

*Supplementary Information*

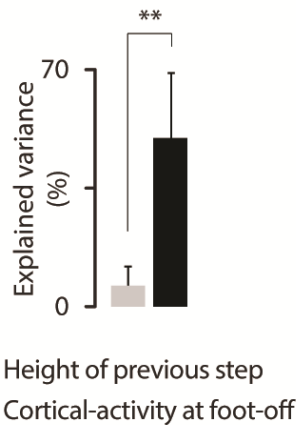
**BRAIN-CONTROLLED MODULATION OF  
SPINAL CIRCUITS IMPROVES RECOVERY  
FROM SPINAL CORD INJURY**

Bonizzato et al.

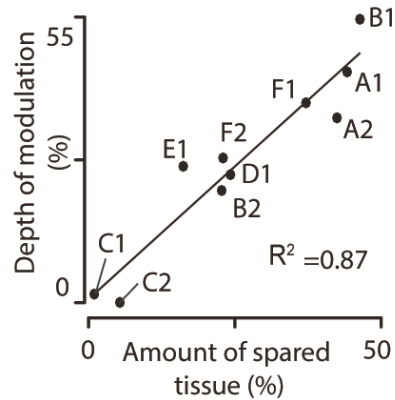
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**a** Variance in step height explained by cortical activity at foot-off

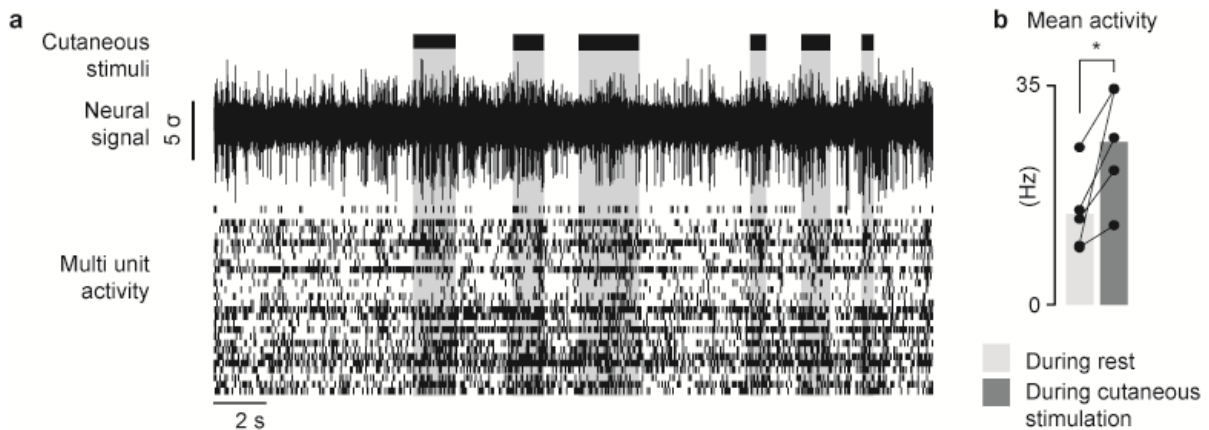
Animal ID	Correlation (r value)
A1	0.77
A2	0.83
B1	0.61
B2	0.67
D1	0.35
E1	0.84
F1	0.64
F2	0.79



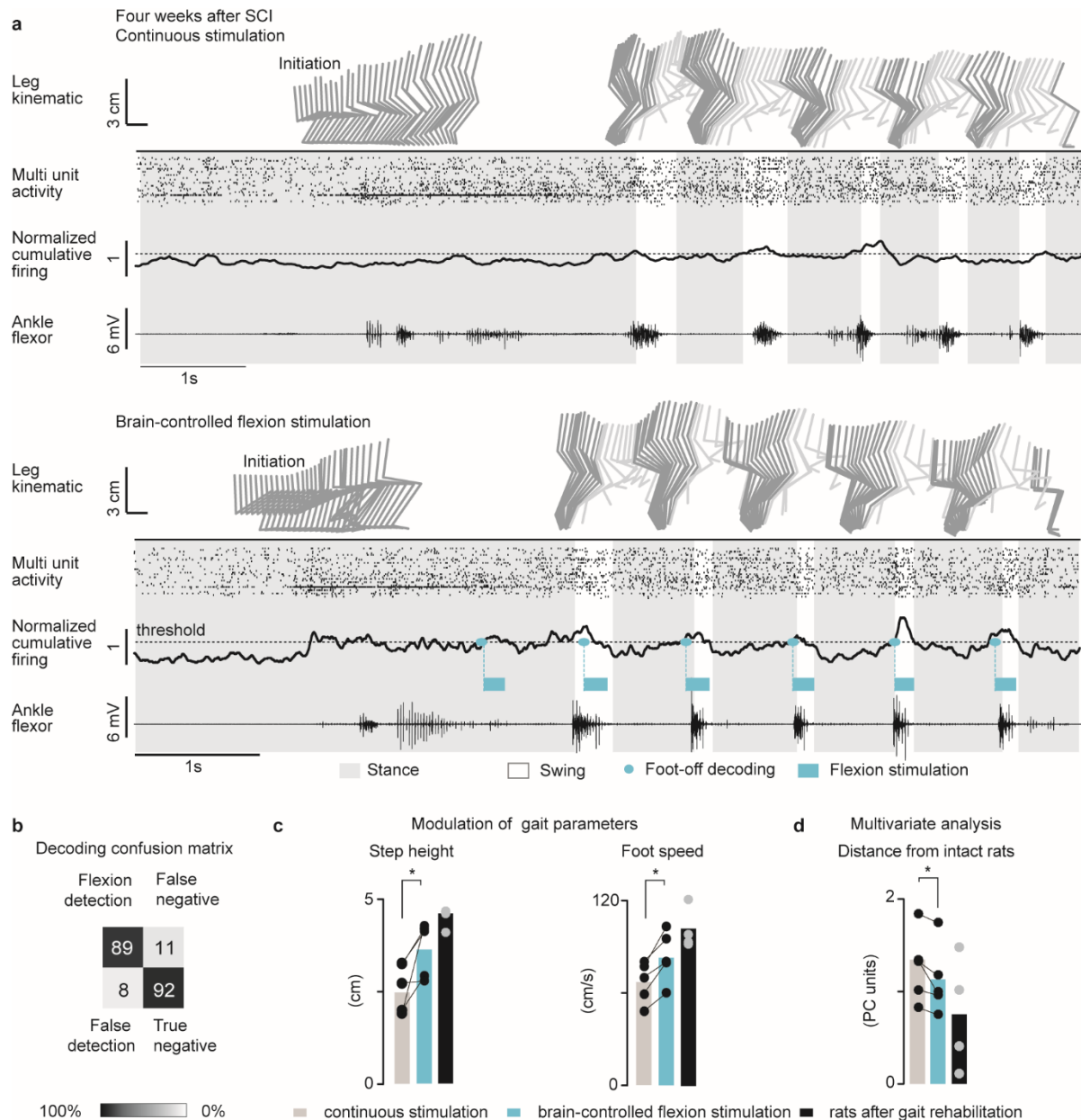
**b** Modulation of cortical ensemble population increases with the amount of spared tissue



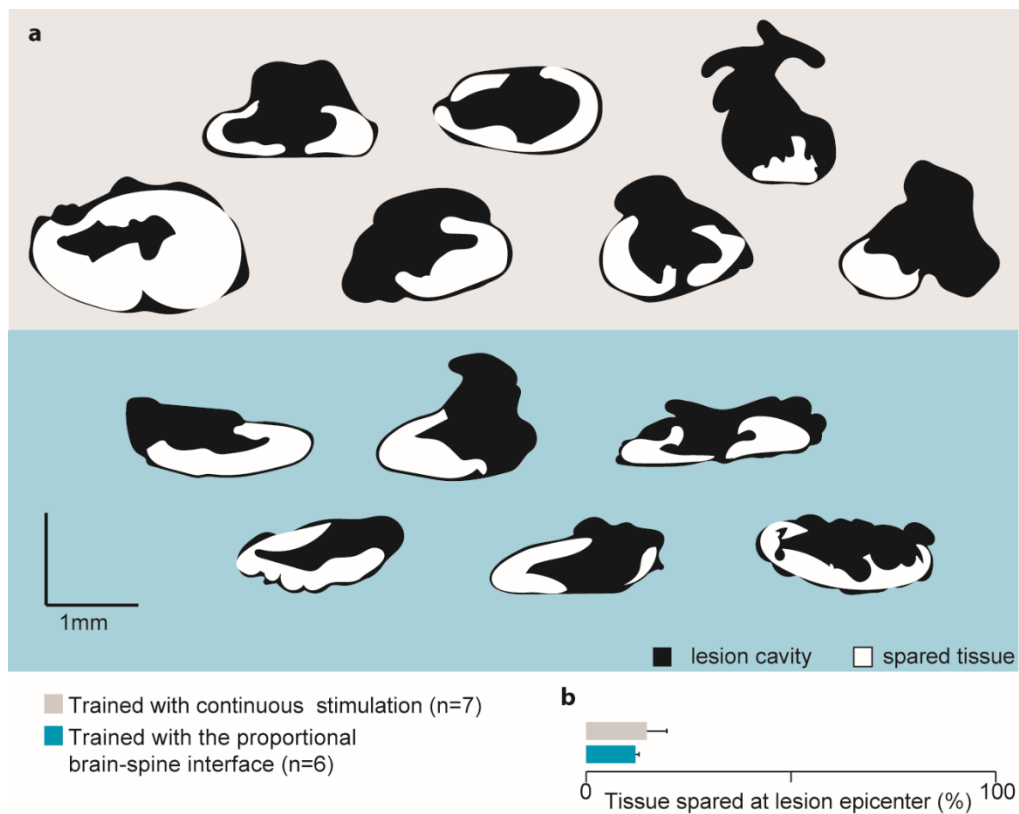
**Supplementary Fig. 1. Modulation of cortical ensemble population correlates with step height, but depends on the amount of spared tissue. (a)** For each rat, the correlation between the cortical activity at foot-off and the step height was calculated. The value of correlation coefficients is reported for each rat. The bar plot reports the mean variance of step height explained by the cortical activity at foot-off measured during the preceding step and for the ongoing step ( $n=8$ , mean  $\pm$  SD). \*\*,  $P < 0.01$ . **(b)** Correlation between the amount of spared tissue (%) and the extent of cortical population ensemble modulation during locomotion for all the experimental rats involved in the design of the brain-spine interface. The modulation is expressed in percent of increase of firing rate during locomotion compared to rest. The labels identifying each rat refer to **Supplementary Table 1**. Note that rats C1 and C2 were excluded from the study due to the absence of modulation in cortical ensemble population due to pronounced tissue damage (outside the targeted range of SCI severity).



**Supplementary Fig. 2. Cortical activity evoked by sensory stimulation of the paw. (a)** Example of cortical activity (single channel and multi-unit activity) in response to successive applications of a pressure on the paw contralateral to the recordings. The horizontal bars and shaded region highlight the time windows over which the stimulation was applied. Recordings were performed at 3 weeks post-injury. **(b)** Bar plot reporting the mean activity measured over all the recorded multi-units during rest and over the period of cutaneous stimulation ( $n=5$ ). \*,  $P < 0.05$ .



**Supplementary Fig. 3. Binary brain–spine interface alleviates locomotor deficits during overground locomotion.** (a) Recordings of bipedal locomotion along the runway at 3 weeks post–injury during continuous stimulation and with the binary brain–spine interface. Conventions are the same as in Fig. 2. (b) Confusion matrix of foot–off event decoding calculated across the 5 rats. (c) Bar plots reporting mean values and individual mean values of parameters modulated during continuous stimulation versus brain–controlled flexion stimulation. The values recorded in rats after gait rehabilitation are reported as a reference. (d) Bar plot reporting the distance from intact rats in the PC space calculated from 55 gait parameters, which thus quantifies locomotor performance. \*,  $P < 0.05$ .



**Supplementary Fig. 4. Quantification of the amount of spared spinal cord tissue. (a)** Reconstruction of the lesion cavity (black) and spared tissue (white) at the epicentre of the contusion for both trained groups. **(b)** Bar plot reporting the amount of spared tissue for the two trained groups (mean  $\pm$  SEM).

Animal ID	Binary BSI on treadmill Fig. 2	Binary BSI overground Supp. Fig. 3	Cortical modulation vs. spared tissue Supp. Fig. 1	Proportional BSI early after SCI Fig. 6	Rehabilitation enabled by proportional BSI Fig. 10	Proportional BSI staircase/overground Fig. 8	Cutaneous paw stimulation Supp. Fig. 2
A1	✓		✓				✓
A2	✓		✓				✓
B1		✓	✓				
B2		✓	✓				
C1			✓				
C2			✓				
D1			✓				
E1	✓	✓	✓				
F1	✓	✓	✓	✓			
F2	✓	✓	✓	✓			
G1				✓			
G2				✓			
G3				✓			
H1					✓		
H2					✓		
H3					✓		
H4					✓		
H5					✓		
H6					✓		
H7					✓		
I1					✓		
I2					✓	✓	
I3					✓	✓	
I4					✓	✓	
I5					✓	✓	
I6					✓	✓	
J1							✓
J2							✓
J3							✓

**Supplementary Table 1. List of experimental procedures conducted per group of rats that participated to the experiments.**

Temporal features of gait	26 Whole limb speed depth
1 Duration of gait cycle	27 Crest elevation depth
2 Speed of animal during stride	28 Thigh elevation depth
3 Stance duration	29 Leg elevation depth
4 Swing duration	30 Foot elevation depth
5 Drag duration	
	Limb coordination
Limb endpoint trajectory	31 Temporal coupling between crest and thigh
6 Step height	32 Temporal coupling between thigh and leg
7 Ankle clearance	33 Temporal coupling between leg and foot
8 Maximal foot speed during swing	34 Correlation between crest and thigh oscillations
9 Foot acceleration at swing onset	35 Correlation between crest and leg oscillations
10 Foot speed at swing onset	36 Correlation between crest and foot oscillations
11 Foot lateral displacement during swing	37 Correlation between thigh and leg oscillations
	38 Correlation between thigh and foot oscillations
Stability	39 Correlation between leg and foot oscillations
12 Stance width	40 Relative duration between crest and thigh angle minima
13 Maximum hip vertical position	41 Relative duration between crest and leg angle minima
14 Minimum hip vertical position	42 Relative duration between crest and foot angle minima
15 Hip oscillation amplitude	43 Relative duration between thigh and leg angle minima
16 Pelvic center of mass vertical motion	44 Relative duration between thigh and foot angle minima
	45 Relative duration between leg and foot angle minima
Joint angles	46 Phase of Crest maximal contraction
17 Hip joint excursion	47 Phase of Hip maximal contraction
18 Knee joint excursion	48 Phase of Knee maximal contraction
19 Ankle joint excursion	49 Phase of Ankle maximal contraction
20 Hip joint speed depth	50 Phase of Foot maximal contraction
21 Knee joint speed depth	51 Lag between crest and thigh maxima
22 Ankle joint speed depth	52 Lag between thigh and leg maxima
23 Foot lateral oscillation	53 Lag between leg and foot maxima
Segmental oscillations	Robotic assistance required
24 Whole-limb excursion amplitude	54 Percentage of body weight supported
25 Whole-limb lateral excursion amplitude	55 Robot vertical force

**Supplementary Table 2. Analysis of kinematic activity: parameters computed for quantification.**