**Poor motor-function recovery after spinal-cord injury in anxiety-model mice with phospholipase C–related catalytically inactive protein type 1 knockout**

情動障害マウスにおける脊髄損傷後運動機能回復の検討

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**Abstract**

Mice with a knockout of phospholipase C (PLC)-related inactive protein type 1 (PRIP1$^{-/-}$ mice) display anxiety-like behavior and altered $GABA_A$-receptor pharmacology. Here we examined associations between anxiety and motor-function recovery in PRIP1$^{-/-}$ mice after a spinal-cord injury (SCI) induced by a moderate contusion injury at the 10th thoracic level. Uninjured PRIP1$^{-/-}$ mice spent less distance than wild-type (WT) mice in the center 25% in an open field test (OFT), indicating anxiety-like behavior. Anxiety behavior increased in both WT and PRIP1$^{-/-}$ mice after SCI. WT and PRIP1$^{-/-}$ mice were completely paralyzed on day 1 after SCI, but gradually recovered until reaching a plateau at around 4 weeks. After SCI, the PRIP1$^{-/-}$ mice had significantly greater motor dysfunction than the WT mice. In WT mice after SCI, the percentage of distance spent in the center 25% of the OFT was correlated with the OFT distance traveled and velocity, and with the reaction time in a plantar pressure-sensitivity mechanical test. In PRIP1$^{-/-}$ mice after SCI, the percentage of distance spent in the center 25% of the OFT was correlated with the OFT distance traveled and with the latency to fall in the rotarod test. Six weeks after SCI, the Iba1 and GFAP expressions were elevated at the lesion epicenter in PRIP1$^{-/-}$ mice, and the spinal-cord atrophy and demyelination were more severe than in WT mice. The axonal

fiber development was also decreased in PRIP1$^{-/-}$ mice, consistent with the poor motor-function recovery after SCI in these mice.

## Introduction

Spinal-cord injury (SCI) causes many physiological complications, including both chronic and acute anxiety and depression. A high proportion of SCI patients experience psychological symptoms, including mood disorders that may strongly influence rehabilitative outcomes and quality of life. One report found that 30% of patients develop mood disorders within six months after SCI.[1] In patients with traumatic SCI, 32.3% had a score consistent with probable anxiety on the Hospital Anxiety and Depression Scale (HADS).[2] However, animal experiments have not shown any correlation between psychological well-being and motor-function recovery.[3]

An abnormality in the $GABA_A$ receptor causes affective disorders.[4] $GABA_A$-receptor functions appear to be regulated by phospholipase C (PLC)-related inactive protein type 1 (PRIP1), which was first identified as a novel inositol 1,4,5-trisphospate [Ins(1,4,5)P3]–binding protein that is homologous to PLC-δ1 but is catalytically inactive.[5] The PRIP-family protein PRIP1 is predominantly expressed in the brain, while PRIP2 is expressed ubiquitously.[6] PRIP1-knockout ($PRIP1^{-/-}$) mice display increased anxiety-like behaviors and altered $GABA_A$-receptor pharmacology,[7] including abnormal pain sensation due to altered $GABA_A$-receptor function in the central nervous system (CNS).[8] The relationships between anxiety and altered sensory-function

mechanisms in anxiety-model mice after SCI are unclear. This study examined associations between anxiety and the recovery of motor function in PRIP1$^{-/-}$ mice after SCI.

## Materials and Methods

### Generation of PRIP-knockdown anxiety-model mice by intrathecal siRNA injection

Experiments were conducted in accordance with the Graduate School of Hirosaki University's Guidelines for Animals and the Central Institute for Animal Experimentation. The experiments used 8-week-old female (20–25 g) mice; their hormonal cycles were synchronized to avoid variability due to estrous cycles. C57BL6 mice (CLEA, Japan, Inc) were used as wild-type (WT) control mice, and PRIP1$^{-/-}$ mice were used as the anxiety-model mice.

Three siRNA target sequences each were designed for the *PRIP1* and *PRIP2* genes, using software provided by iGENE Therapeutics Inc. (Tokyo, Japan), which synthesized the siRNA. The siRNA (0.15 pmol of each/5 μl) was injected (0.45 pmol/animal) into the subarachnoid space between the L5 and L6 vertebrae using the hemagglutinating virus of Japan envelope (HVJ-E) vector system (GenomeONE; Ishihara Sangyo Kaisha Ltd., Osaka, Japan).[9]

### SCI model

WT and PRIP1$^{-/-}$ mice were anesthetized with 1% isoflurane in a mixture of 30%

oxygen. The mice underwent sham laminectomy only (WT-sham and PRIP1$^{-/-}$sham mice) at the 10th thoracic level (T10) or laminectomy with contusive SCI at the same level (WT-SCI and PRIP1$^{-/-}$SCI mice). SCI was induced using a commercially available device (IH impactor, Precision Systems and Instrumentation, Lexington, KY, Kentucky, USA) as described previously.[10] This device delivers a rapid, defined-force impact (60 kdyn) with a stainless steel-tipped impounder to create a consistent contusion injury. The initial touch point of the impactor with the dura was determined using the vibrator mode of the impactor tip, and from there a 1.5-mm displacement was applied to the spinal cord. Force-curve readings revealed an average value and standard deviation of 63.3 ± 3.1 kdyn.

**Behavior analyses**

*Open field test (OFT) to assess anxiety-like behavior and motor function*

The open field test is one of the most common procedures used in animal psychology studies.[11] Spontaneous exploratory behavior was evaluated with a OFT apparatus (24 × 24 cm) placed in a quiet room illuminated with white light.[12] The floor of the apparatus was divided equally into nine squares (8 × 8 cm$^2$). A mouse was placed by itself into the open field on the central square, and its spontaneous behavior was

recorded by video tracking system (Capture Star Clever Sys, Inc. Reston, Virginia, USA) for 10 minutes before being scored by an observer blinded to the experimental conditions.

An animal's very first exposure to the OFT can be used to assess changes in emotionality induced by exposure to a novel environment.[12] Rodents tend to stay in close contact with the walls of the open field apparatus in which they are placed.[13] Compared to normal rats, rats with emotional disorders make fewer entries into the central part of the arena.[14] We calculated the total distance traveled by the mouse, the average velocity, and the percentage of walking distance that fell within the center 25% of the open field (TopScan. Clever Sys., Inc. Reston, Virginia, USA). The percentage of distance spent in the center 25% of the field (IC-25) was calculated by dividing the walking distance spent in the center 25% area by the total walking distance. A decrease in the walking distance of travel through the center 25% indicates increased anxiety (Fig. 1A). In addition, the total walking distance and average acceleration were measured to evaluate motor function.

*The Basso Mouse Scale (BMS)*

Hind-limb motor function was evaluated before and for every week after SCI until 6 weeks using the BMS locomotor rating test.[15,16] Behavior was scored at the same time each day by well-trained investigators who were blinded to the treatment groups.

*Rotarod test*

Neurological function and motor coordination were evaluated by placing the mouse on a rod rotating at 10 rpm (Rotarod, Ugo Basile, Varese, Italy) and measuring the time (in seconds) until the mouse fell off onto a platform below,[17,18] thereby activating it to record the time of latency to fall off the rod. The maximum measurement time was 120 seconds. Each test involved three trials.

*Dynamic plantar pressure-sensitivity test (Mechanical test)*

Mechanical nociceptive thresholds for paw withdrawal were assessed by pressing filaments in the sole of the hind paw using a commercially available device set to automatic strength, and measuring the length of the time and the amount of pressure required for the mouse to lift its hind limb (The Dynamic Plantar Aesthesiometer, Ugo Basile, Varese, Italy). Both hind paws were tested. The mouse was acclimatized to the testing area for 30 min before testing.[19,20]

*Plantar heat-sensitivity test (Heat test)*

Hind-paw plantar thermal sensitivity was tested by Hargreaves' method (A method to measure cutaneous hyperalgesia to thermal stimulation in unrestrained animals) using a Plantar Test Apparatus (Ugo Basile, Varese, Italy).[21] The mouse was placed unrestrained in a clear plastic compartment (11 cm × 17 cm × 14 cm). When the mouse was stationary and not attending to the tester or stimulus, an infrared radiant heat source (25 watts) was applied through a glass floor to the middle of the plantar surface of the hind paw, between the foot pads. A photocell automatically stopped the heat source and the timer when the mouse lifted its paw. The maximum period of heat was 20 seconds, at which point the heat cut off automatically to prevent tissue damage. If the mouse could not stand normally, it was held gently to assist paw placement. Each test involved five trials on each hind paw, with at least one minute between trials, and a randomized order of testing to minimize avoidance behaviors. The latency (in seconds) of withdrawal from the heat source was recorded, together with any other behavior indicating attention to the stimulus, including sniffing, licking, looking at the affected paw, or attacking the stimulus. The high and low latencies were dropped for each paw, and the remaining six latencies were averaged for each mouse.[22]

**Histological analysis**

Animals were anesthetized and transcardially perfused with 4% paraformaldehyde in 0.1 M PBS at 6 weeks after laminectomy alone or 2 and 6 weeks after laminectomy with SCI. The spinal cords were removed, embedded in OCT compound (Sakura Finetechnical Co. Ltd., Tokyo, Japan), and cryosectioned at 20 μm in the axial plane (Leica CM3050 S, Germany). The spinal cords were histologically evaluated by hematoxylin-eosin (HE) staining, Luxol fast blue (LFB) staining, and immunohistochemistry.

For immunohistochemistry, tissue sections were stained with the following primary antibodies: anti-glial fibrillary acidic protein (GFAP) (ab4674, Abcam Alexa Fluor, Cambridge, Massachusetts, USA), anti-ionized calcium-binding adapter molecule 1 (Iba1) (SC-28530, Santa Cruz Biotechnology Inc., Dallas, Texas, USA), and anti-neurofilament M (NF-M) (AB5735 EMD Millipore Sigma-Aldrich, Shinagawa, Japan) and with secondary antibodies (A11042 and A11055 Alexa Fluor, Life Technology, Yokohama, Japan). We also used a biotinylated secondary antibody (A11042 A11055 Alexa Fluor, Life Technology, Yokohama, Japan) after exposure to 0.3% $H_2O_2$ for 30 minutes at room temperature to inactivate endogenous peroxidase, and signals were

enhanced with the Vectastain ABC kit (Vector Laboratories, Inc. Burlingame, USA). Nuclei were stained with 4,6-diamidino-2-phenylindole and Hoechst 33258.

**Quantitative analyses of stained spinal-cord sections**

Images of stained tissue sections were captured with a BZ-X700 fluorescence microscope (BZ-X700, Keyence, Osaka, Japan), manually outlined, and quantified. For HE-stained or LFB-stained sections, images were captured at the epicenter of the lesion and 0.5 mm and 1 mm rostral and caudal to the epicenter in axial sections at 40× magnification (n = 5 each); stained areas in the axial sections were measured with the BZ-X700 software. The white matter area was also measured. We automatically captured five regions from each animal in axial sections 4-mm caudal to the lesion epicenter, which was at the T10 level.

For immunohistochemistry, the maximum intensity in the lesion area was measured using the BZ-Analysis application (BZ-X700, Keyence, Osaka, Japan). The $Iba1^{+}GFAP^{+}$ area at the epicenter of the lesion in axial sections was quantified (n = 5). For cell counts, five regions were automatically captured in axial sections at the (T10 level) and 4-mm caudal to the lesion epicenter, and the total $NF\text{-}M^{+}$ area was quantified using light density at 40× magnification (n = 5, each). The total $NF\text{-}M^{+}$ area was also quantified (n = 3).

**Statistical analysis**

All data were presented as mean ± SEM. GFAP and Iba1 immunostaining data were compared across groups using one-way ANOVA followed by the Tukey–Kramer test. The OFT, BMS, rotarod, and LFB and HE staining data were analyzed by repeated-measures two-way ANOVA followed by the Tukey–Kramer test. Associations between anxiety and motor or sensory function were examined by Spearman's rank correlation. R-squared correlation analysis and P-values were calculated with Pearson’s correlation coefficient using SPSS Version 22 (I.B.M. Corporation, Armonk, New York, USA). $P < 0.05$ was considered significant.

## Results

### Behavior analysis

*OFT anxiety assessment*

The IC-25 was significantly lower for PRIP1$^{-/-}$ than WT mice prior to injury (Fig. 1A and 1B). At day 14 after injury, the PRIP$^{-/-}$sham IC-25 was the same as prior to injury, but the IC-25 decreased for the WT-sham, WT-SCI, and PRIP1$^{-/-}$SCI groups. The IC-25 gradually increased for the WT-sham group after injury, but gradually decreased for the WT-SCI and PRIP1$^{-/-}$SCI groups.

*Motor and sensory function*

The BMS score was 0 (complete paralysis) on day 1 after contusive SCI, followed by a gradual recovery that leveled off at around 4 weeks. BMS scores for the WT-SCI and PRIP1$^{-/-}$SCI groups were similar on days 14 and 21 after injury, but the motor function was significantly worse in the PRIP1$^{-/-}$SCI mice on days 7, 28, 35, and 42 (Fig. 2A). WT mice and PRIP1$^{-/-}$SCI mice showed significant decreases in both the total walking distance and the acceleration after injury compared with before injury (Fig. 1C, D). The latency to fall in the rotarod test, which reflects coordinated movement, was significantly shorter for PRIP1$^{-/-}$ mice than WT mice prior to injury

(Fig. 2B), and the times were significantly reduced for both groups after SCI. In the dynamic plantar test, the reaction times showed that the PRIP1$^{-/-}$SCI mice had significant hyposensitivity compared with the WT-sham group before injury (Fig. 2C, D). There were no significant differences in the heat test results at any point between the groups, either before or after injury (Fig. 2E).

*Correlation between anxiety and motor/sensory function*

We examined correlations between anxiety and motor-sensory function at each time point (Tables 1, 2). In the WT-SCI group, the IC-25 at 4 and 6 weeks post-injury was correlated with the OFT distance (R = 0.782, P = 0.002, R = 0.813, P = 0.001), and velocity (R = 0.773, P = 0.002, R = 0.781, P = 0.002). At 2 weeks post-injury, the IC-25 was correlated with the reaction time in the mechanical test (R = 0.568, P = 0.043). In the PRIP1$^{-/-}$ SCI group, the IC- 25 at 2 and 6 weeks was correlated with the OFT distance (R = 0.714, P = 0.047, R = 0.708, P = 0.05), and the IC-25 at 4 weeks was correlated with the rotarod latency to fall (R = 0.711, P = 0.048). Table 3 shows the correlations of IC-25 with parameters in all of the SCI model mice. In the total SCI group, the IC-25 was correlated with the BMS (R = -0.536, P = 0.026) at 2 weeks post-injury and with the OFT distance (R = 0.463, P = 0.04) at 6 weeks post-injury. At pre-

injury, the IC-25 was correlated with the OFT velocity (R = -0.585, P = 0.017) and mechanical test results (reaction time) (R = -0.510, P = 0.044). Thus, in the total SCI model mouse group, the IC-25 was correlated with motor-sensory function at pre-injury and with motor function at post- injury.

**Histological analysis**

*Atrophic change and demyelination after SCI*

Atrophic changes and demyelination of the injured spinal cord were examined 6 weeks after SCI by HE and LFB staining (Fig. 3A, B). Compared to WT mice, the transverse area of the spinal cord was smaller around the injury (in sections 0.5 mm cranial to the epicenter and 0.5 mm and 1 mm caudal from the epicenter) in PRIP1$^{-/-}$ mice, indicating atrophy. White matter at the lesion epicenter was severely demyelinated (Fig 3C, D).

*Iba1$^{+}$-cell infiltration, GFAP$^{+}$-astrocyte glial scars, and sparse axonal fibers*

Six weeks after SCI, immunostaining in PRIP1$^{-/-}$ mice showed extensive inflammation-cell infiltration and elevated GFAP$^{+}$ cell counts in the center of the lesion (Fig. 4A, D-). Iba1 immunoreactivity, which was found in both gray and white matter structures in WT mice, was elevated in both gray and white matter in the PRIP1$^{-/-}$ mice

(Fig. 4A, C). Quantitative analysis revealed significantly more Iba1$^{+}$ cells at the lesion epicenter in PRIP1$^{-/-}$ mice than in WT mice.

GFAP immunoreactivity, found in white matter in the WT mice, was increased in the same areas in PRIP1$^{-/-}$ mice, with significantly more GFAP$^{+}$ cells at the epicenter in PRIP1$^{-/-}$ mice (Fig. 4D). Comparatively few NF-M$^{+}$ axons were observed in PRIP1$^{-/-}$ than WT mice at the lesion epicenter and perilesional area (Fig. 4B, E).

## Discussion

The novelty of this study was the examination of functional recovery after SCI in an anxiety mouse model with $GABA_A$-receptor knockdown. We observed more spinal-cord atrophy and demyelination in the $PRIP1^{-/-}$ group than in the WT group. There were significantly more $Iba1^+$ inflammatory cells and $GFAP^+$ cells at the injury site in $PRIP1^{-/-}$ mice than in WT mice. There were relatively few $NF\text{-}H^+$ axons at the rim of the lesion site in the $PRIP1^{-/-}$ group. Consequently, $PRIP1^{-/-}$ mice had poor motor-function recovery after SCI compared to WT mice. Anxiety was correlated with motor function in the $PRIP1^{-/-}$ mice.

Up to 60% of patients with a spinal-cord injury suffer from anxiety.[23] A previous study in rats showed that on day 21 after SCI, the OFT IC-25 activity was reduced in anxiety/depression and depression groups relative to the non-anxiety group, and that SCI-model rats demonstrated anxiety-like behavior in IC-25 and shock-probe burying tests.[3] In our study as well, both WT and $PRIP1^{-/-}$ mice displayed increased anxiety-like behavior after SCI, indicating that SCI induced anxiety in the animal models regardless of their innate social tendency or background. We also found that on day 14 after injury, the $PRIP^{-/-}$sham IC-25 was the same as prior to injury, while the IC-25 decreased for the WT-sham group. Therefore, anxiety was induced by the laminectomy-only

procedure in the WT-sham group. This discrepancy in the sham models may have been due to the low IC-25 score in the PRIP$^{-/-}$sham group at pre-injury.

Anxiety was correlated with motor function in the PRIP1$^{-/-}$ mice and with motor sensory function in the WT mice. A previous study found no correlation between motor recovery and behavioral tests for depression and anxiety in male rats.[3] As described in the limitations, this discrepancy may be due to gender differences.

In the present study, inflammation in the CNS was elevated in the anxiety-model mice after SCI, which is consistent with previous reports showing that inhibiting $GABA_A$-receptor activity augments inflammatory responses.[24] SCIs include primary and secondary injury processes; the secondary injury includes such events as the breakdown of the blood–spinal cord barrier (BSCB), neuroinflammation, oxidative stress, neuronal injury, and ischemic dysfunction.[25] Inflammation plays a crucial role in the onset of SCI, and inflammatory reactions from local tissue damage can increase the extent of secondary damage.[26] Our present study demonstrated that motor-function recovery after SCI was impaired in PRIP1$^{-/-}$mice, which have $GABA_A$-receptor abnormalities that might contribute to the inflammatory response and secondary injury observed throughout the SCI lesion and adjacent tissue. The PRIP1$^{-/-}$ mice had widespread GFAP$^+$ astrocyte migration and glial-scar formation with few

neurofilaments, resulting in spinal-cord atrophy and a loss of myelin-sheath area. These factors may have impaired the recovery of post-SCI motor and sensory function in the PRIP1$^{-/-}$ mice compared to WT mice, although the mechanisms involved should be investigated in more detail.

Some limitations should be noted for this study. First, we used only female mice. Compared to males, female rats spend more time traveling and less time in one spot in the OFT, which indicates that females are more anxious.[27] Female rats are also reported to have an advantage over male rats in functional recovery after SCI,[28] possibly due to the influence of the sex hormone estrogen. PRIP1$^{-/-}$ mice showed behavioral abnormalities in response to various noxious stimuli.[8] PRIP1-deficient mice may be more vulnerable to inflammation, and in our study, the immune response appeared to contribute to the poor motor-function recovery in PRIP1$^{-/-}$ mice after SCI.

Second, the reaction times in the mechanical pressure-sensitivity tests showed significant hyposensitivity in PRIP1$^{-/-}$ uninjured mice compared to WT mice. Thus, an impairment in motor function prior to injury in PRIP1$^{-/-}$ mice may have influenced the behavior analysis after SCI.

Third, anxiety-like behavior was measured only by the OFT IC-25, with a decrease in IC-25 activity interpreted as a passive anxiety-like sign. It may be useful to

consider additional methods for evaluating anxiety-like behavior.

## Conclusion

In this study, spinal-cord atrophy and demyelination after SCI were more pronounced in anxiety-model PRIP1$^{-/-}$ mice than in WT mice. PRIP1$^{-/-}$ mice showed more inflammatory-cell infiltration, a larger glial-scar area, fewer axonal fibers, and worse motor function recovery compared toWT mice after SCI.


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## Author Disclosure Statement

No competing financial interests exist.

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Fig 1

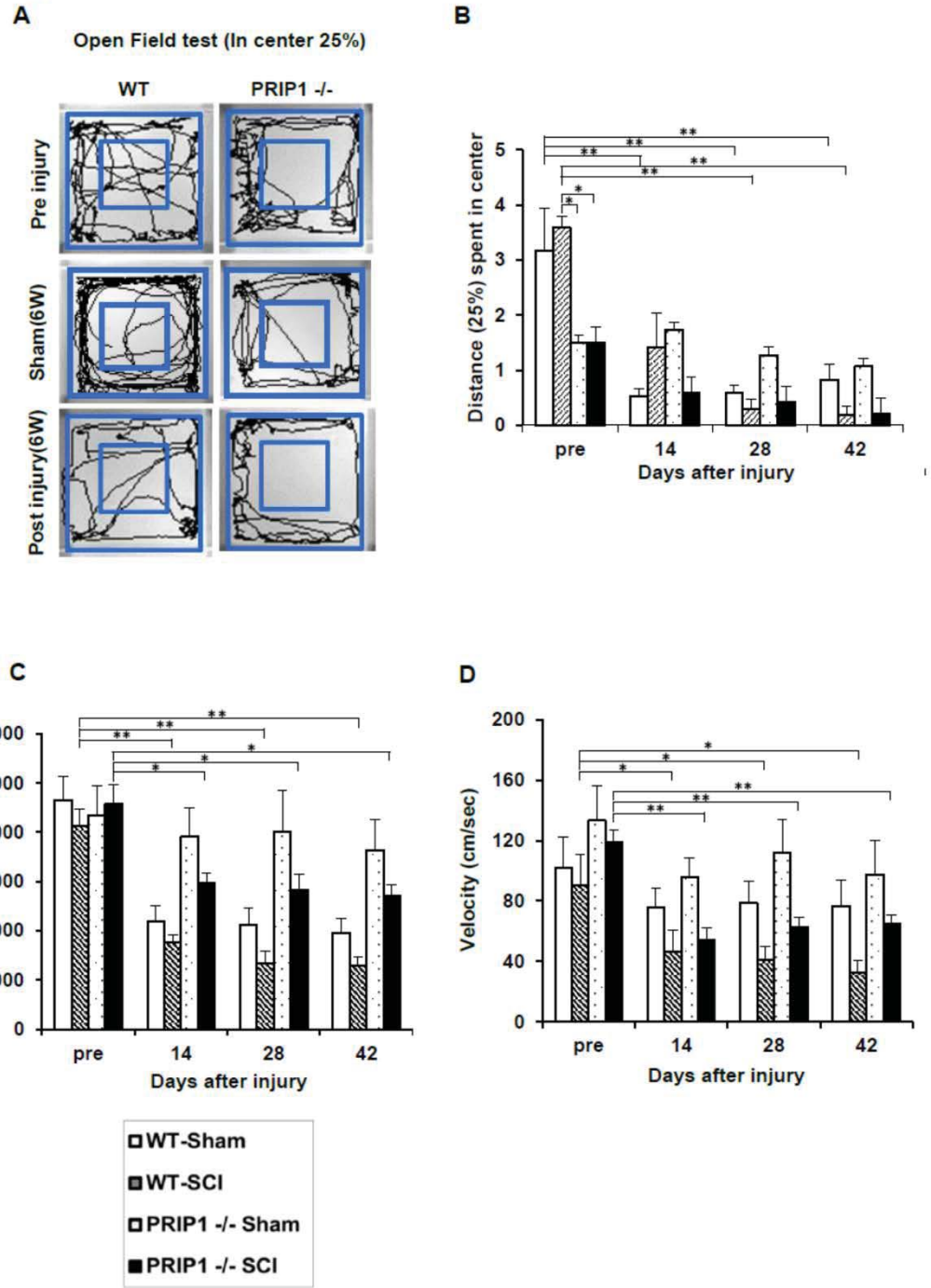
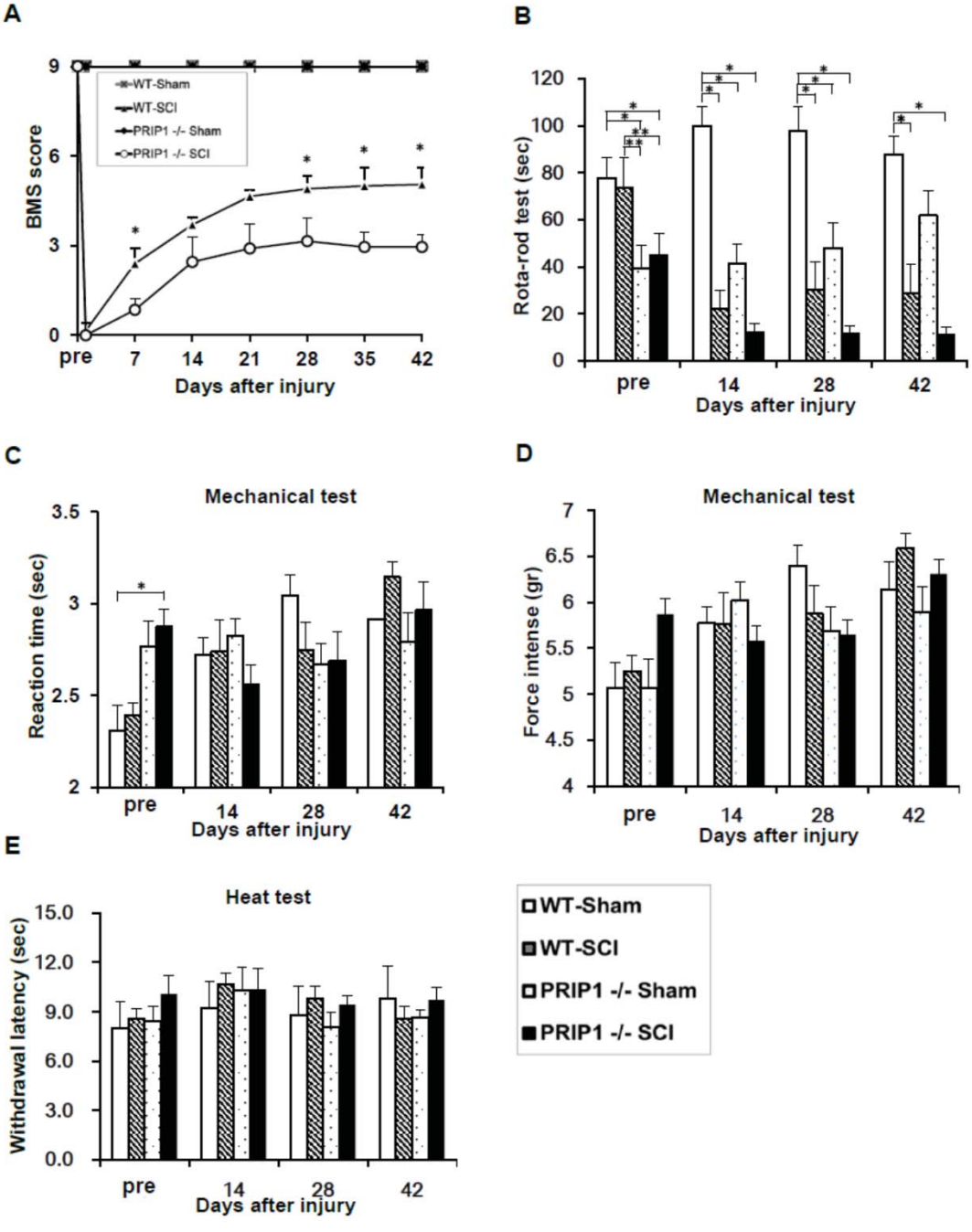

A
Open Field test (In center 25%)
WT
PRIP1 -/-
Pre injury
Sham(6W)
Post injury(6W)
B
Distance (25%) spent in center
pre
14
28
42
Days after injury
C
Walking distance (mm)
pre
14
28
42
Days after injury
D
Velocity (cm/sec)
pre
14
28
42
Days after injury
WT-Sham
WT-SCI
PRIP1 -/- Sham
PRIP1 -/- SCI

Fig 2


A
B
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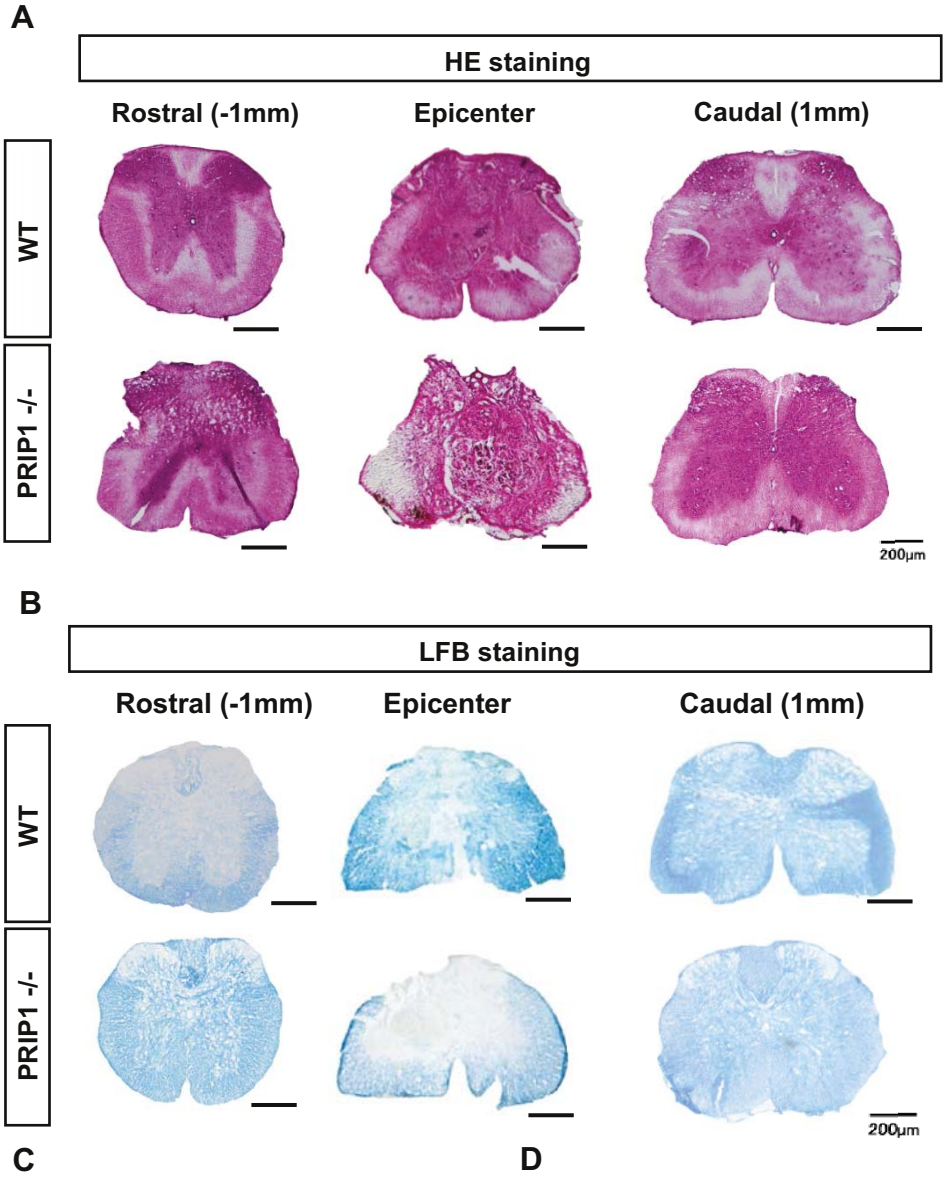
BMS score
WT-Sham
WT-SCI
PRIP1 -/- Sham
PRIP1 -/- SCI
pre
7
14
21
28
35
42
Days after injury
Rota-rod test (sec)
Mechanical test
Reaction time (sec)
Force intense (gr)
Heat test
Withdrawal latency (sec)
WT-Sham
WT-SCI
PRIP1 -/- Sham
PRIP1 -/- SCI

Fig 3


A
HE staining
Rostral (-1mm)
Epicenter
Caudal (1mm)
WT
PRIP1 -/-
200μm
B
LFB staining
Rostral (-1mm)
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PRIP1 -/-
200μm

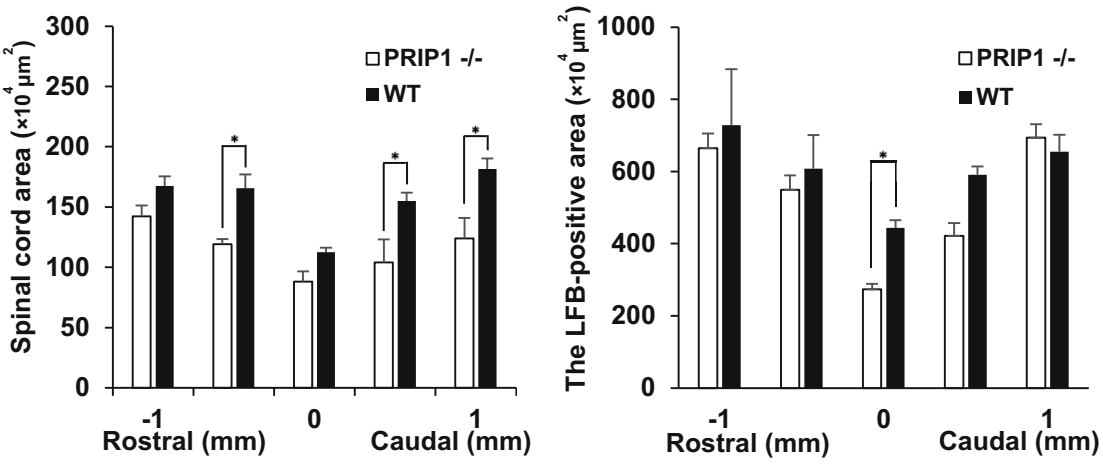
C
Spinal cord area (×10⁴ μm²)
300
250
200
150
100
50
0
PRIP1 -/-
WT
*
*
*
-1
0
1
Rostral (mm)
Caudal (mm)
D
The LFB-positive area (×10⁴ μm²)
1000
800
600
400
200
0
PRIP1 -/-
WT
*
-1
0
1
Rostral (mm)
Caudal (mm)

Fig 4

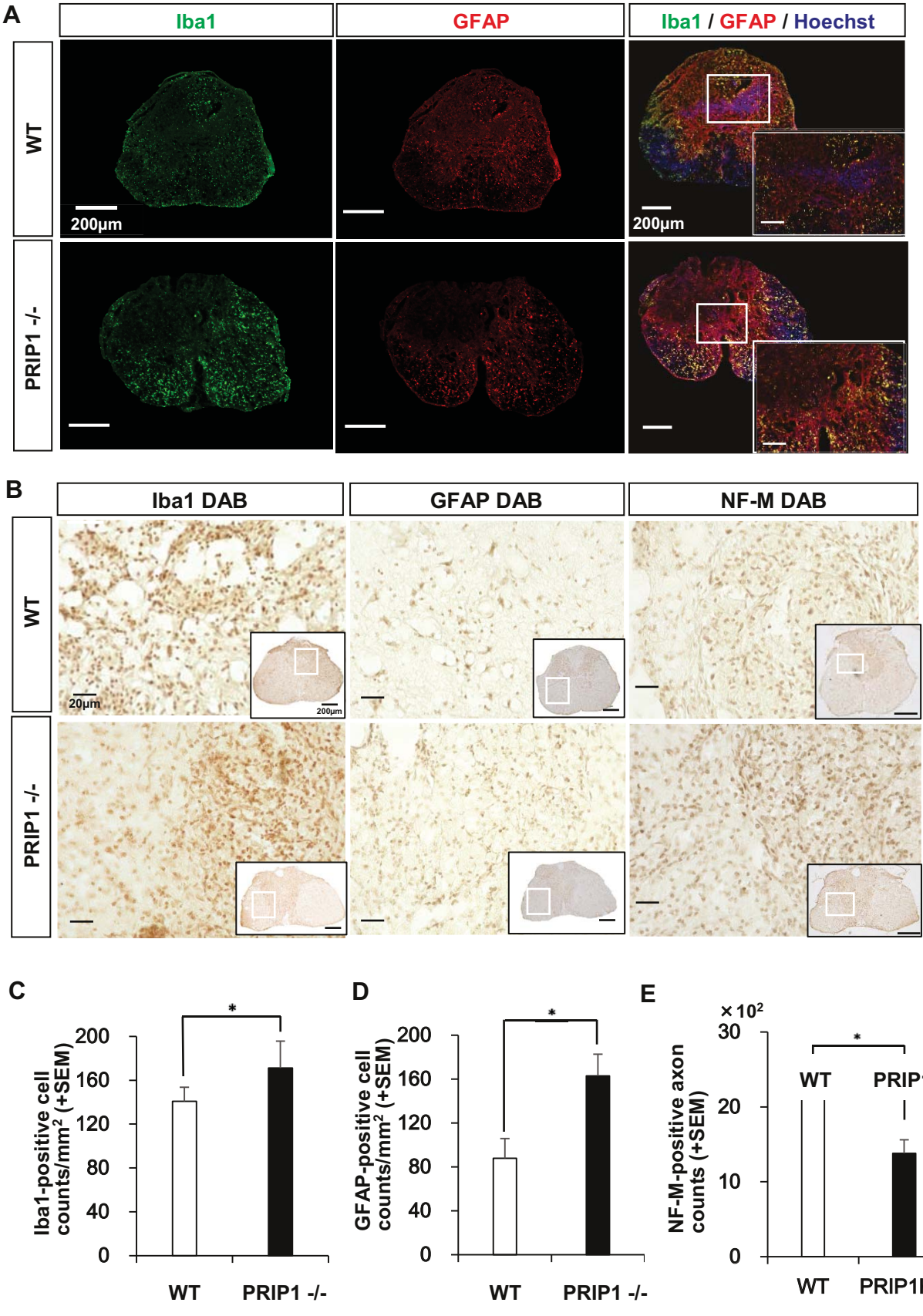
A
Iba1
GFAP
Iba1 / GFAP / Hoechst
WT
PRIP1 -/-
200μm
200μm
B
Iba1 DAB
GFAP DAB
NF-M DAB
WT
PRIP1 -/-
20μm
200μm
C
Iba1-positive cell counts/mm² (+SEM)
200
160
120
80
40
0
*
WT
PRIP1 -/-
D
GFAP-positive cell counts/mm² (+SEM)
200
160
120
80
40
0
*
WT
PRIP1 -/-
E
×10²
NF-M-positive axon counts (+SEM)
30
20
10
0
*
WT
PRIP1 -/-
WT
PRIP1KO

**Table 1. Correlations with IC-25 in WT-SCI mice.**

| | Pre | 2W | 4W | 6W |
|---|---|---|---|---|
| BMS (point) | | 0.575 (-0.172) | 0.755 (-0.096) | 0.842 (-0.062) |
| OFT distance (mm) | 0.596 (-0.162) | 0.452 (-0.229) | 0.002* (0.782) | 0.001* (0.813) |
| OFT velocity (mm/sec) | 0.823 (-0.069) | 0.540 (-0.187) | 0.002* (0.773) | 0.002* (0.781) |
| Rota-rod (sec) | 0.288 (-0.319) | 0.245 (-0.348) | 0.827 (-0.068) | 0.836 (-0.064) |
| Mechanical test : reaction time (sec) | 0.245 (-0.347) | 0.043* (-0.568) | 0.419 (-0.245) | 0.743 (-0.101) |
| Mechanical test : force intense (gr) | 0.404 (-0.253) | 0.063 (-0.528) | 0.536 (-0.189) | 0.721 (-0.110) |
| Heat test (sec) | 0.674 (-0.129) | 0.628 (-0.149) | 0.160 (-0.413) | 0.420 (-0.245) |

In the WT-SCI group, the OFT IC-25 (percentage of time spent in the center 25%) was correlated with the OFT distance and velocity at 4 and 6 weeks, and with the reaction time in the mechanical plantar test at 2 weeks.

P (R) P < 0.05: statistically significant. R 0 to -1: negative relationship; R 0 to 1: *positive relationship.

**Table 2. Correlations with IC-25 in PRIP1$^{-/-}$SCI mice**

| | Pre | 2W | 4W | 6W |
|---|---|---|---|---|
| BMS (point) | | 0.188 (-0.518) | 0.234 (-0.476) | 0.813 (-0.101) |
| OFT distance (mm) | 0.083 (-0.647) | 0.047* (0.714) | 0.731 (-0.145) | 0.050* (0.708) |
| OFT velocity (mm/sec) | 0.272 (-0.443) | 0.102 (-0.619) | 0.504 (-0.279) | 0.127 (-0.586) |
| Rota-rod (sec) | 0.588 (-0.228) | 0.320 (-0.405) | 0.048* (0.711) | 0.863 (-0.073) |
| Mechanical test : reaction time (sec) | 0.771 (-0.123) | 0.349 (-0.383) | 0.886 (-0.061) | 0.493 (-0.286) |
| Mechanical test : force intense (gr) | 0.778 (-0.120) | 0.399 (-0.347) | 0.966 (-0.018) | 0.601 (-0.220) |
| Heat test (sec) | 0.608 (-0.216) | 0.570 (-0.238) | 0.487 (-0.289) | 0.774 (-0.122) |

In the PRIP1$^{-/-}$SCI group, the OFT IC-25 (percentage of time spent in the center 25%) was correlated with the OFT distance of at 2 weeks and with the time to fall in rotarod tests at 4 weeks.

P (R) P < 0.05: statistically significant. R: 0 to -1: negative relationship; R 0 to 1: *positive relationship.