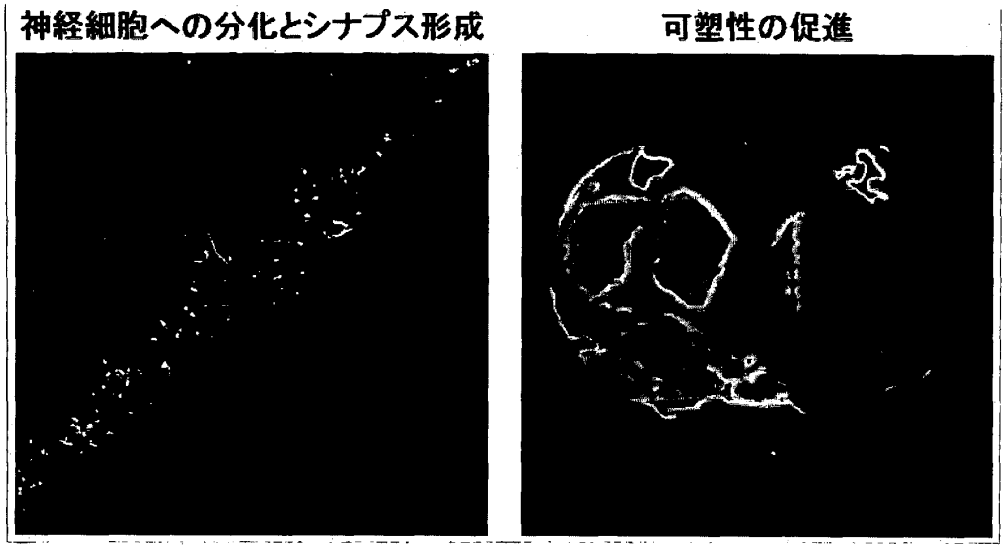
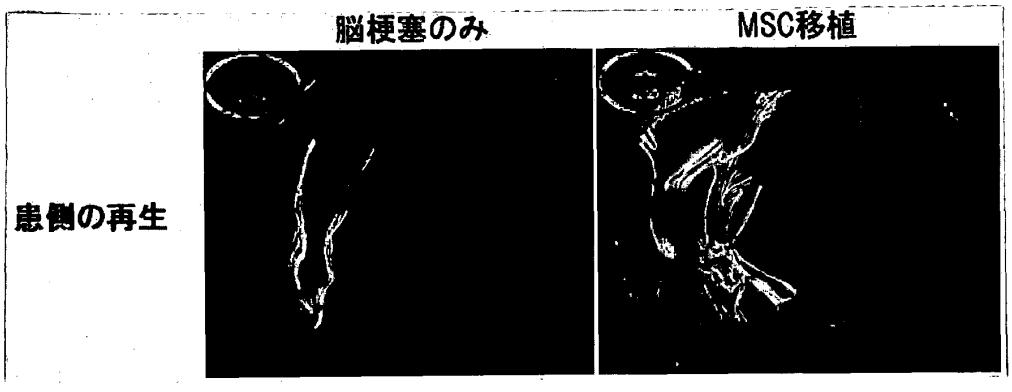
図面

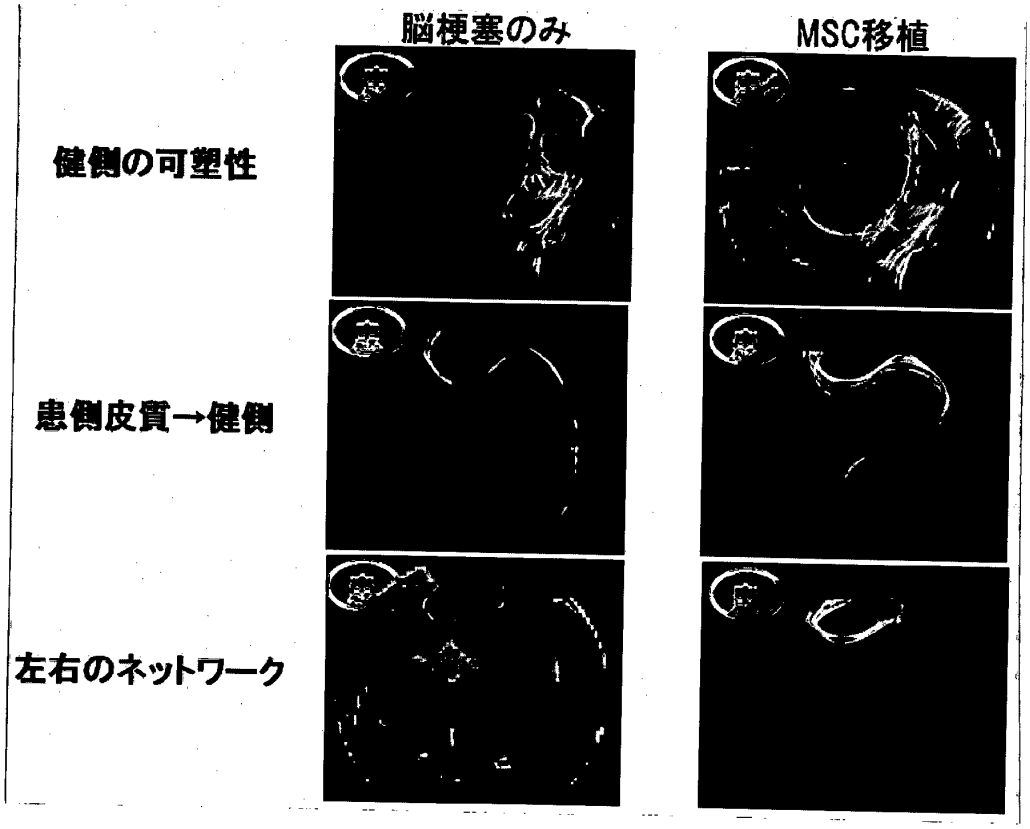
[図１]



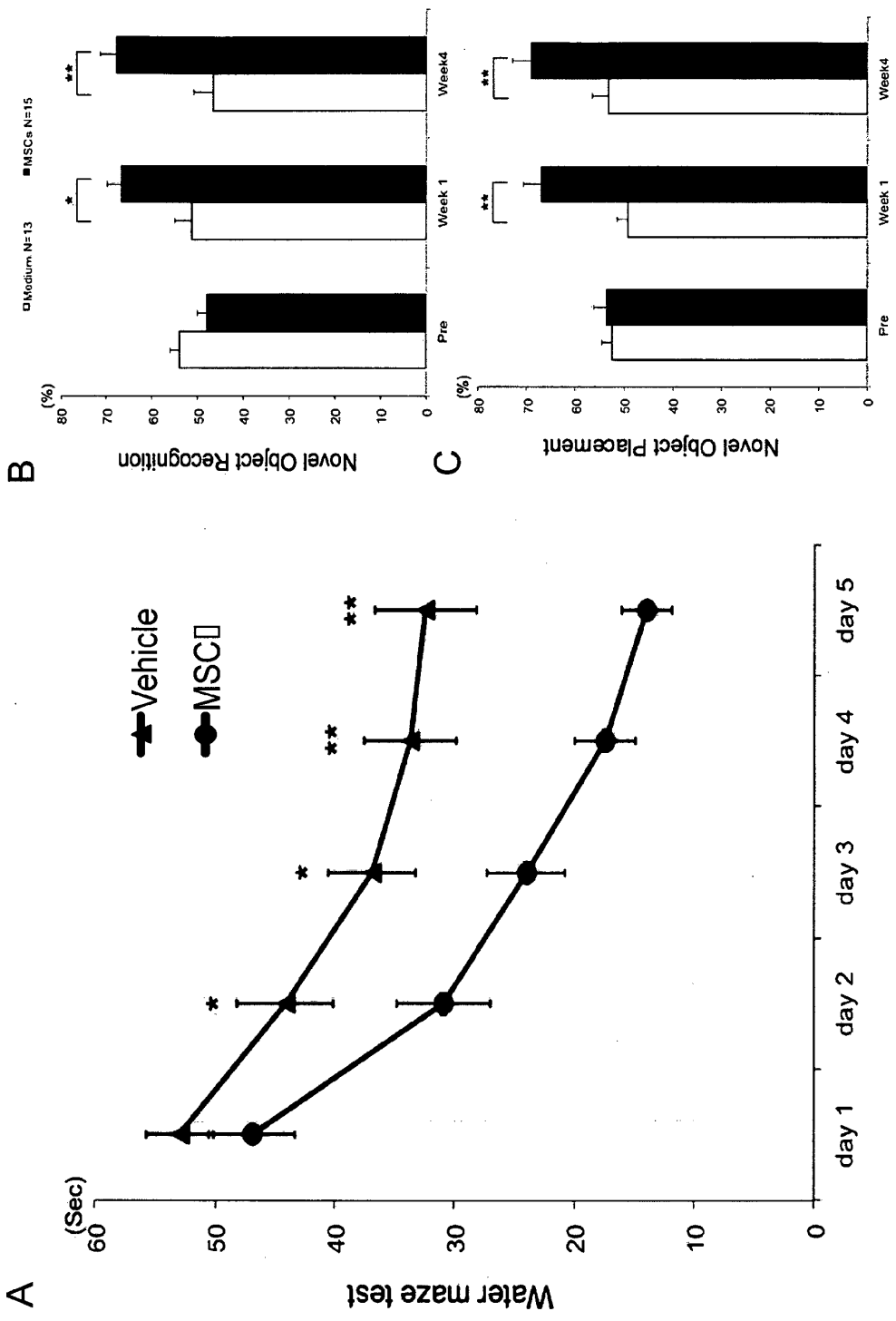
[図２]



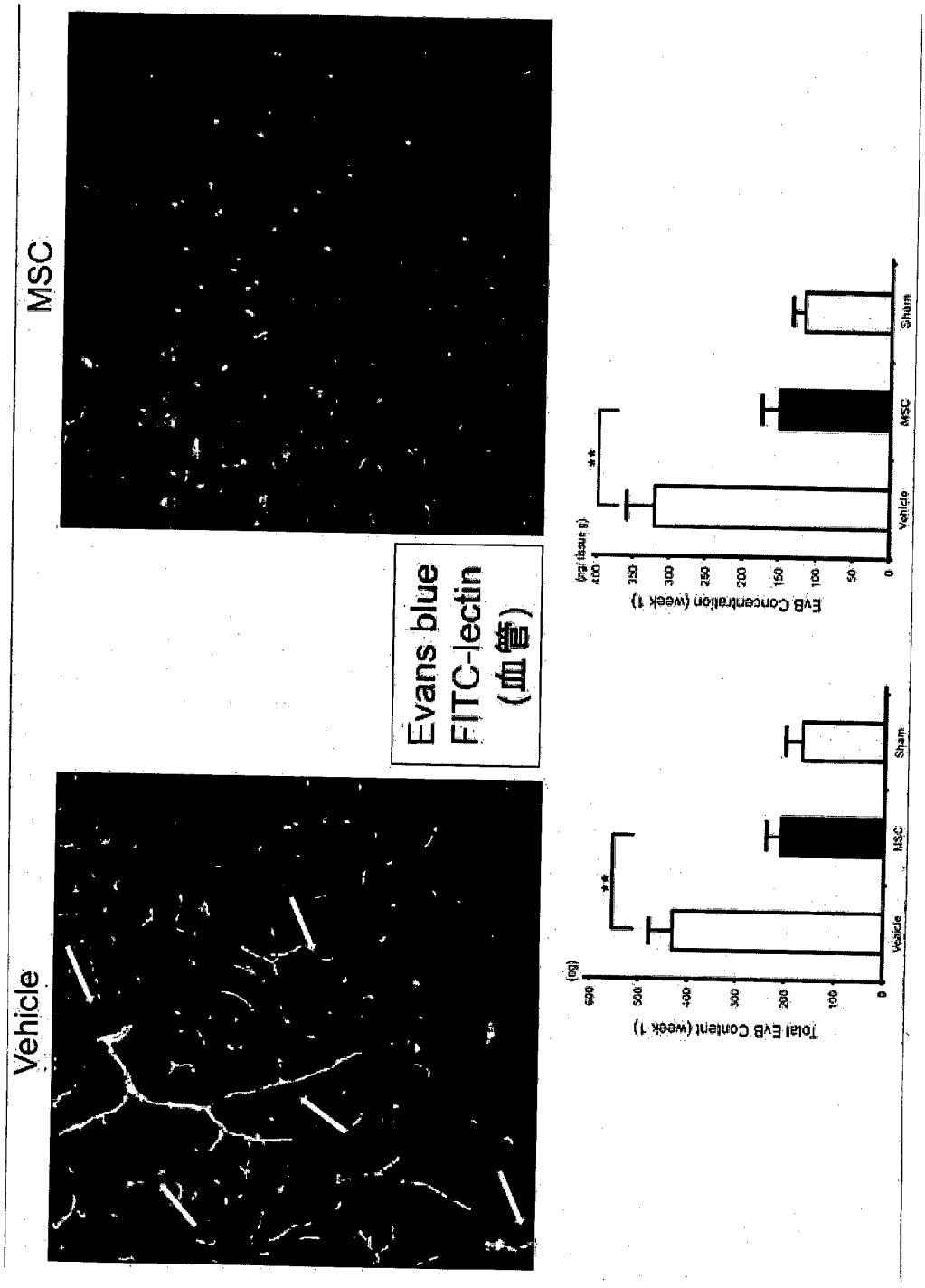
[図３]



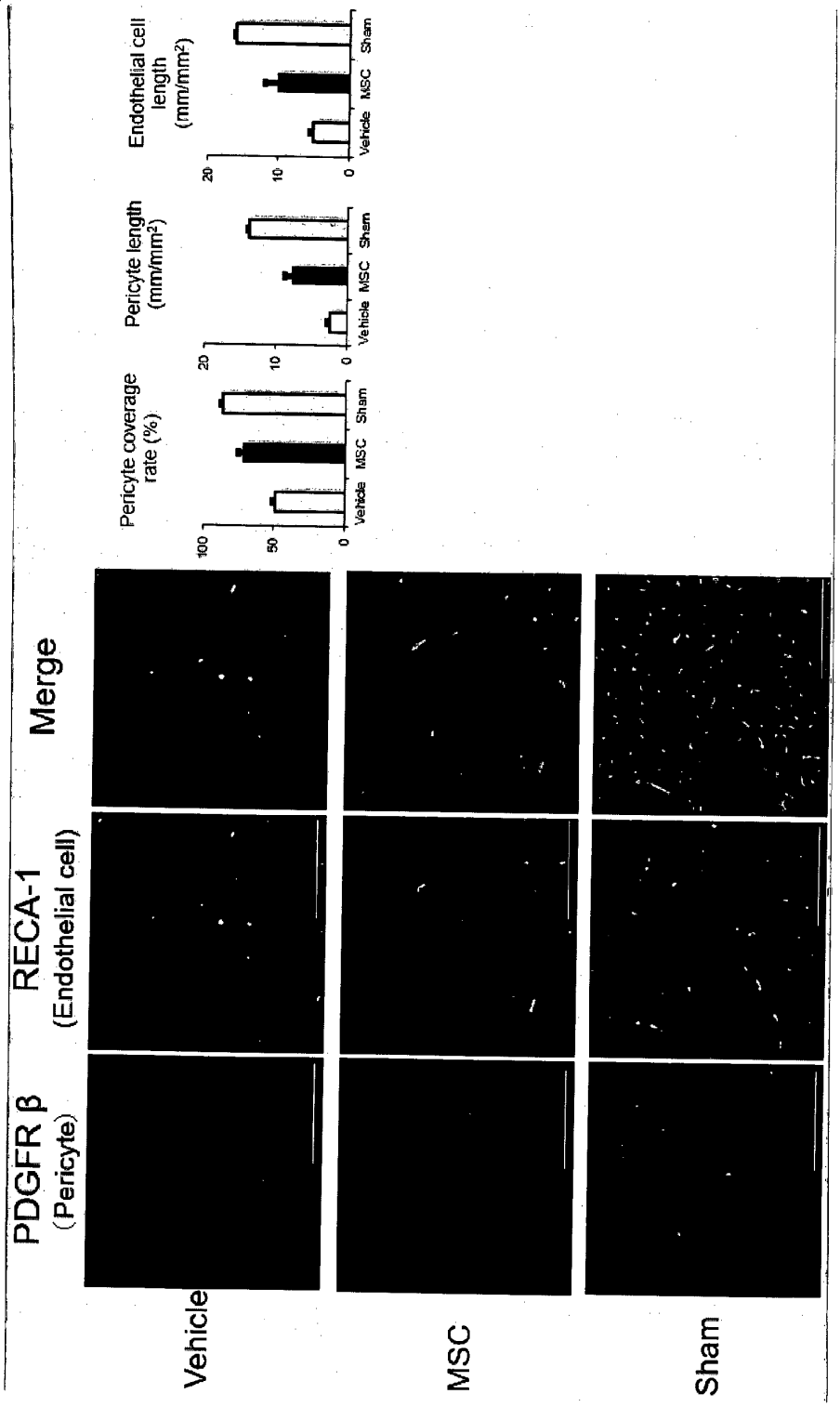
[図4]


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
**
**

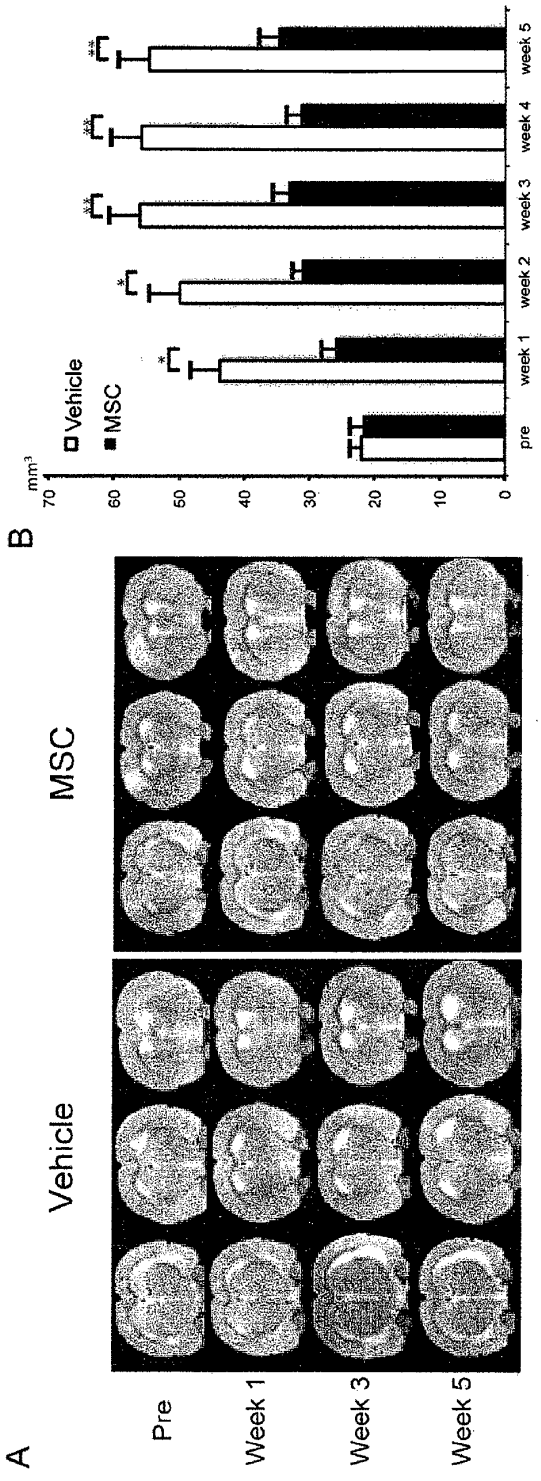
[図5]


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

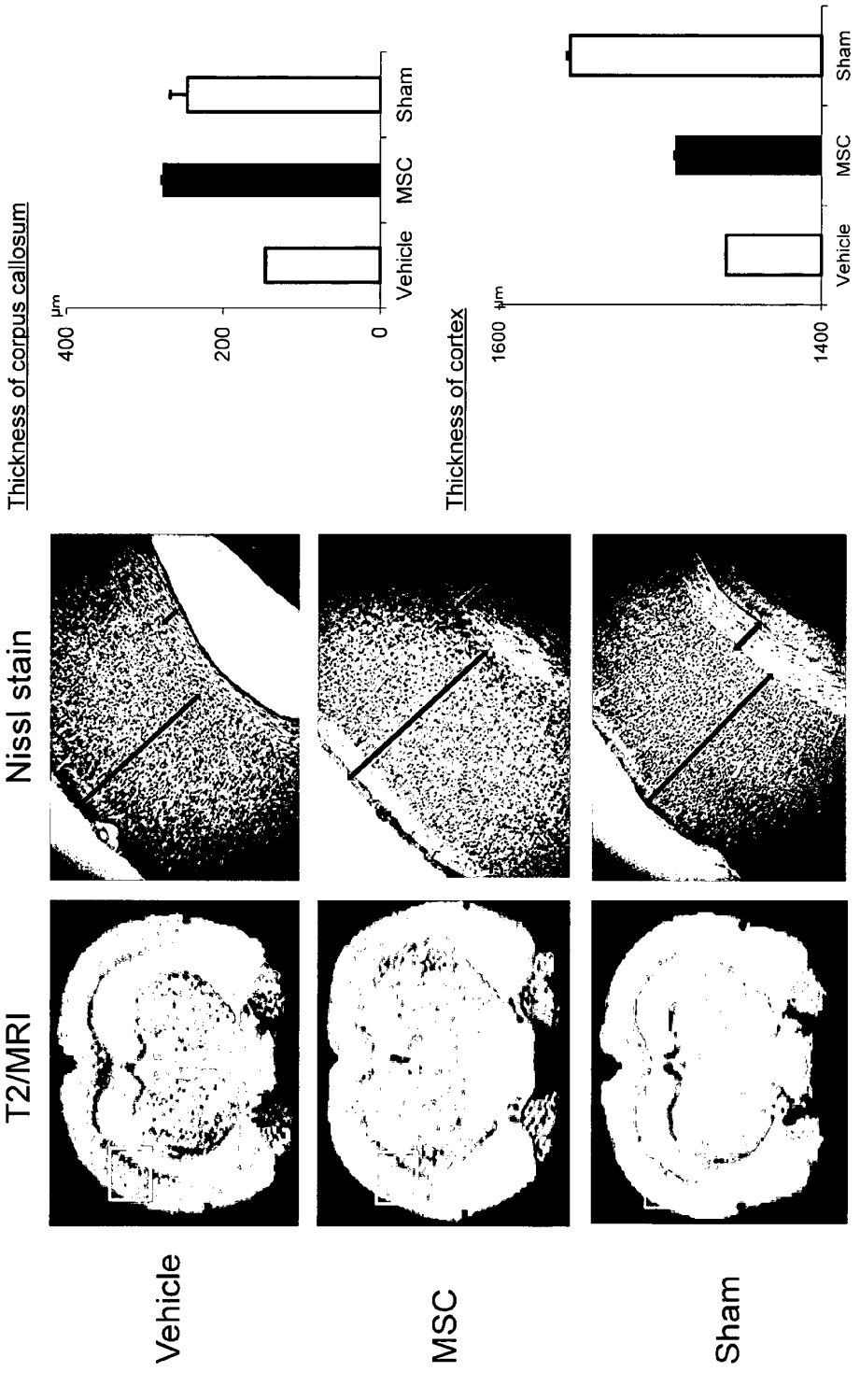
[図6]


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

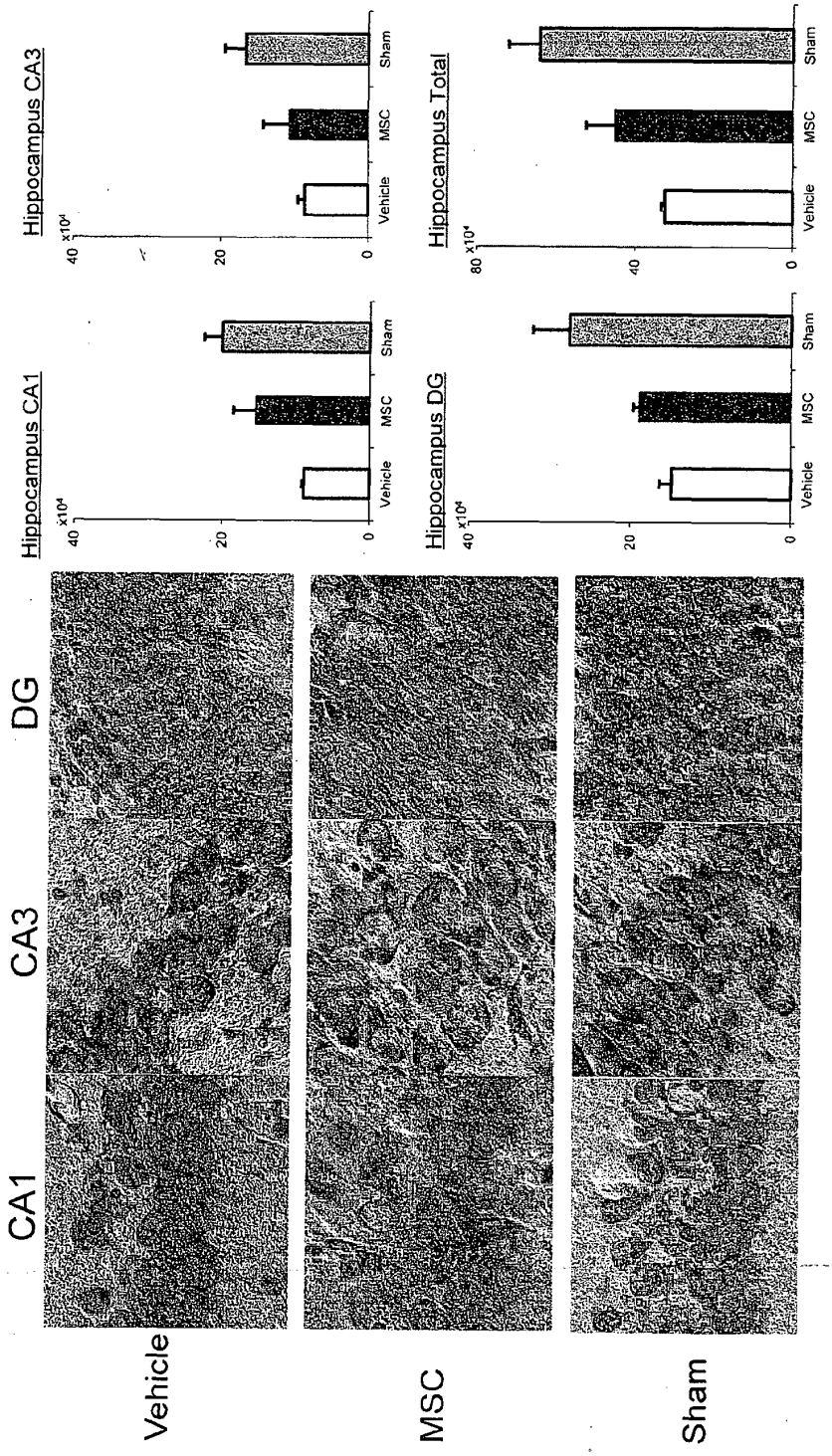
[図7]


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

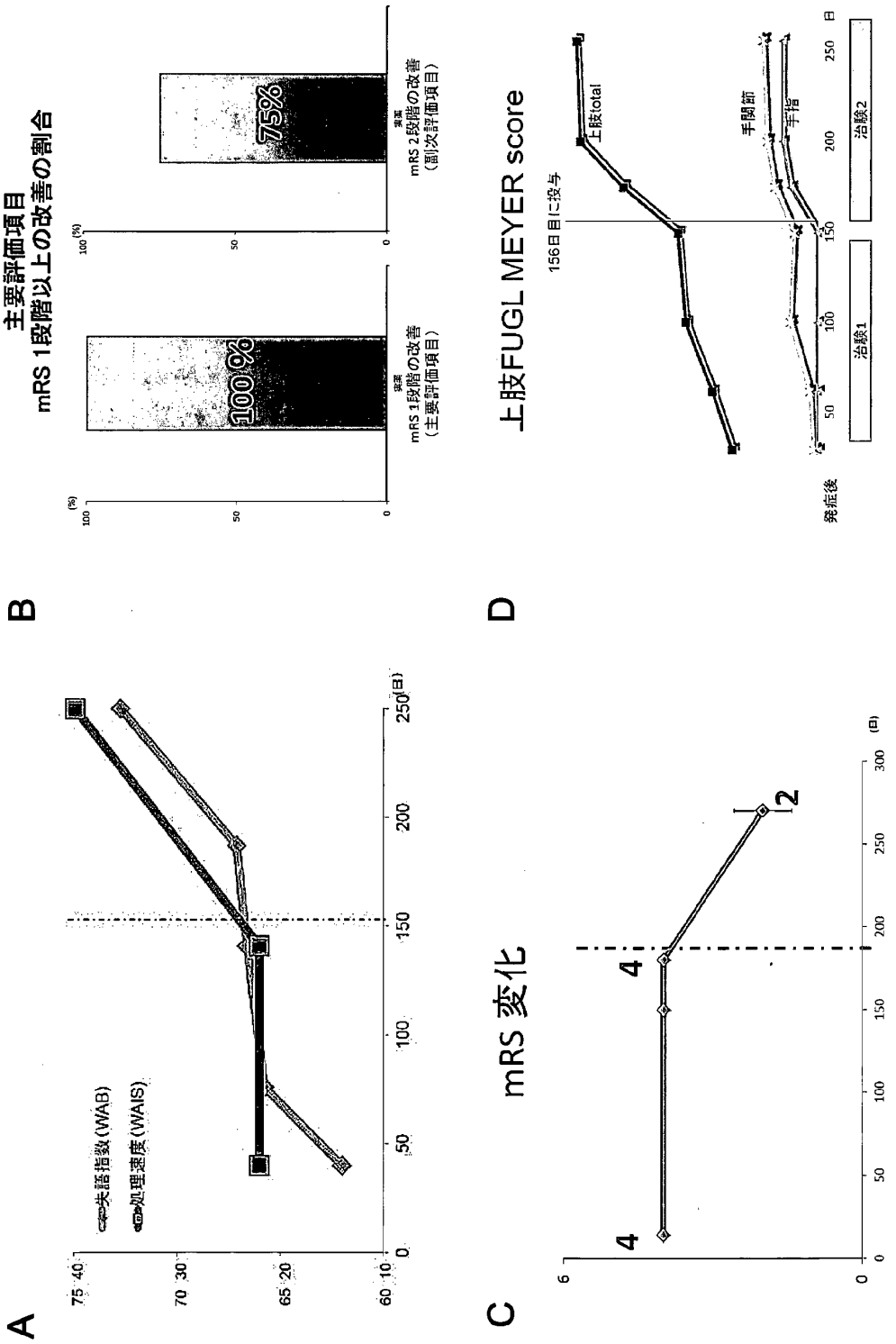
[図８]


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

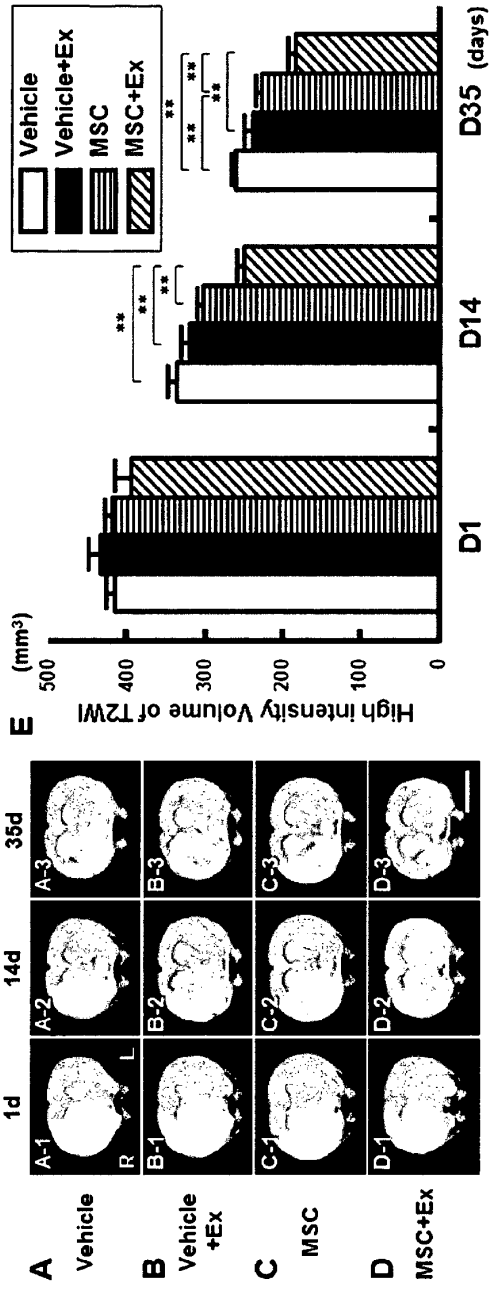
[図9]


CA1
CA3
DG
Vehicle
MSC
Sham
Hippocampus CA1
Hippocampus CA3
Hippocampus DG
Hippocampus Total
x10⁴
Vehicle
MSC
Sham

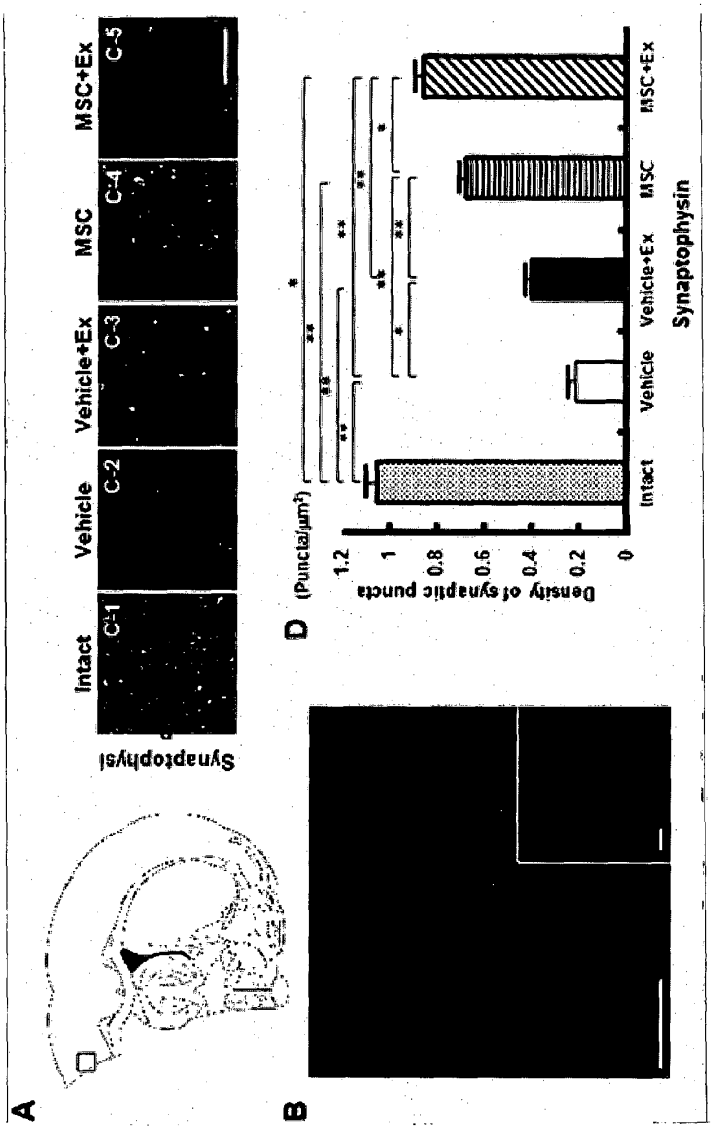
［図１０］


A
失語指数 (WAB)
処理速度 (WAIS)
B
主要評価項目
mRS 1段階以上の改善の割合
100%
75%
mRS 1段階の改善
（主要評価項目）
mRS 2段階の改善
（副次評価項目）
C
mRS 変化
D
上肢FUGL MEYER score
156日目に投与
上肢total
手関節
手指
治験1
治験2
発症後

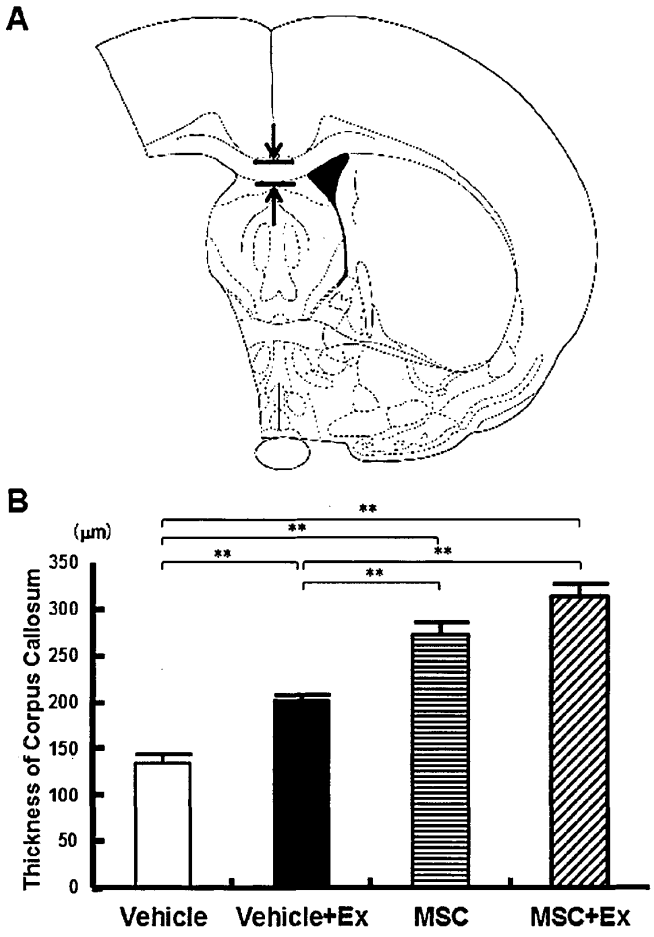
[図１１]


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
**

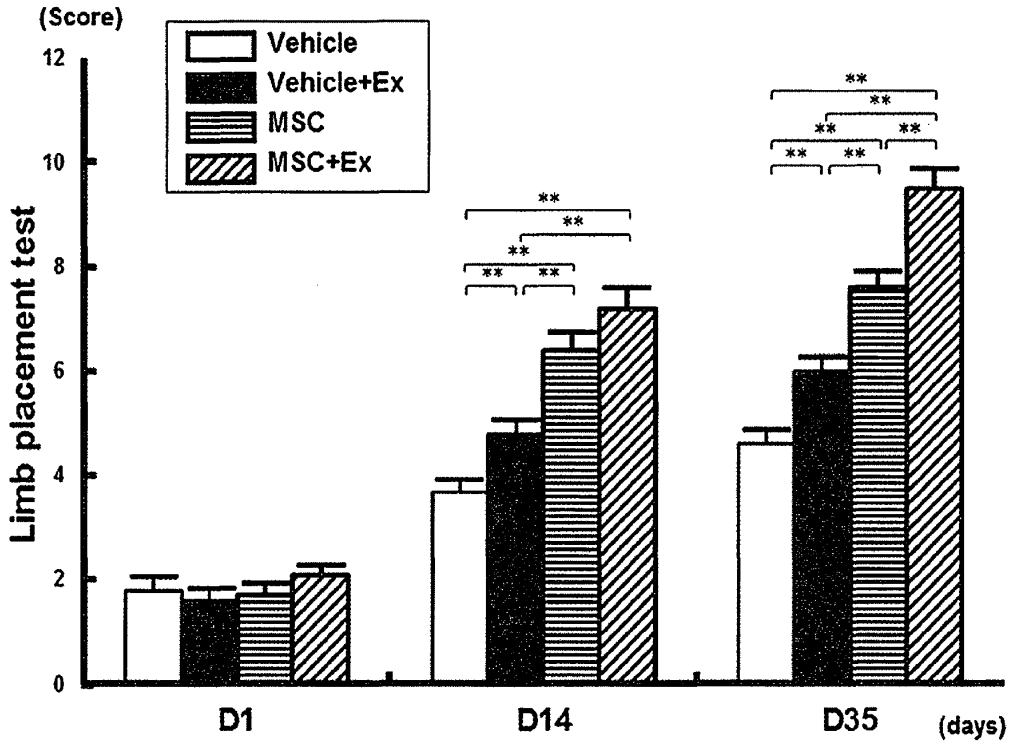
[図１２]


A
Intact
Vehicle
Vehicle+Ex
MSC
MSC+Ex
C-1
C-2
C-3
C-4
C-5
Synaptophysin
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

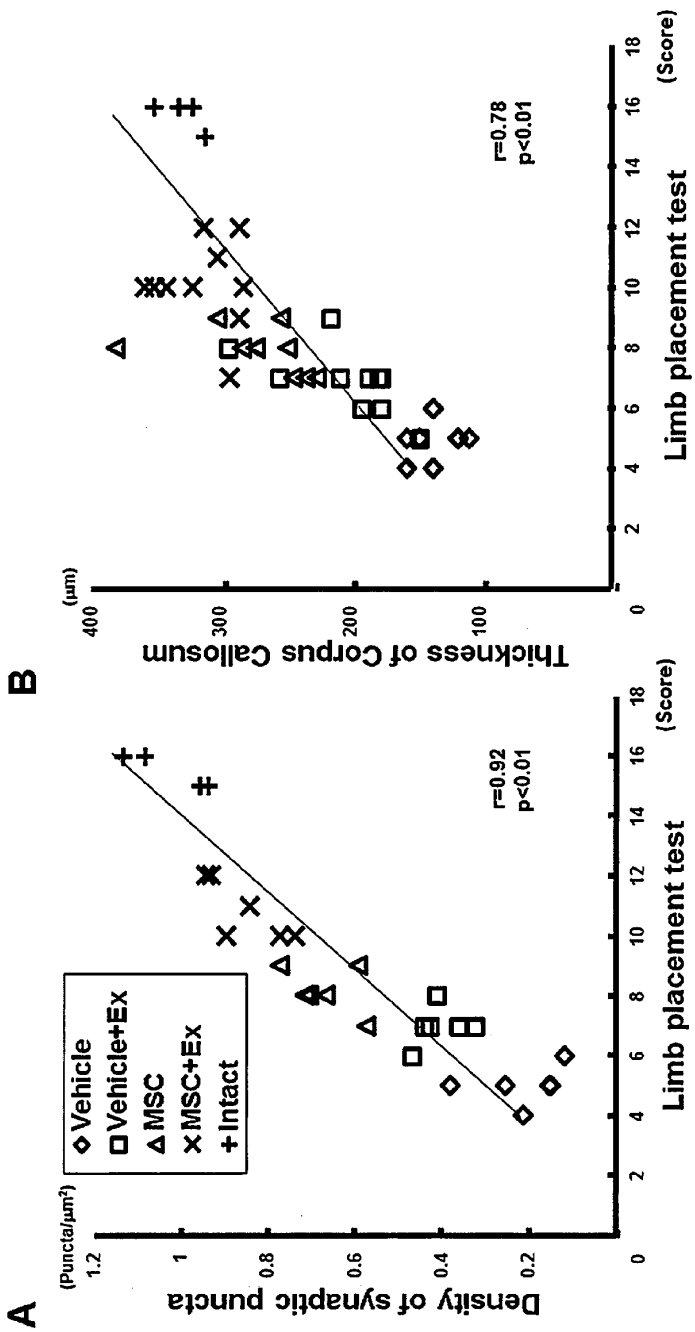
[図１３]


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

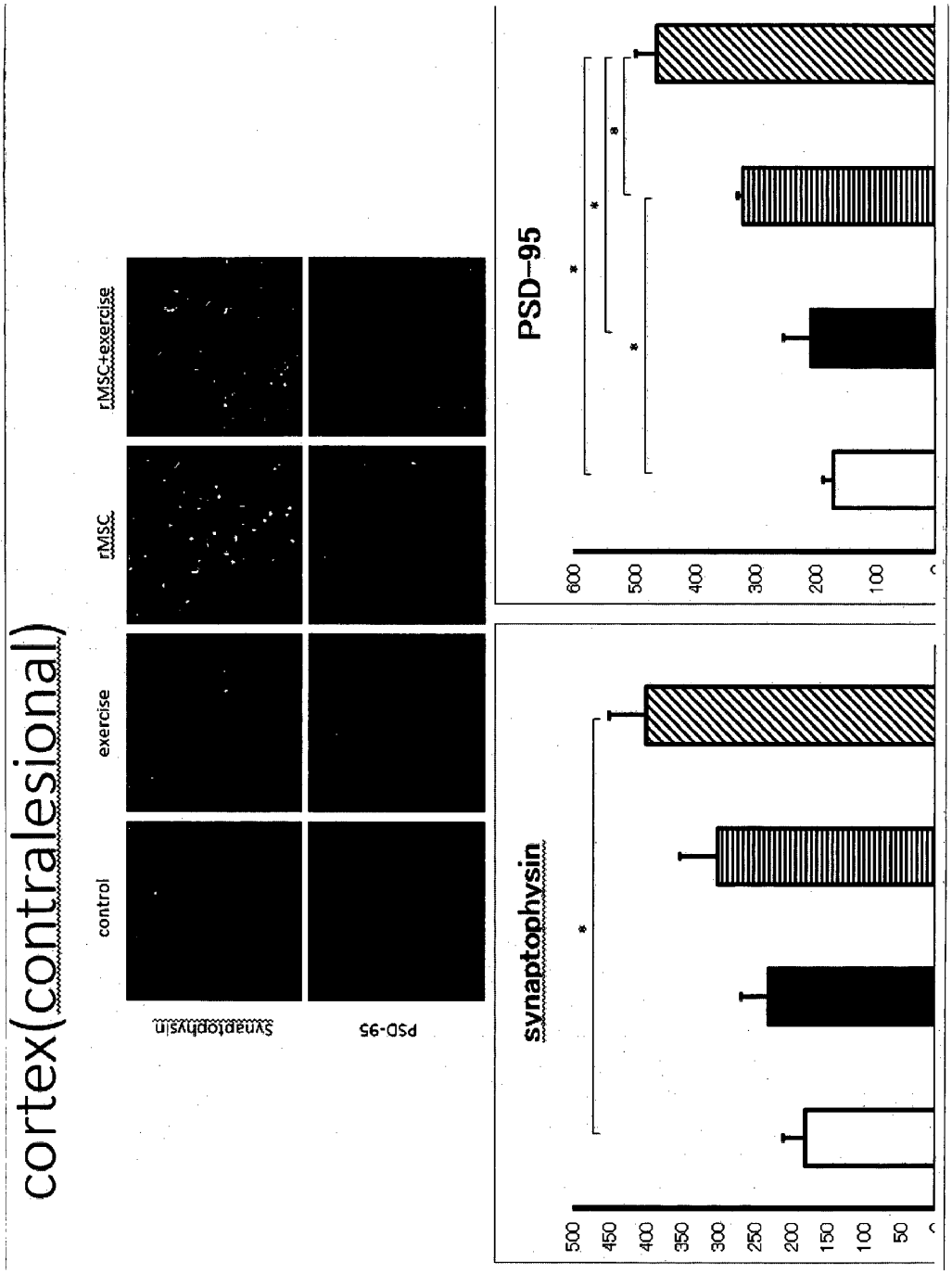
[図１４]


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

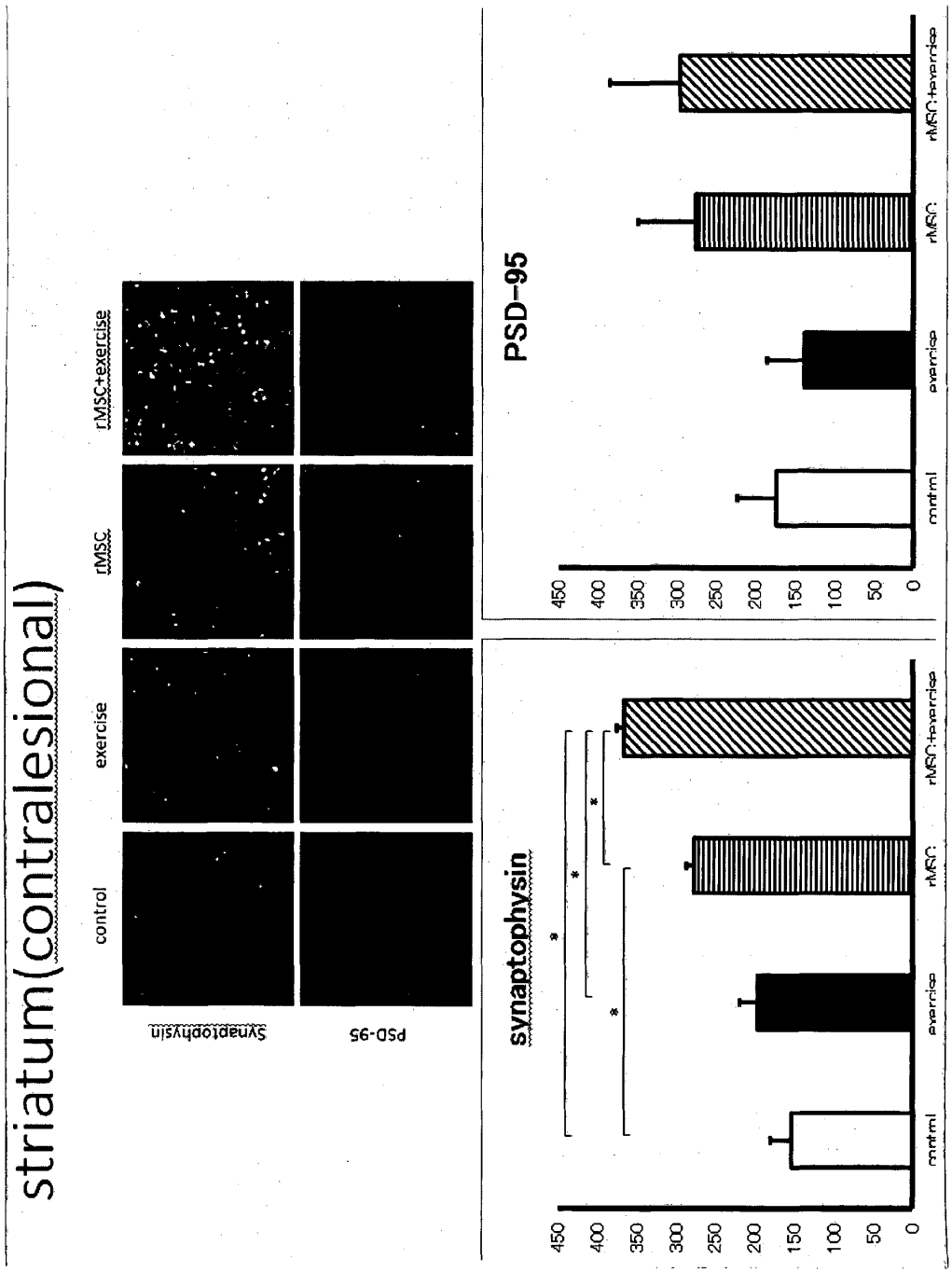
[図１５]


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

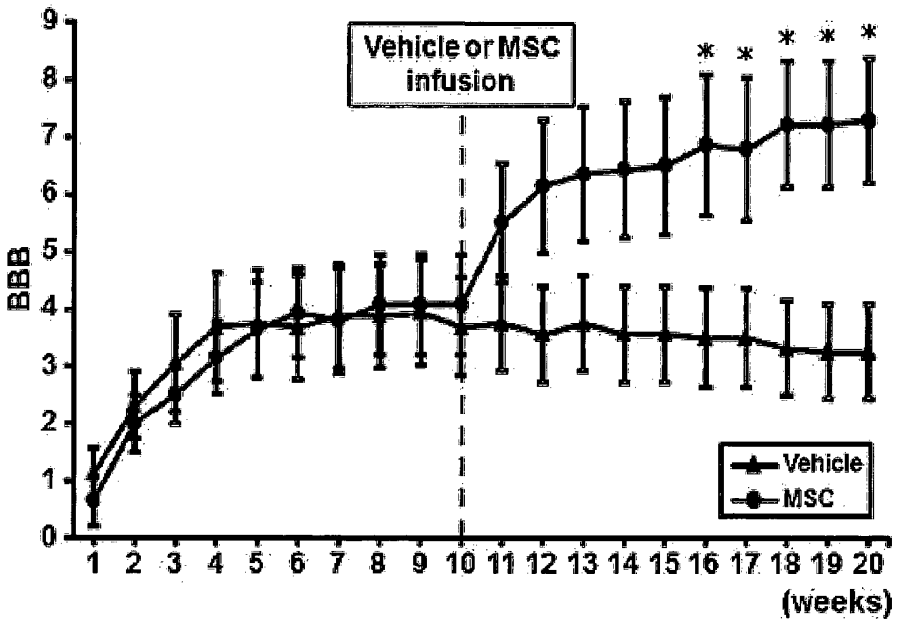
[図１６]


cortex(contralesional)
control
exercise
rMSC
rMSC+exercise
synaptophysin
PSD-95
synaptophysin
PSD-95
500
450
400
350
300
250
200
150
100
50
600
500
400
300
200
100

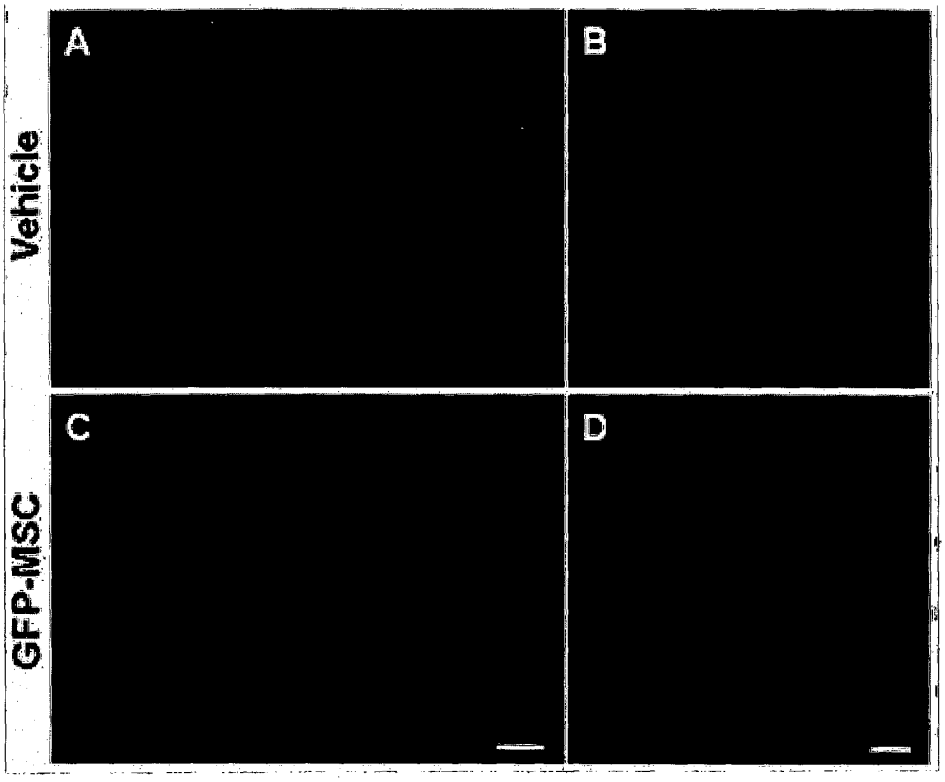
[図17]


striatum(contralesional)
control
exercise
rMSC
rMSC+exercise
Synaptophysin
PSD-95
synaptophysin
PSD-95
0
50
100
150
200
250
300
350
400
450
control
exercise
rMSC
rMSC+exercise

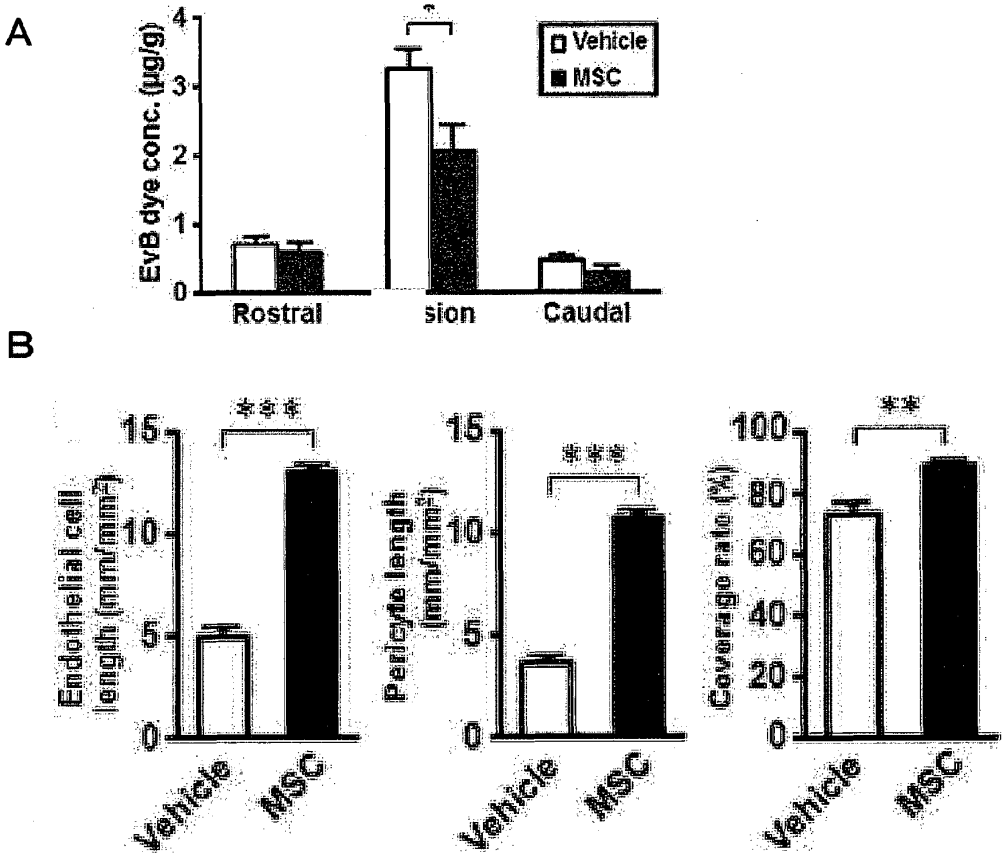
[図１８]


Vehicle or MSC infusion
BBB
(weeks)
Vehicle
MSC
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
*
*
*
*
*

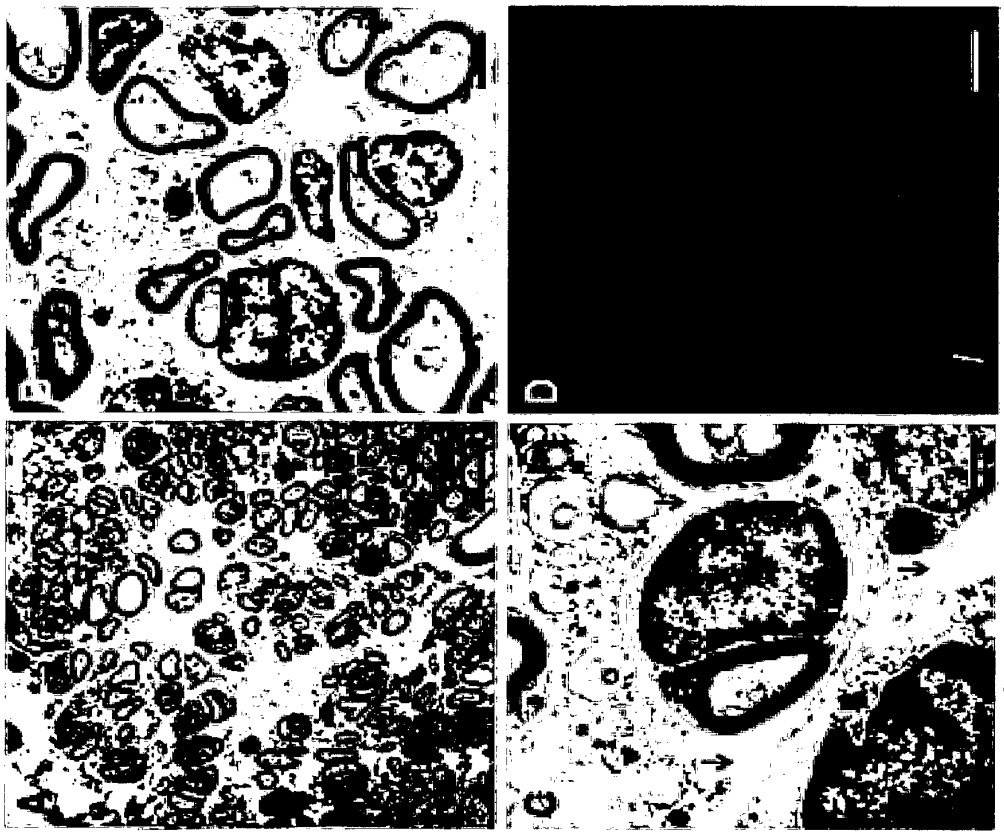
[図１９]

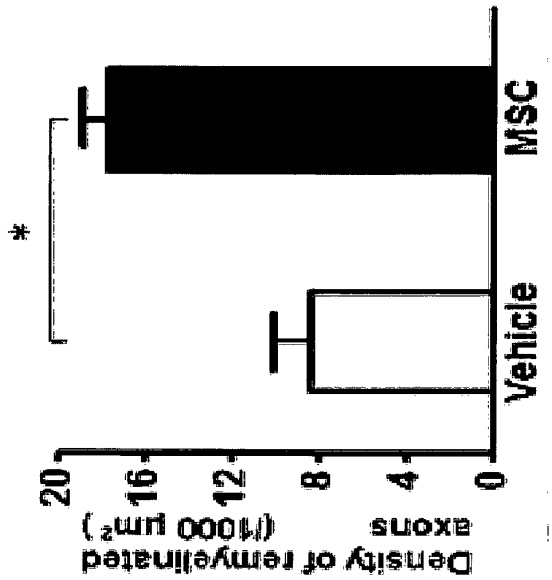


[図２０]

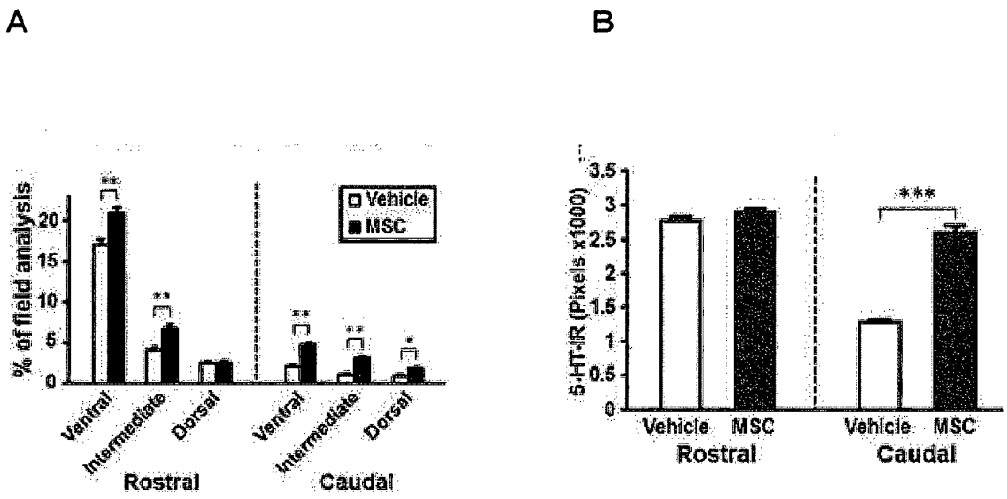

A
EvB dye conc. (μg/g)
Vehicle
MSC
Rostral
sion
Caudal
B
Endothelial cell length (mm/mm²)
Pericyte length (mm/mm²)
Coverage rate (%)
Vehicle
MSC

[図２１]

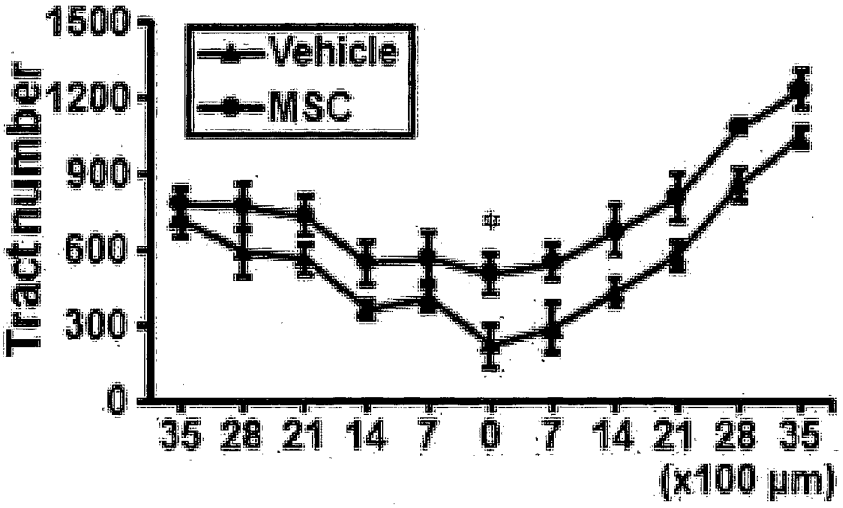

B
D
C


Density of remyelinated axons (/1000 μm²)
0
4
8
12
16
20
Vehicle
MSC
*

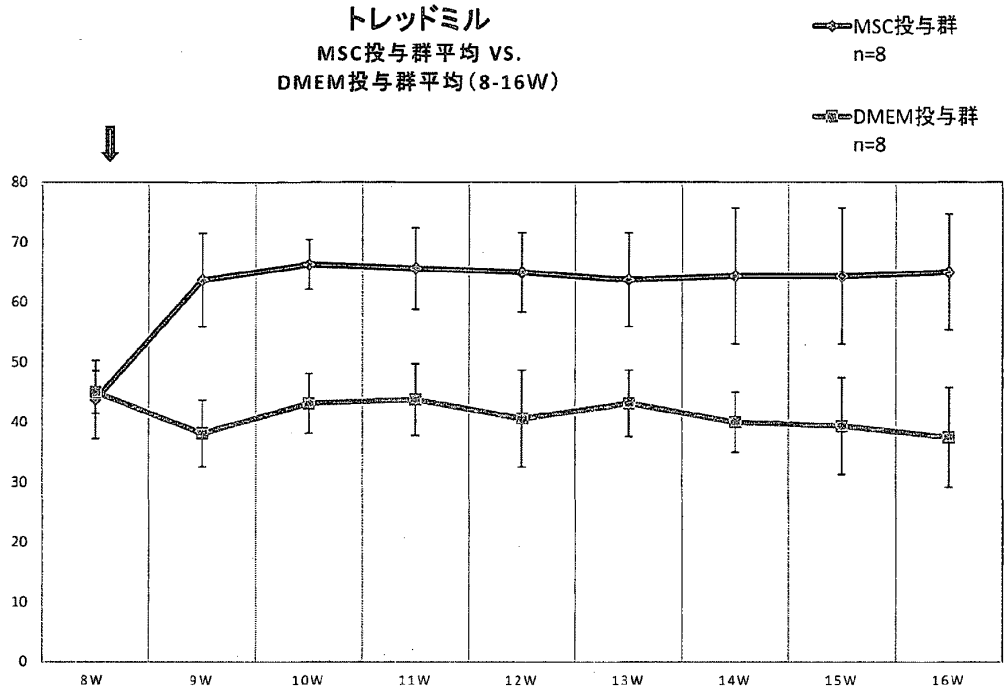
[図２２]


A
B
% of field analysis
Vehicle
MSC
Ventral
Intermediate
Dorsal
Rostral
Caudal
5-HT-IR (Pixels x1000)
***

[図２３]


Tract number
Vehicle
MSC
(x100 μm)

[図２４]


トレッドミル
MSC投与群平均 VS.
DMEM投与群平均(8-16W)
MSC投与群
n=8
DMEM投与群
n=8
80
70
60
50
40
30
20
10
0
8W
9W
10W
11W
12W
13W
14W
15W
16W