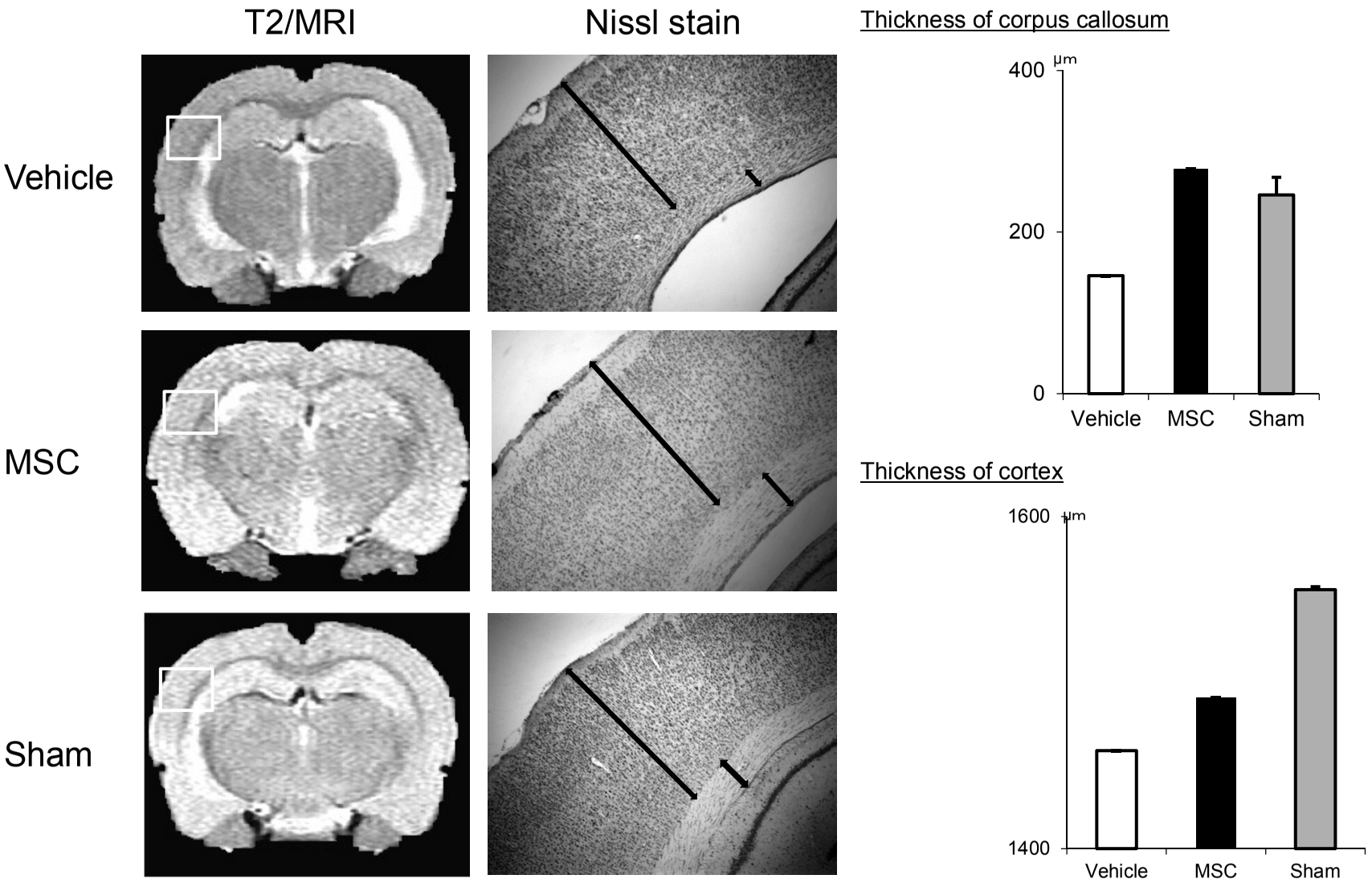

T2/MRI
Nissl stain
Vehicle
MSC
Sham
Thickness of corpus callosum
400 μm
200
0
Vehicle
MSC
Sham
Thickness of cortex
1600 μm
1400
Vehicle
MSC
Sham

FIG.9

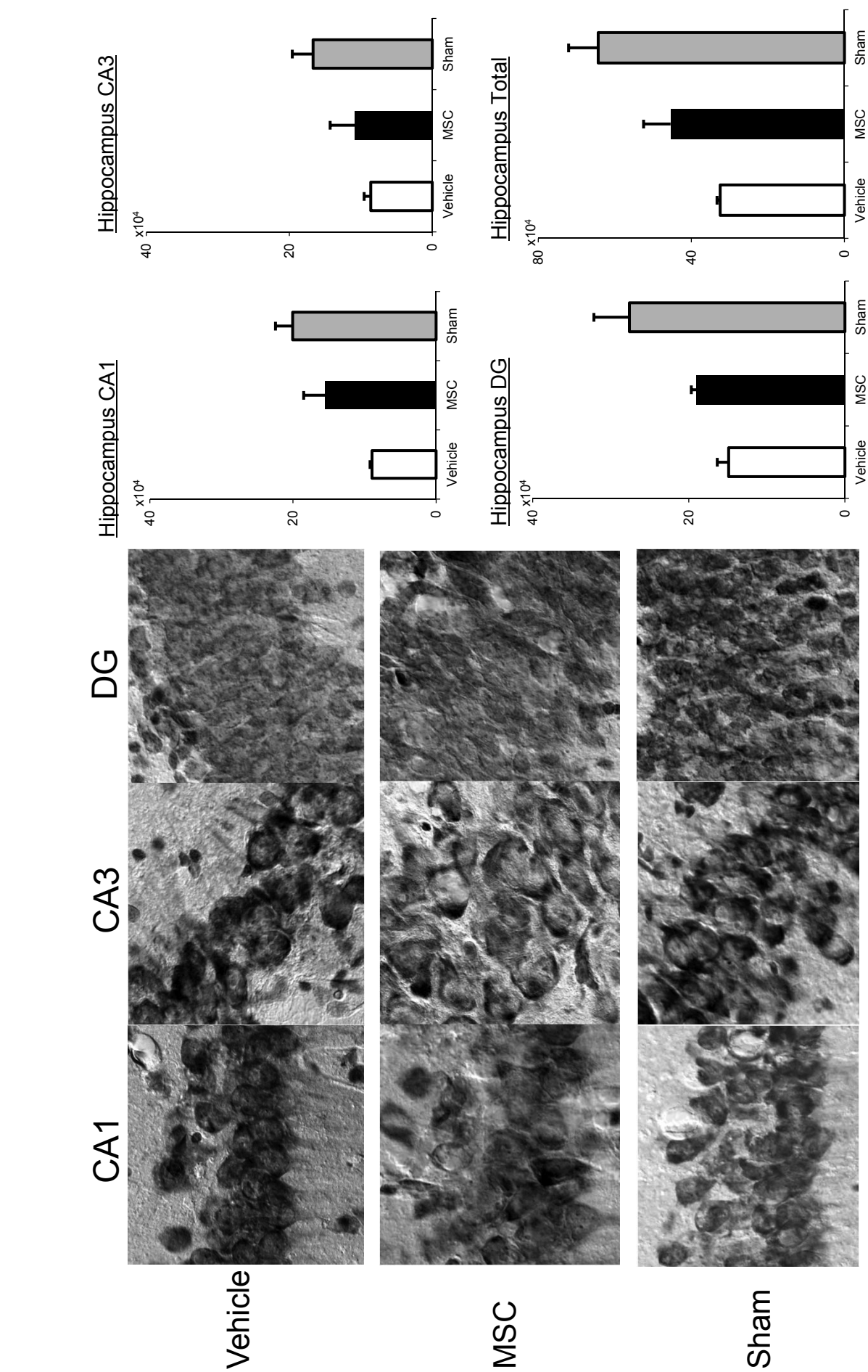

CA1
CA3
DG
Vehicle
MSC
Sham
Hippocampus CA1
Hippocampus CA3
Hippocampus DG
Hippocampus Total
x10^4
0
20
40
80
Vehicle
MSC
Sham

FIG.10

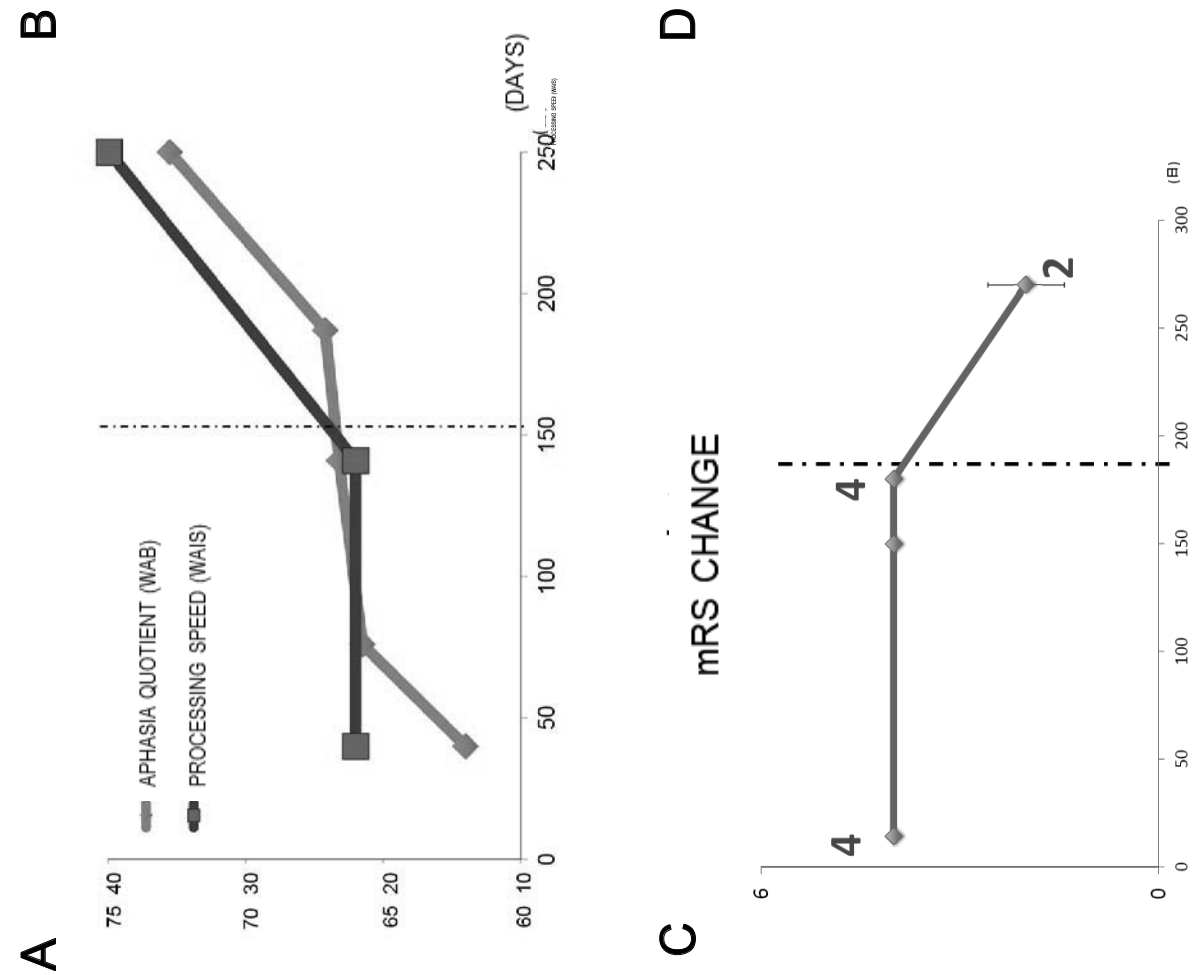

A
APHASIA QUOTIENT (WAB)
PROCESSING SPEED (WAIS)
(DAYS)
B
PRIMARY ENDPOINT
PERCENTAGE OF THOSE WITH IMPROVEMENT BY ONE OR MORE mRS LEVELS
100 %
75%
ACTIVE DRUG IMPROVEMENT BY 1 mRS GRADE (PRIMARY ENDPOINT)
ACTIVE DRUG IMPROVEMENT BY 2 mRS GRADES (SECONDARY ENDPOINT)
C
mRS CHANGE
4
4
2
D
UPPER LIMB FUGL MEYER SCORE
ADMINISTRATION ON DAY 156
TOTAL UPPER LIMB
WRIST
FINGER
AFTER ONSET
CLINICAL TRIAL 1
CLINICAL TRIAL 2

FIG.11

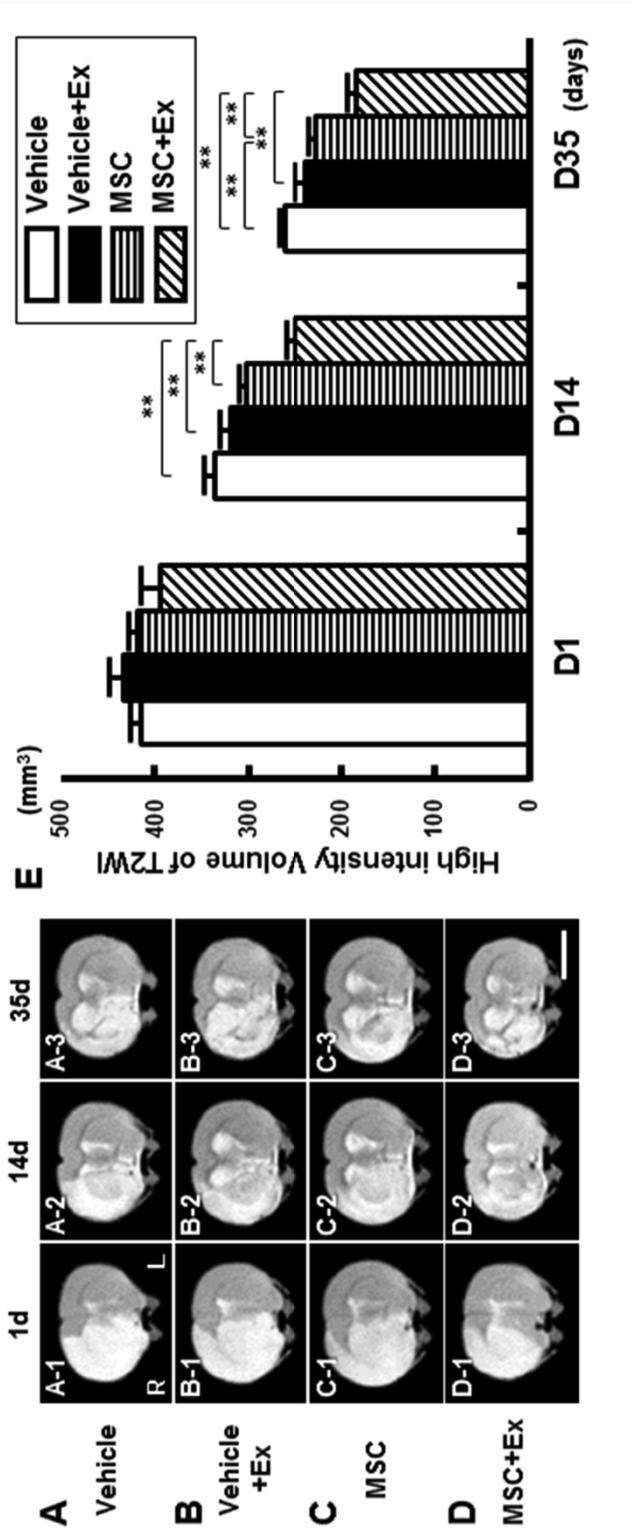

A
Vehicle
B
Vehicle +Ex
C
MSC
D
MSC+Ex
1d
14d
35d
A-1
A-2
A-3
B-1
B-2
B-3
C-1
C-2
C-3
D-1
D-2
D-3
R
L
E
High intensity Volume of T2WI
(mm3)
500
400
300
200
100
0
D1
D14
D35
(days)
Vehicle
Vehicle+Ex
MSC
MSC+Ex
**

FIG.12

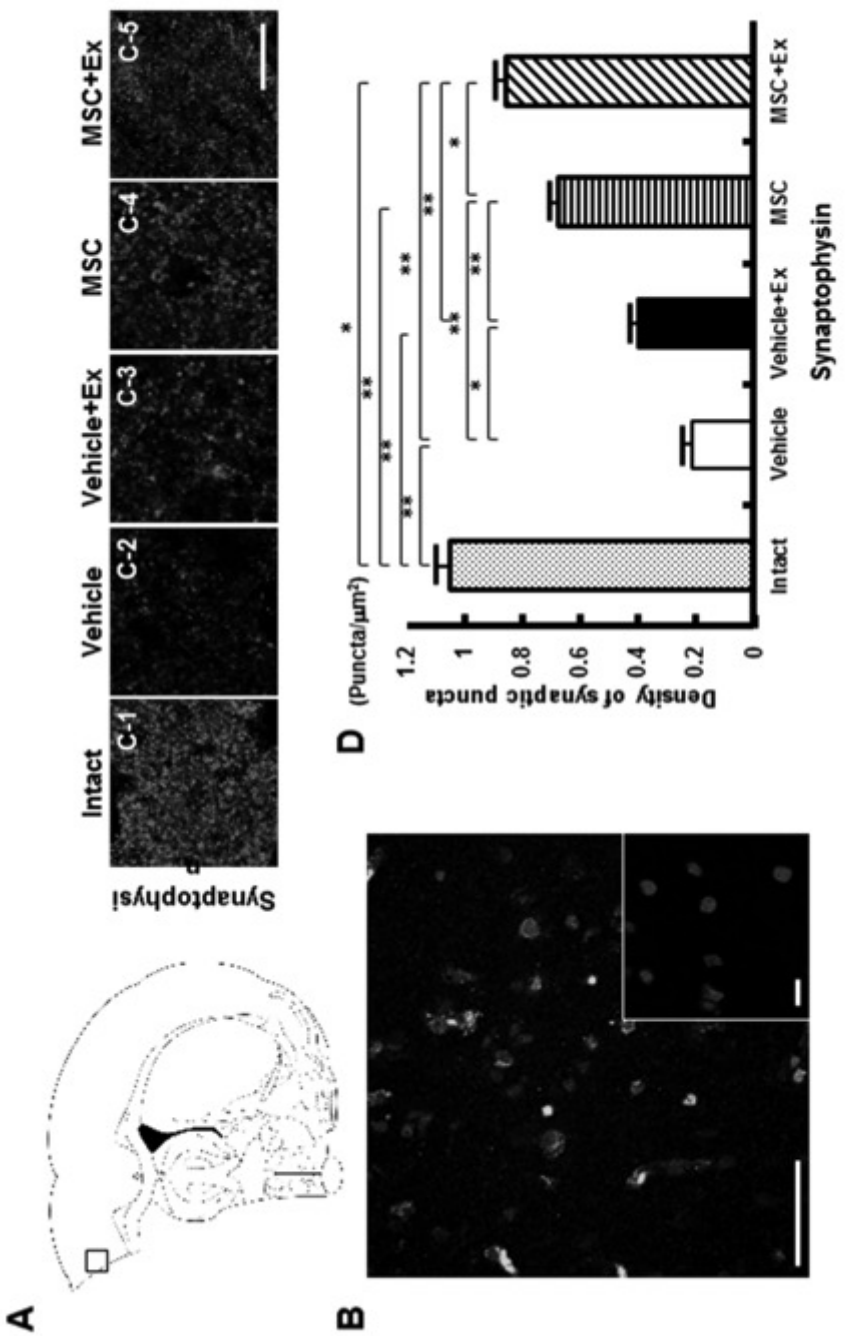

A
Intact
Vehicle
Vehicle+Ex
MSC
MSC+Ex
C-1
C-2
C-3
C-4
C-5
Synaptophysi
B
D
Density of synaptic puncta
(Puncta/μm²)
1.2
1
0.8
0.6
0.4
0.2
0
Intact
Vehicle
Vehicle+Ex
MSC
MSC+Ex
Synaptophysin

FIG.13

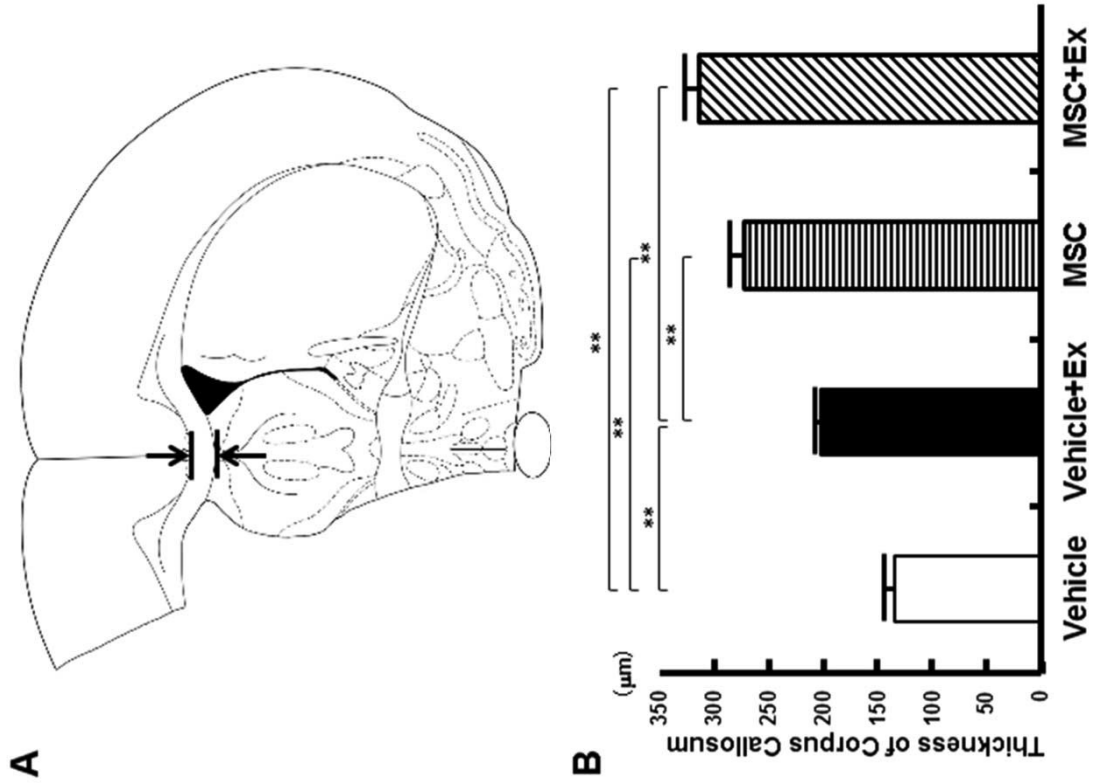

A
B
Thickness of Corpus Callosum
(μm)
350
300
250
200
150
100
50
0
**
**
**
**
**
Vehicle
Vehicle+Ex
MSC
MSC+Ex

FIG.14

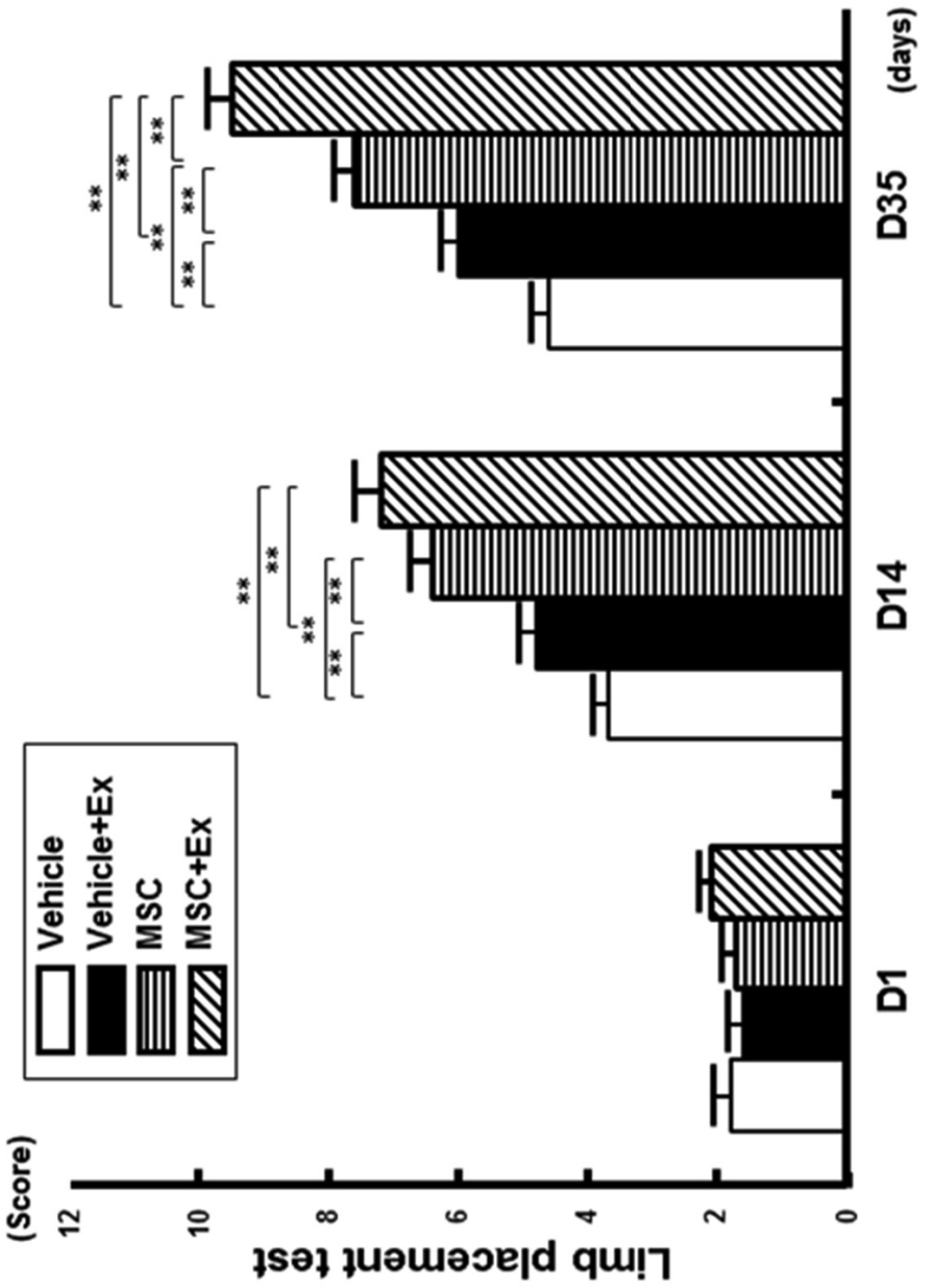
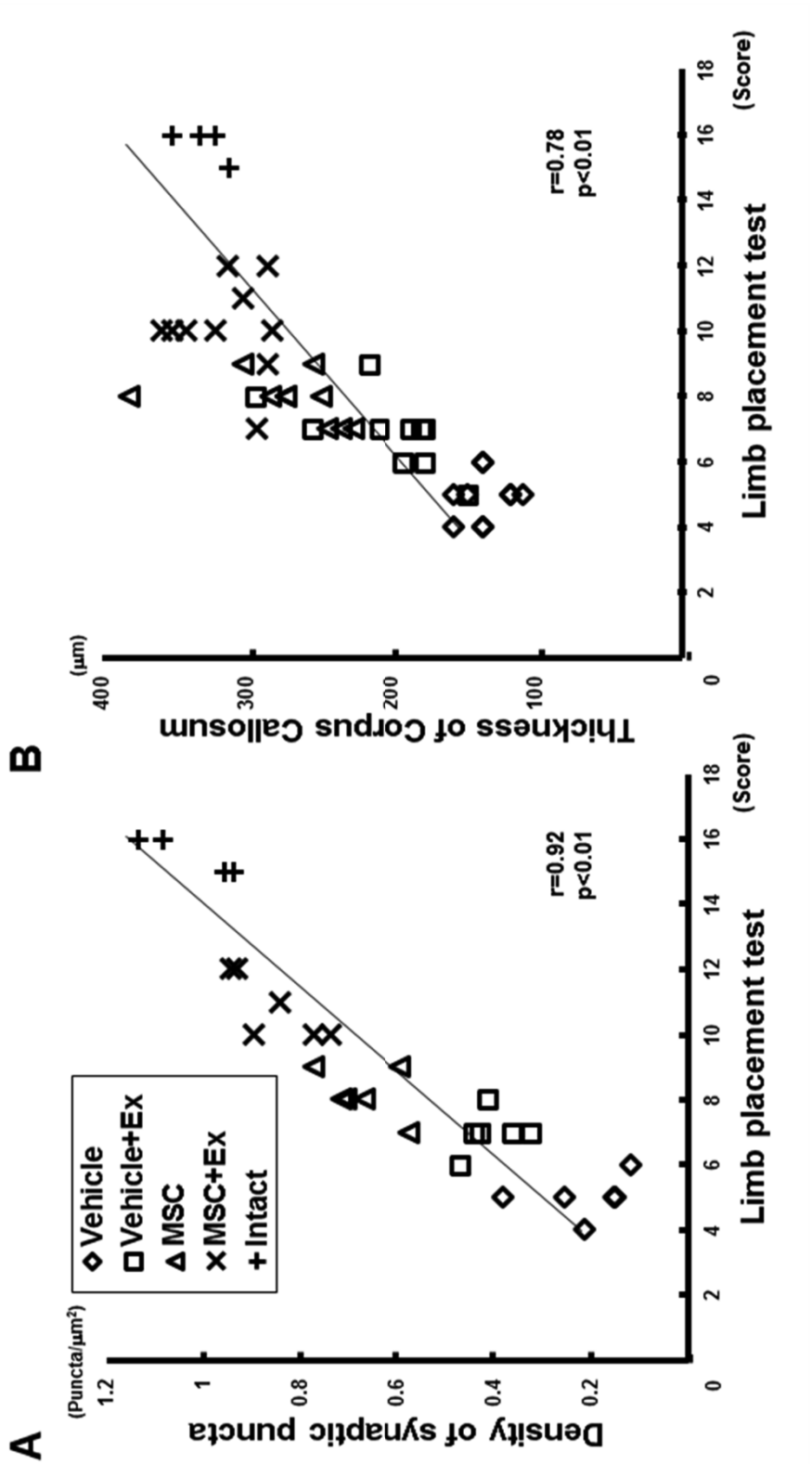

Limb placement test
(Score)
12
10
8
6
4
2
0
D1
D14
D35
(days)
Vehicle
Vehicle+Ex
MSC
MSC+Ex
**

FIG.15


A
Density of synaptic puncta
(Puncta/μm²)
1.2
1
0.8
0.6
0.4
0.2
0
2
4
6
8
10
12
14
16
18
Limb placement test
(Score)
Vehicle
Vehicle+Ex
MSC
MSC+Ex
Intact
r=0.92
p<0.01
B
Thickness of Corpus Callosum
(μm)
400
300
200
100
0
2
4
6
8
10
12
14
16
18
Limb placement test
(Score)
r=0.78
p<0.01

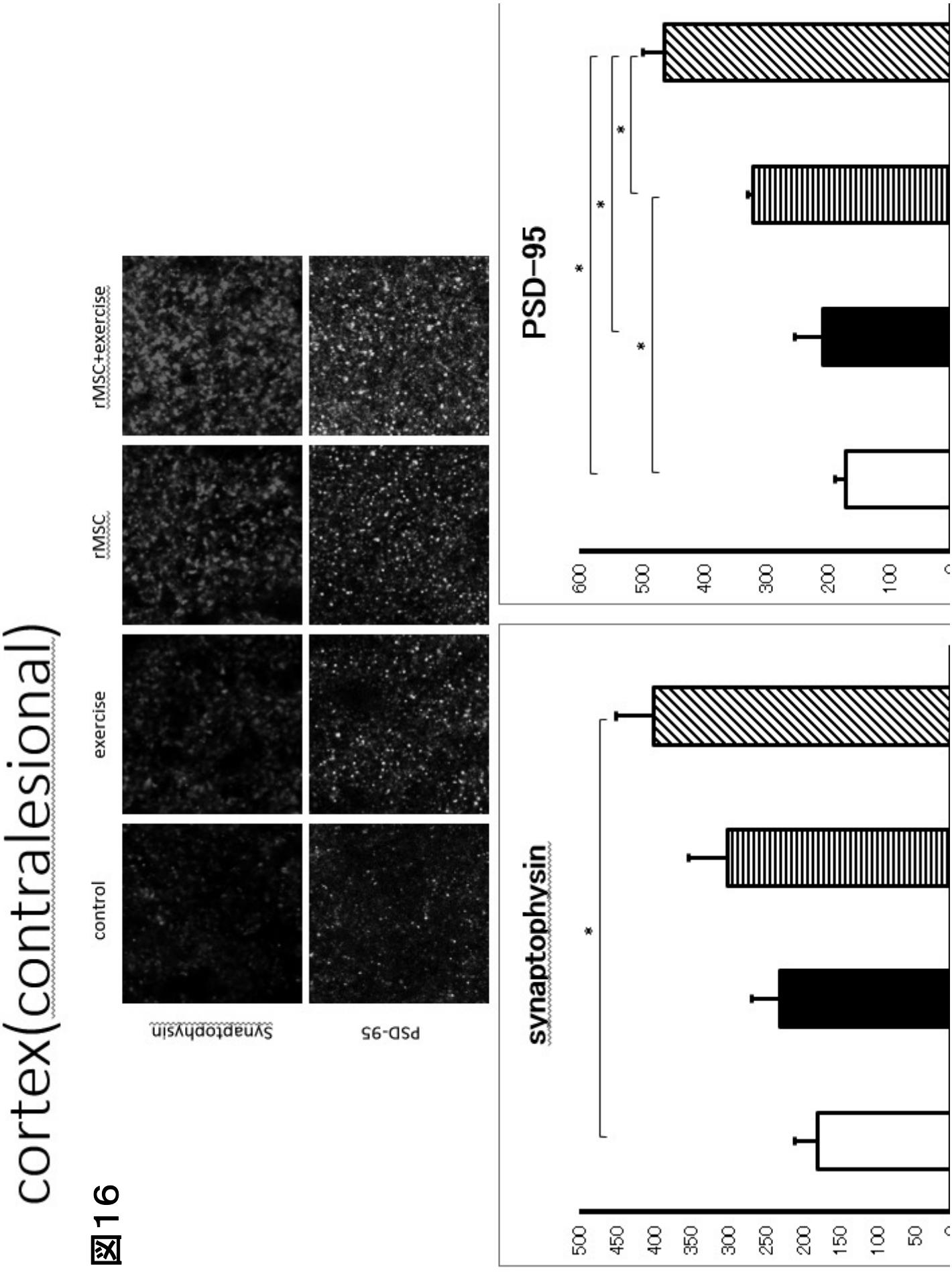
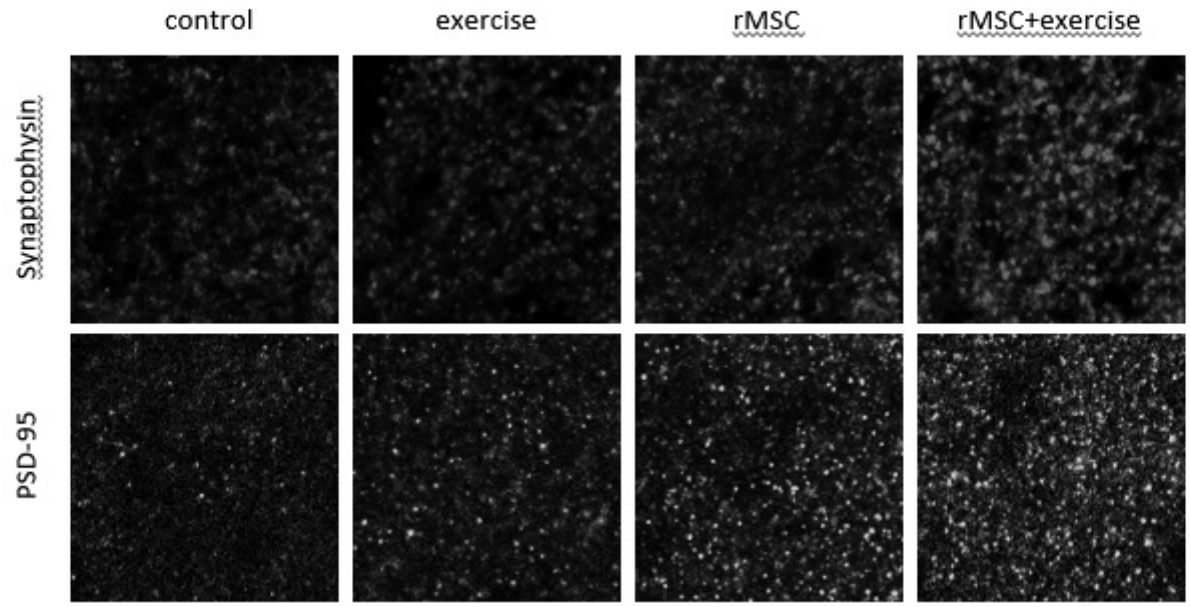
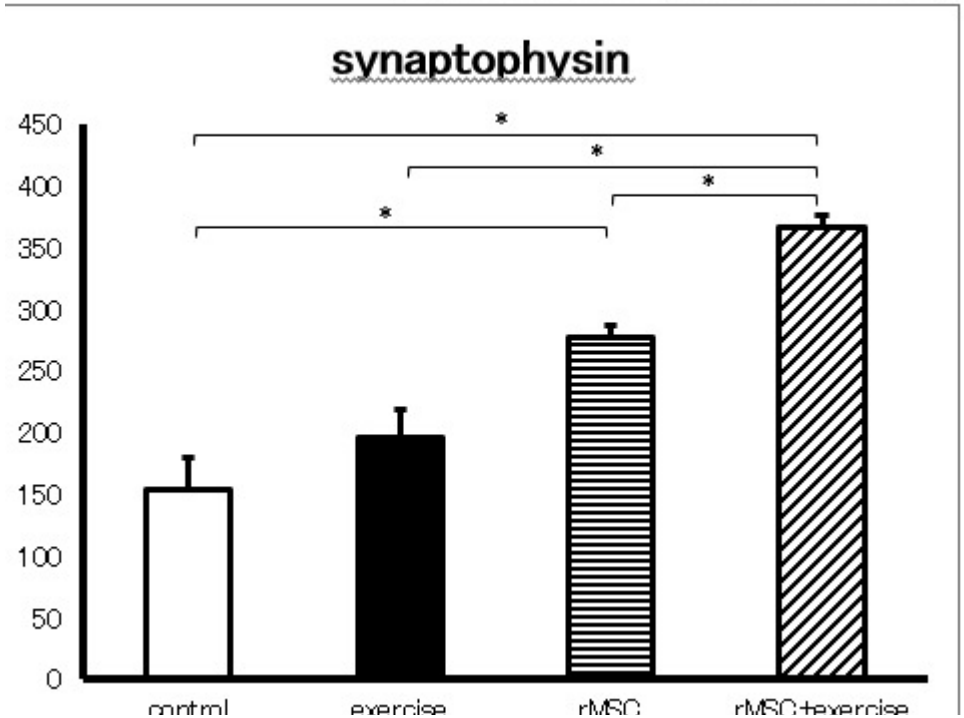

cortex(contralesional)
control
exercise
rMSC
rMSC+exercise
Synaptophysin
PSD-95
PSD-95
synaptophysin

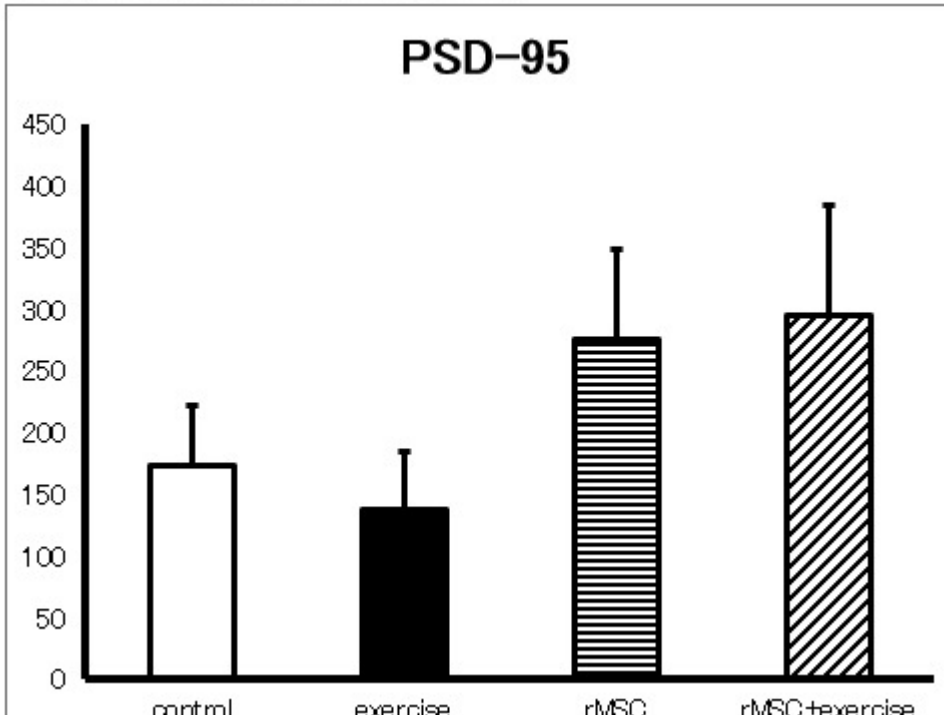
図16

striatum(contralesional)

FIG.17







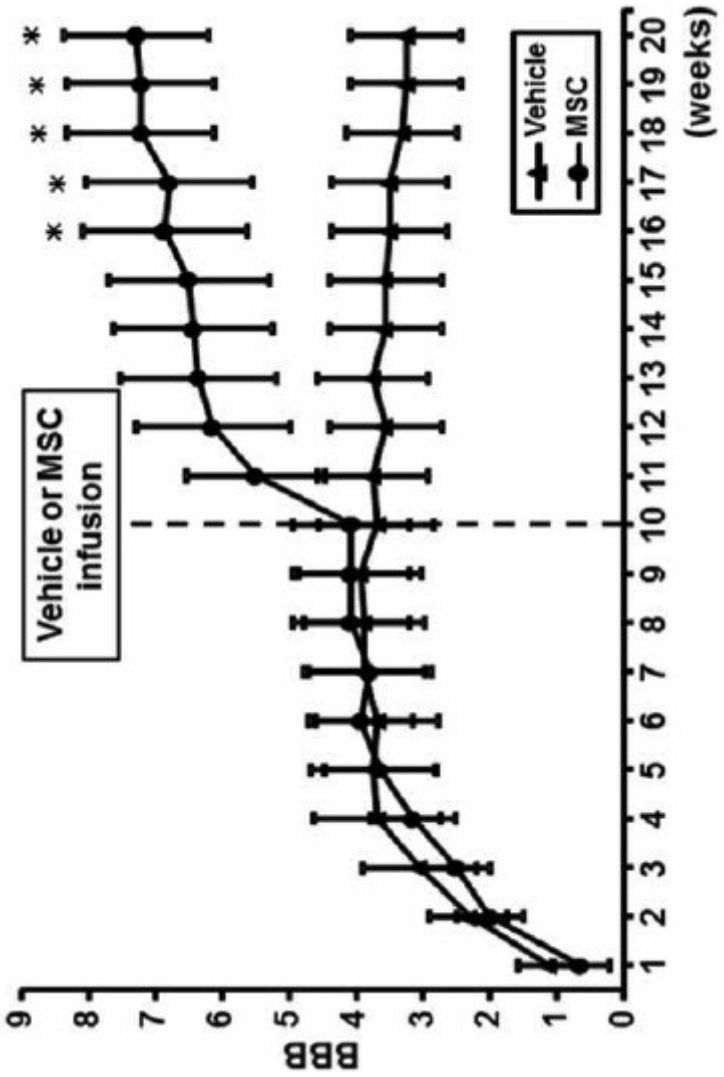

BBB
0
1
2
3
4
5
6
7
8
9
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
(weeks)
Vehicle or MSC infusion
* * * * * *
Vehicle
MSC

FIG.18

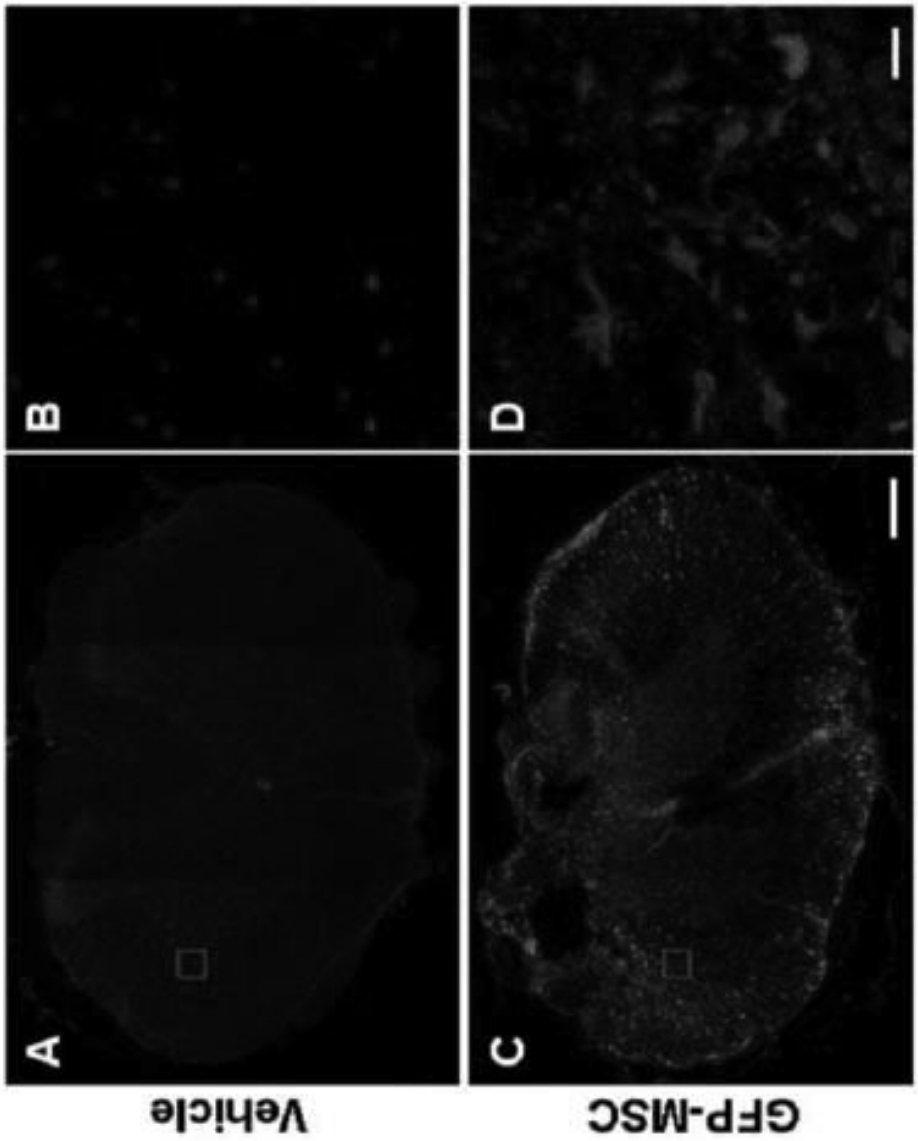


FIG.19

FIG.20

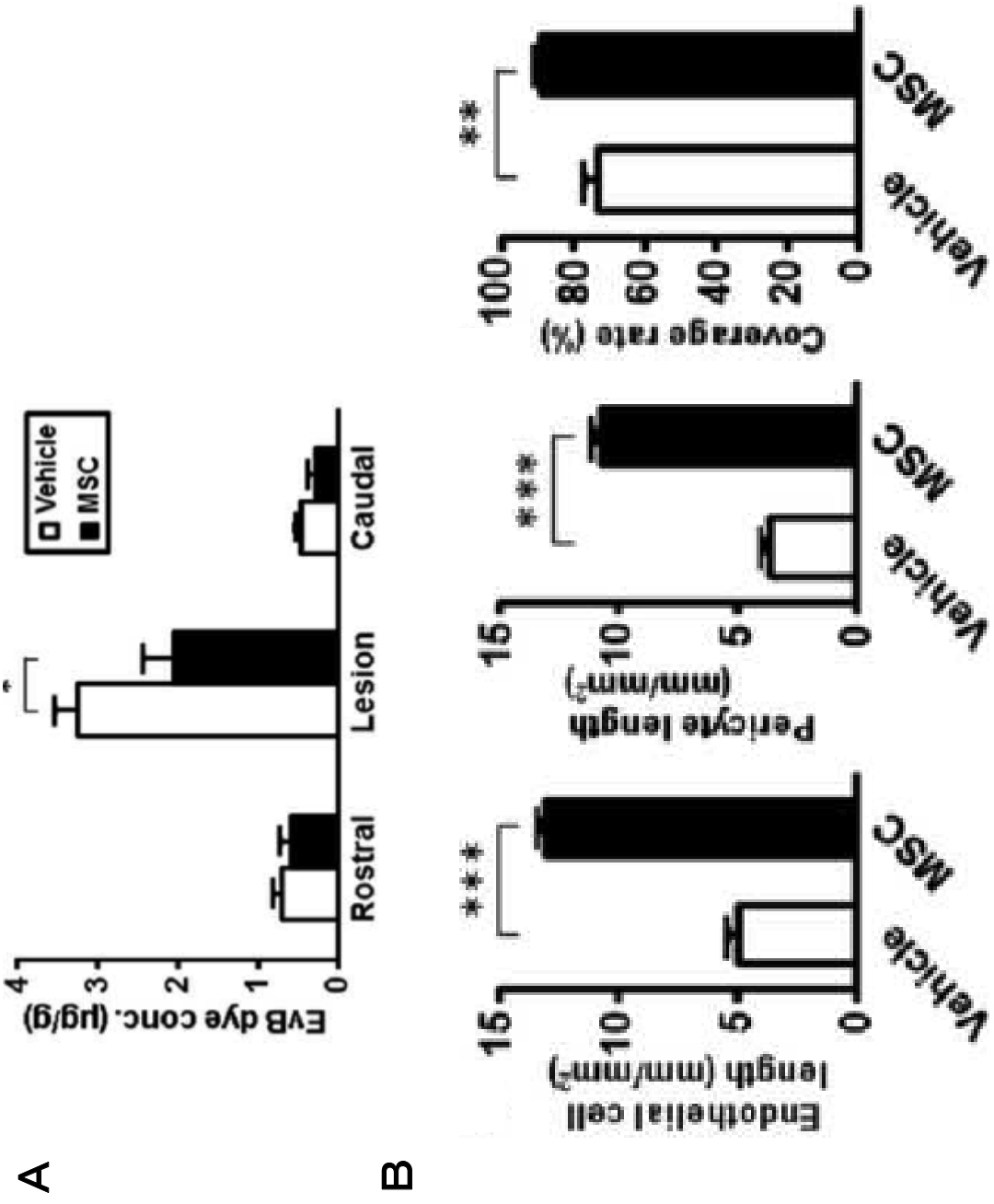

A
EvB dye conc. (μg/g)
0
1
2
3
4
Rostral
Lesion
Caudal
Vehicle
MSC
*
B
Endothelial cell length (mm/mm²)
Pericyte length (mm/mm²)
Coverage rate (%)
0
5
10
15
0
20
40
60
80
100
***
**
Vehicle
MSC

FIG.21

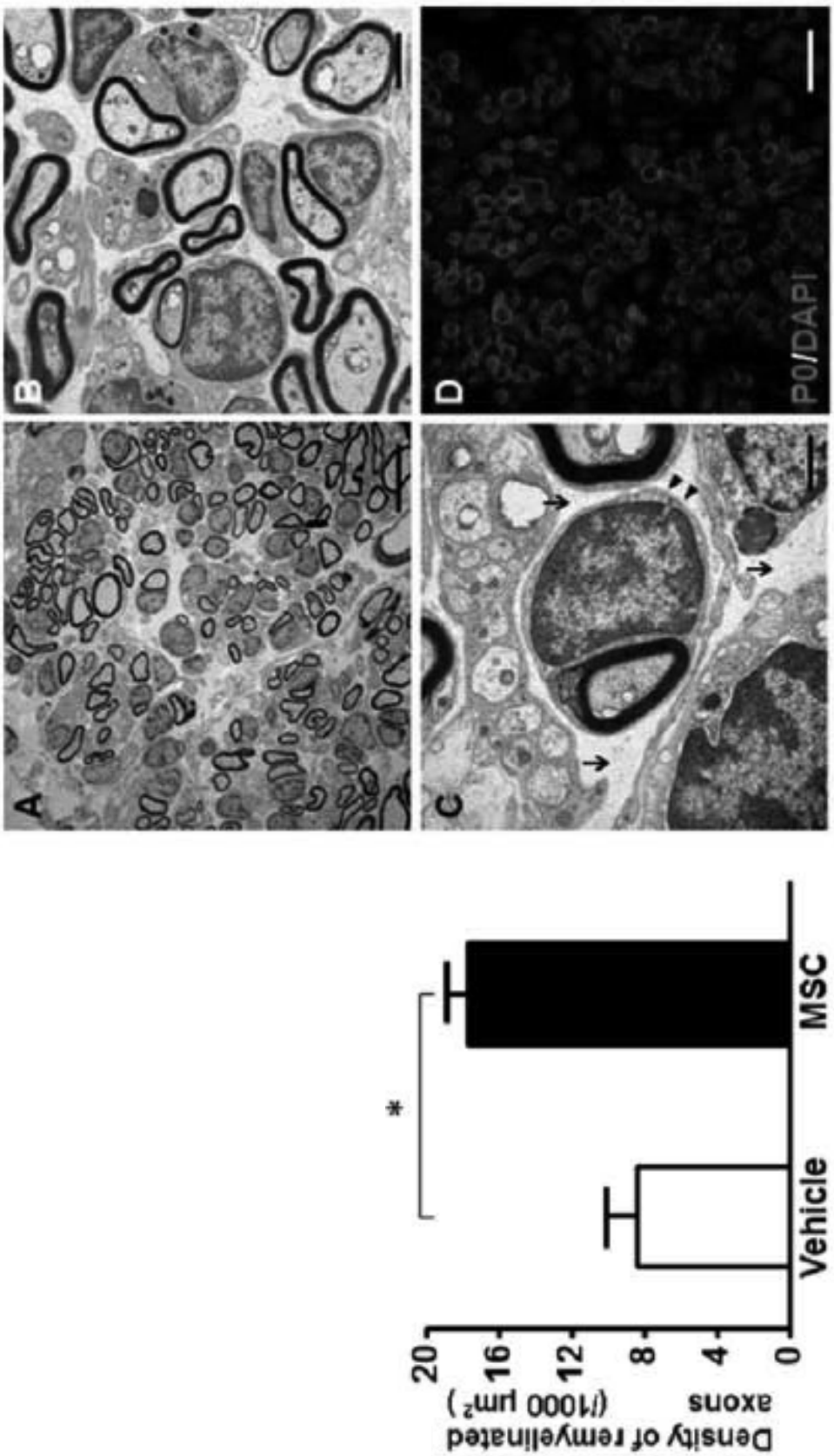
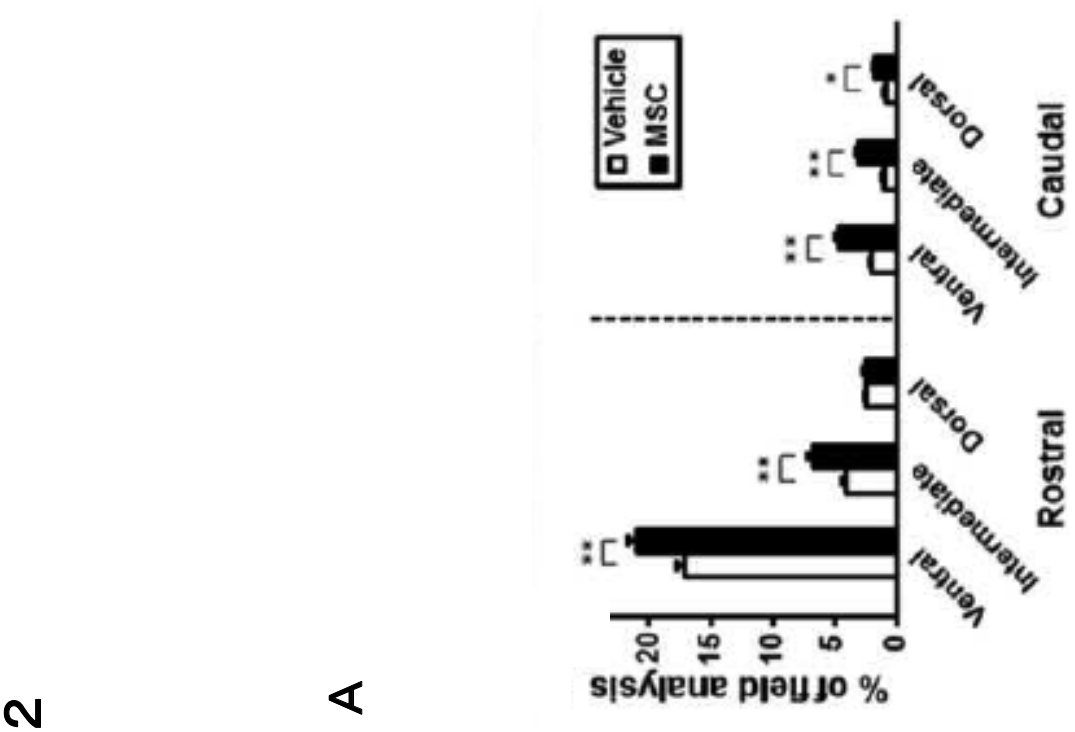

A
B
C
D
P0/DAPI
Density of remyelinated axons (/1000 μm²)
20
16
12
8
4
0
*
Vehicle
MSC

FIG.22


A
% of field analysis
20
15
10
5
0
Vehicle
MSC
Ventral
Intermediate
Dorsal
Rostral
Ventral
Intermediate
Dorsal
Caudal
B
5-HT-IR (Pixels x1000)
3.5
3
2.5
2
1.5
1
0.5
0
***
Vehicle
MSC
Rostral
Vehicle
MSC
Caudal

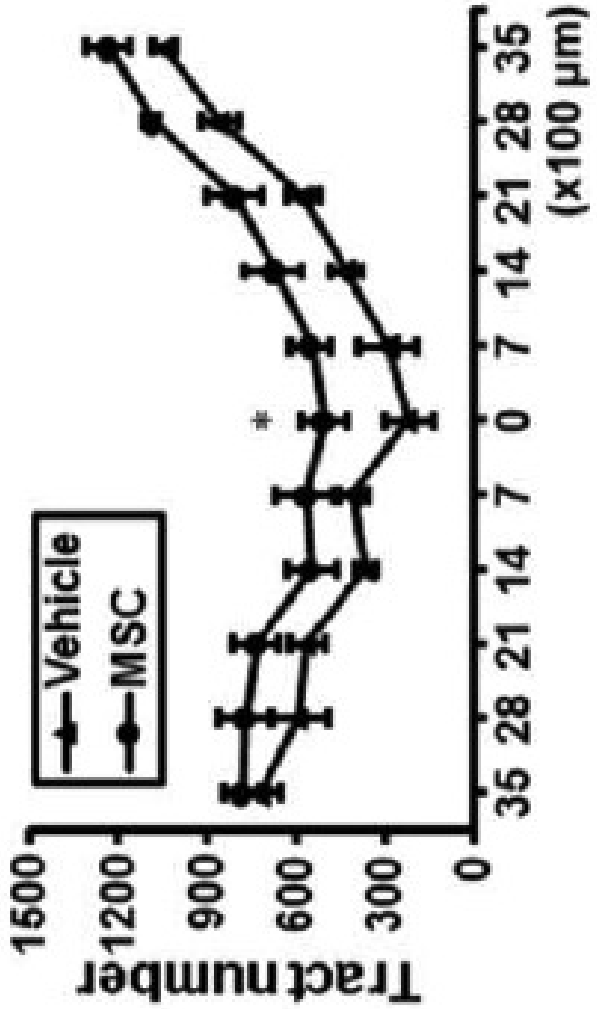
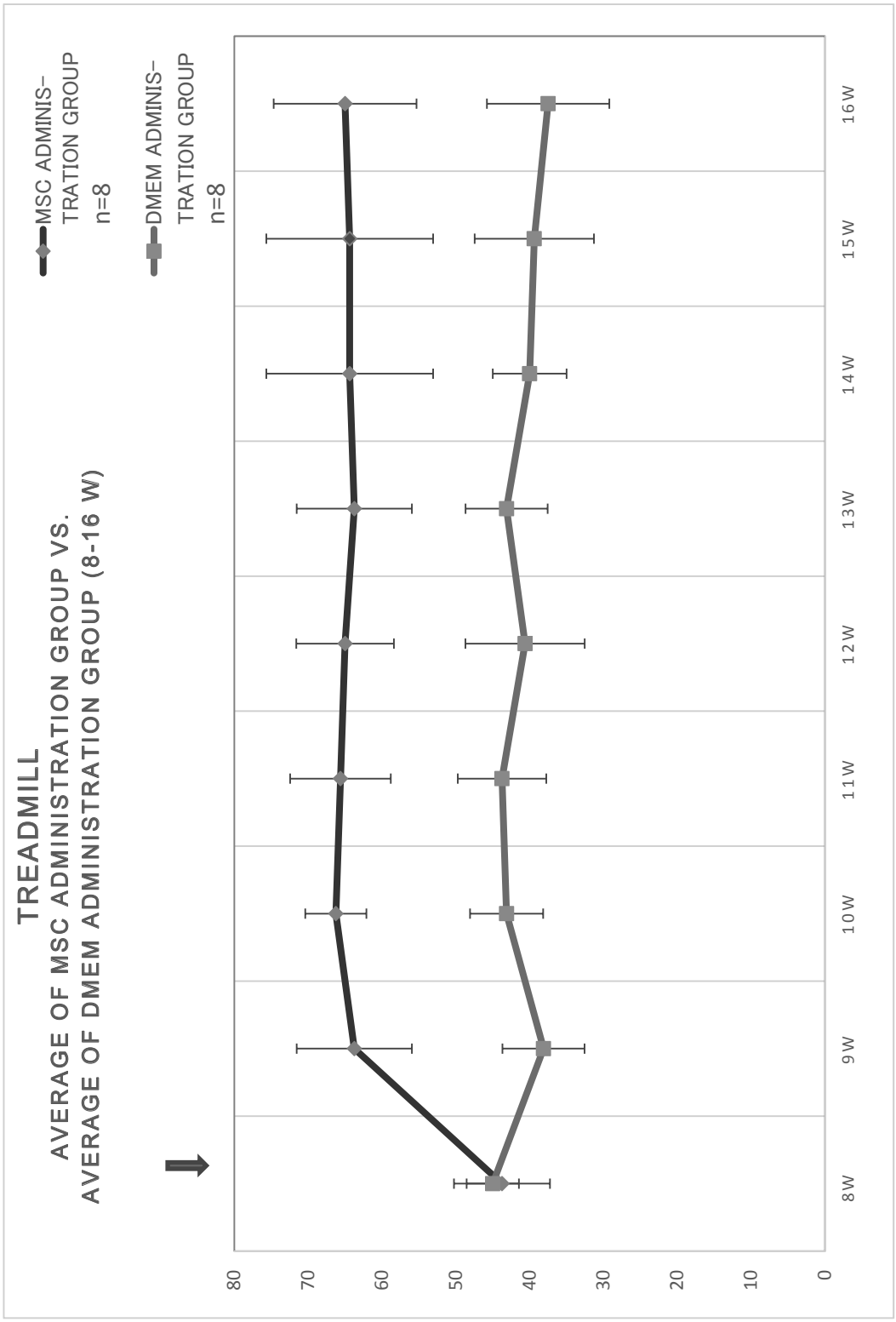

Tract number
1500
1200
900
600
300
0
35 28 21 14 7 0 7 14 21 28 35
(x100 μm)
Vehicle
MSC
*

FIG.23

FIG.24


TREADMILL
AVERAGE OF MSC ADMINISTRATION GROUP VS.
AVERAGE OF DMEM ADMINISTRATION GROUP (8-16 W)
MSC ADMINIS-
TRATION GROUP
n=8
DMEM ADMINIS-
TRATION GROUP
n=8
80
70
60
50
40
30
20
10
0
8W
9W
10W
11W
12W
13W
14W
15W
16W