Restoring Voluntary Control of Locomotion after Paralyzing Spinal Cord Injury

By:
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Presented by: Brian Morris

- (Van Der Brand et. al. 2012 Science)

JOURNAL

Rubia van den Brand et al., SCIENCE **336:**1182-1185 (June 1, 2012)

- Science/ AAAS

Author/lab

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Grégoire Courtine

Lab Mission

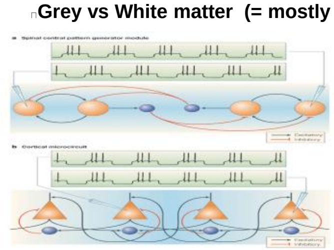
- Our mission is to design innovative interventions to restore sensorimotor functions after CNS disorders, especially spinal cord injury, and to translate our findings into effective clinical applications capable of improving the quality of life of people with neuromotor impairments.

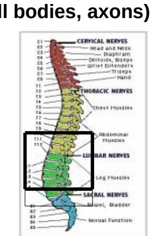
Background on the Lab

- Kay, Simone: Lab Technicians
- Quentin, Joachim, Jack, Nadia, Pavel, Rubia: Post-Docs
- Michèle, Lucia, Isabel, Eduardo, Silvestro: PhD students

Some important terms

- **Central Pattern Generator (CPG):** A circuit capable of
- creating rhythmic motor output without rhythmic input
- **Cervical/Thoracic/Lumbar/sacral**
- 7 cervical, 13 thoracic (ribs bearing), 6 lumbar
- **Grey vs White matter (= mostly cell bodies, axons)**





Previous Research

- Transformation of nonfunctional spinal circuits into
- functional states after the loss of brain input. (Courtine et al., 2008)

- Previous work done on rats and zebrafish
- Mechanism for rehabilitation of circuits
- studied in most cases, not well understood

Introduction

- Activity based spinal motor output training
- - activation of cortical neurons
- Hypothesis: Re-establish supraspinal control of locomotion
- Electrical and chemical stimulation
- Over-ground trained vs treadmill

Methods

- Video http://www.sciencemag.org/content/suppl/2012/05/30/336.6085.1182.DC1.html

Results

- Regain of function, automated vs. sensory ques
- Remodeling of circuits, and bypass of lesions
- Over ground vs treadmill
- Density of CST axons in each case
- Correlation between motor cortex and Cortical Spinal Tracts
- Cortex necessity
- Seratonergic inputs
- Figures

Figures

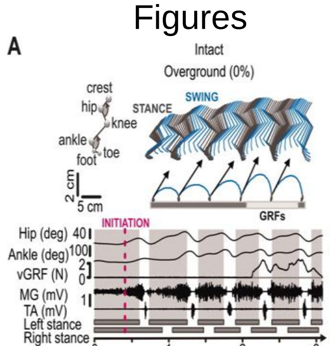
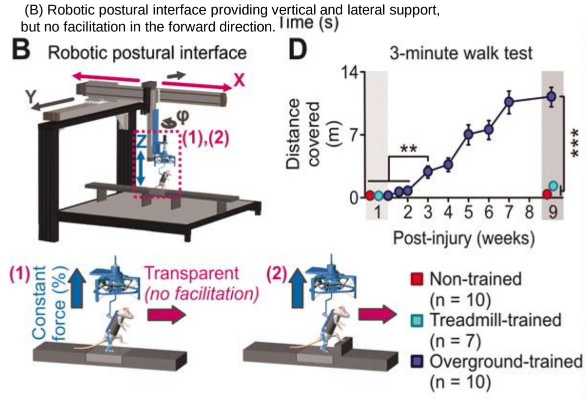
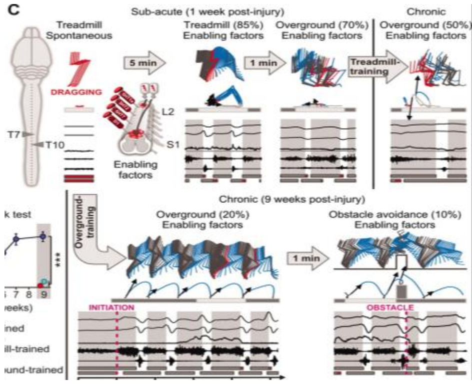


Fig. 1.Multisystem neuroprosthetic training restores voluntary locomotion after paralyzing SCI.
(A) Left hindlimb kinematics, hindlimb end-point trajectory and velocity vector, vertical ground reaction forces (vGRF), as well as electromyographic (EMG) activity of medial gastrocnemius (MG) and TA muscles during bipedal locomotion in an intact rat.

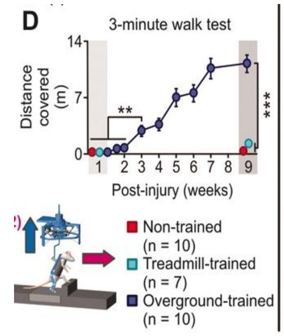
Figures contd.

(B) Robotic postural interface providing vertical and lateral support, but no facilitation in the forward direction.





(C) Representative left hindlimb stepping patterns recorded under the various experimental conditions 1 and 9 weeks post SCI.



(D) Distance covered in 3 min during bipedal locomotion.%, Body weight support. **P < 0.01. ***P < 0.001. Error bars, SEM

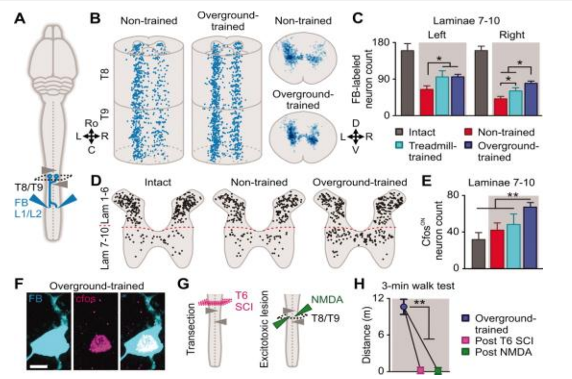
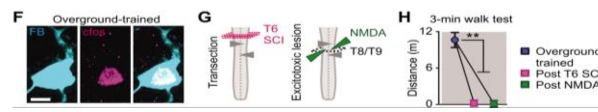
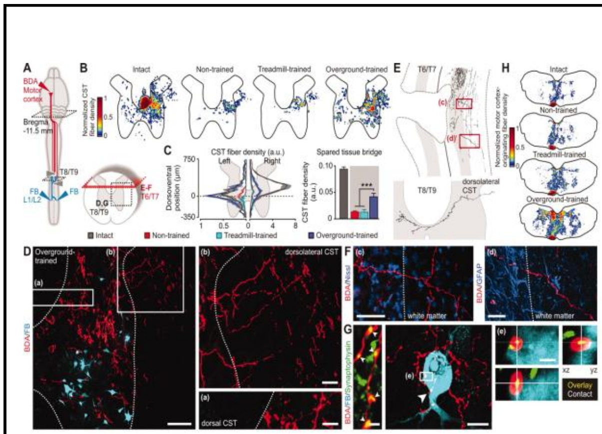


Fig. 2. Multisystem neuroprosthetic training promotes the formation of intraspinal detours that relay supraspinal information. Diagram illustrating anatomical experiments. (B) Longitudinal and transverse views of three-dimensional (3D) reconstructions of Fast blue–labeled (FB) neurons between the lesions. L, left; R, right; Ro, rostral; C, caudal; D, dorsal; V, ventral. (C) Counts (n = 6 to 9 rats per group) of FB neurons in laminae 7 to 10 of T8/T9 segments after 45 min of continuous locomotion. (D) C-fos expression patterns in T8/T9 segments. (E) Counts (n = 5 to 7 rats per group) of c-fos ON neurons in laminae 7 to 10 after continuous locomotion.



(F) Colocalization of FB and c-fos. Scale bar, 10 mm.
(G) Overground-trained rats received a complete T6 SCI (n = 2) or T8/T9 NMDA microinjections (n = 3).
(H) Distance covered in 3 min before and after the lesions.
*P < 0.05. **P < 0.01. Error bars, SEM.



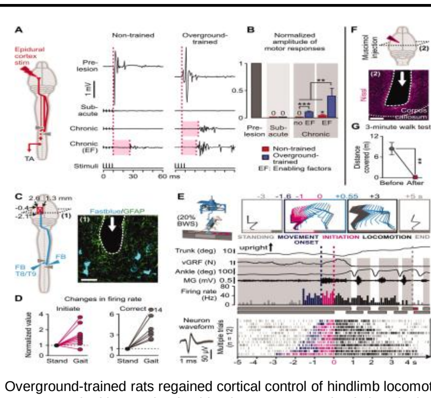


Fig. 4. Overground-trained rats regained cortical control of hindlimb locomotion.
(A) Responses evoked by a train of epidural motor cortex stimulations in the left
(B) TA muscle in a nontrained and overgroundtrained rat. (B) Mean (n = 5 rats per group)
(C) amplitude of responses.

Discussion

- Importance of remodeling: use dependent vs complete regeneration
- Implications for future: robots or not

Answers to questions

1: (Answer in class) Define a Central Pattern Generator (CPG)
in one sentence.: A circuit capable of creating rhythmic
motor output without rhythmic input

2: Where were the lesions in the spinal cord made?
Why were these locations chosen?:
T7/T10, to eliminate supraspinal input without complete lesion

3: How did they stimulate the cord after injury?:
Electrical stimulation (L2, S1) and a drug coctail of Seratonin
agonists and Dopamine

References

http://courtine-lab.epfl.ch/ Lab/author

Magazine
http://www.sciencemag.org/search?author1=Gr%C3%A9goire+Courtine&sortspec=date&submit=Submit

Prof Courtine: www.google.com/images

CPG:http://www.nature.com/nrn/journal/v6/n6/images/nrn1686-f1.jpg

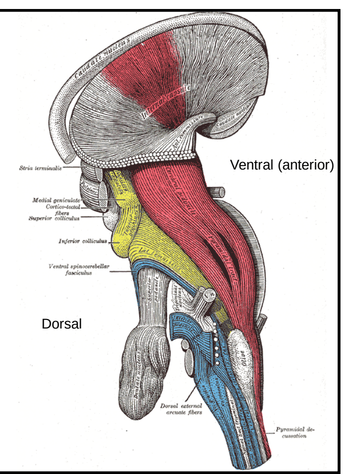
Blue spinal cord injury picuture:
http://blog.billhurst.com/lawyer-login-panel/wp-content/uploads/2011/03/spinal-cord.jpg

Treadmill picture: http://www.rehabmed.emory.edu/pt/images/spinal_1.jpg
Courtine et al., Nat. Med. 14, 69 (2008).

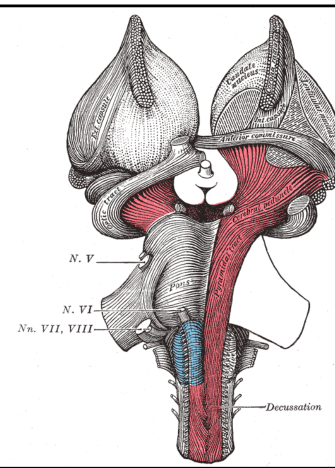
See also Video of Grégoire Courtine explaining results of this paper

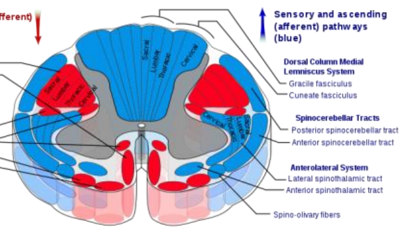
http://actu.epfl.ch/news/walking-again-after-spinal-cord-injury-2

Corticospinal tract (in red)
From Grey's anatomy



Ventral view of cortico-spinal motor tract – Pyramidal tract and pyramidal decussation (caudal to the pons)





Cross section of spinal cord showing sensory bundles (in blue) and motor bundles in red. The lateral pyramidal tracts project to the limbs, the ventral (anterior) tracts project to the trunk.

[Neuroanatomy - The **Corticospinal Tract** in 3D - YouTube](http://www.youtube.com/watch?v=9BaWBGRVxp8)

www.youtube.com/watch?v=9BaWBGRVxp8Jul 19, 2009 - 3 min - Uploaded by BrainwashedSoftware
Visit http://www.brainwashedsoftware.com for more information. This is the **corticospinal tract** as seen in Axiom **...**

http://www.youtube.com/watch?v=9BaWBGRVxp8