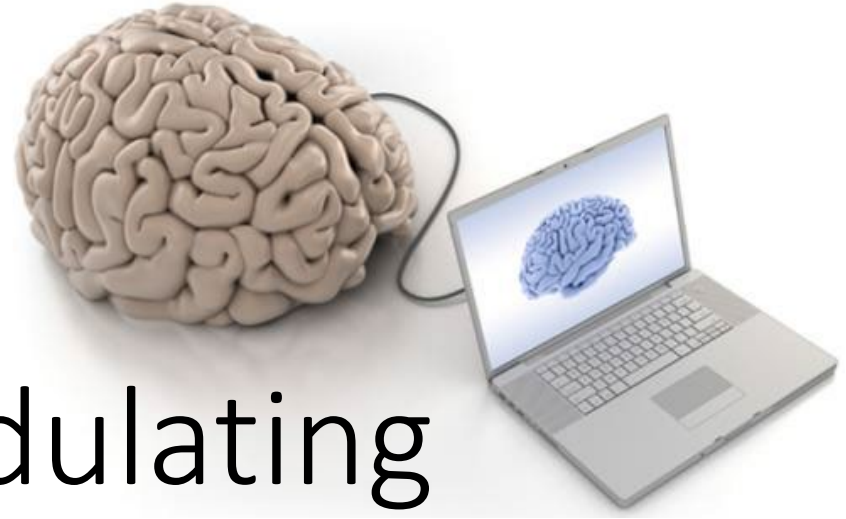

Interrogating and Modulating Sensorimotor Circuits

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Violeta Pellicer Morata, PhD

Nasreen Nemati, MS

Samiha Khan, MS

Solomon Mesfin, MS

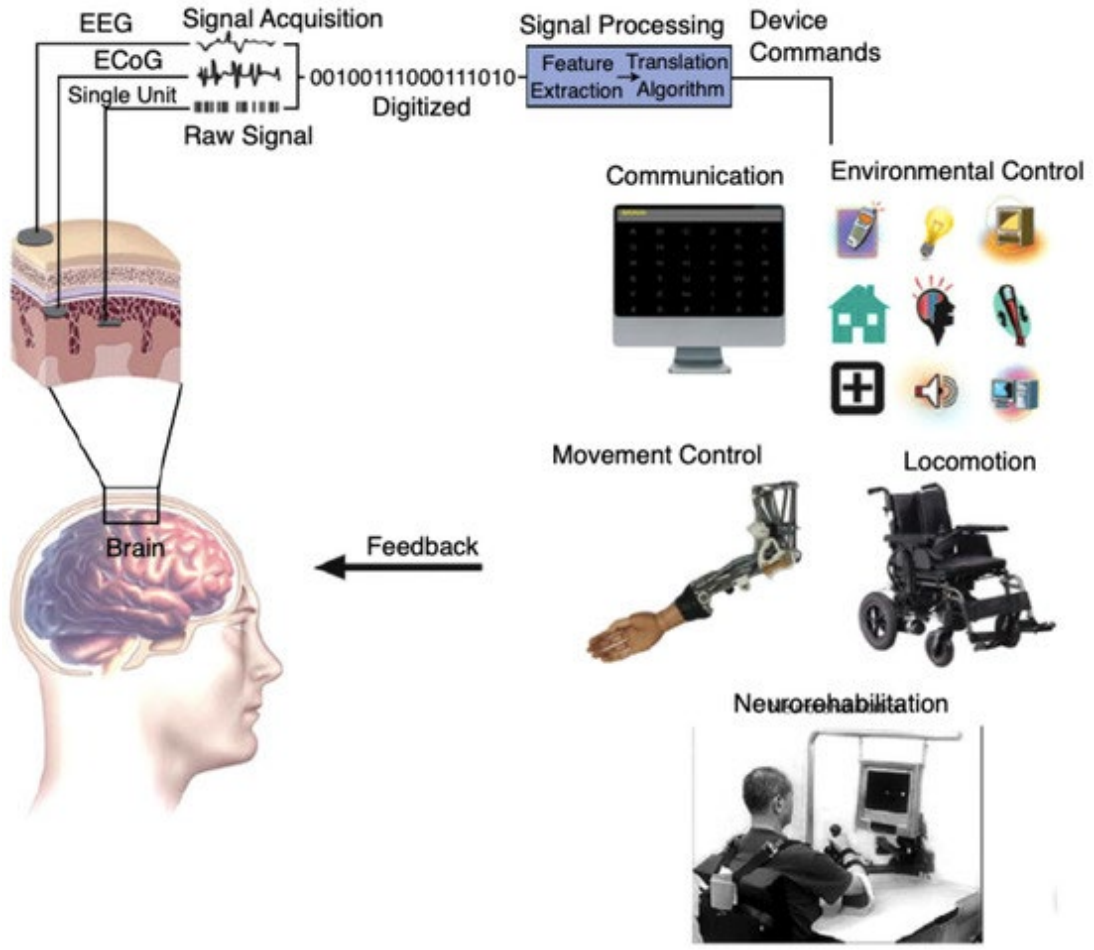
Cesar Gutierrez Mendoza, BS

Lauren Carter

Brain-Computer Interfaces

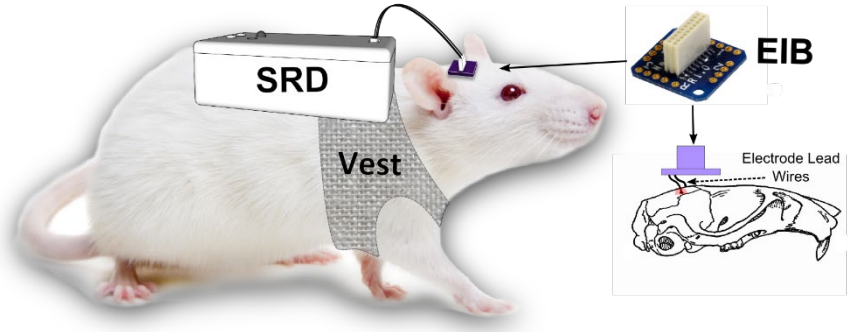
www.theverge.com/2014/6/12/5804708/world-cup-first-kick-paralyzed-man-in-mind-controlled-exoskeleton

World Cup 2014 kicked off by paralyzed man in mind-controlled robot suit



Kawala-Sterniuk, et al. *Brain Sci.* **2021**. https://doi.org/10.3390/brainsci11010043

Overview



Telemetry-controlled simultaneous stimulation-and-recording device (SRD)

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- 1.7 million amputees in US, 70% suffer from phantom limb pain
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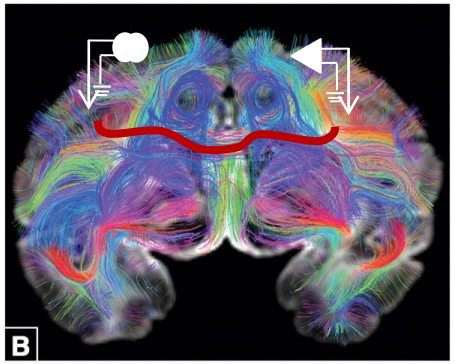

Schmahmann J D et al. Brain 2007;130:630-653

Repetitive intracortical microstimulation may

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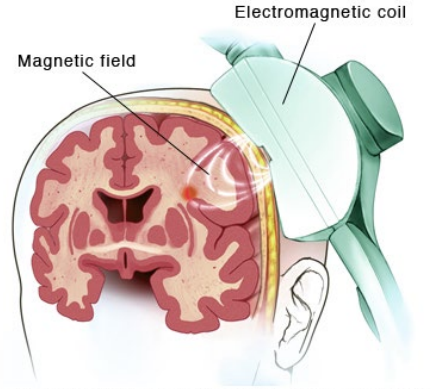
- induce cortical remodeling in patients suffering from stroke

Transcranial Magnetic Stimulation

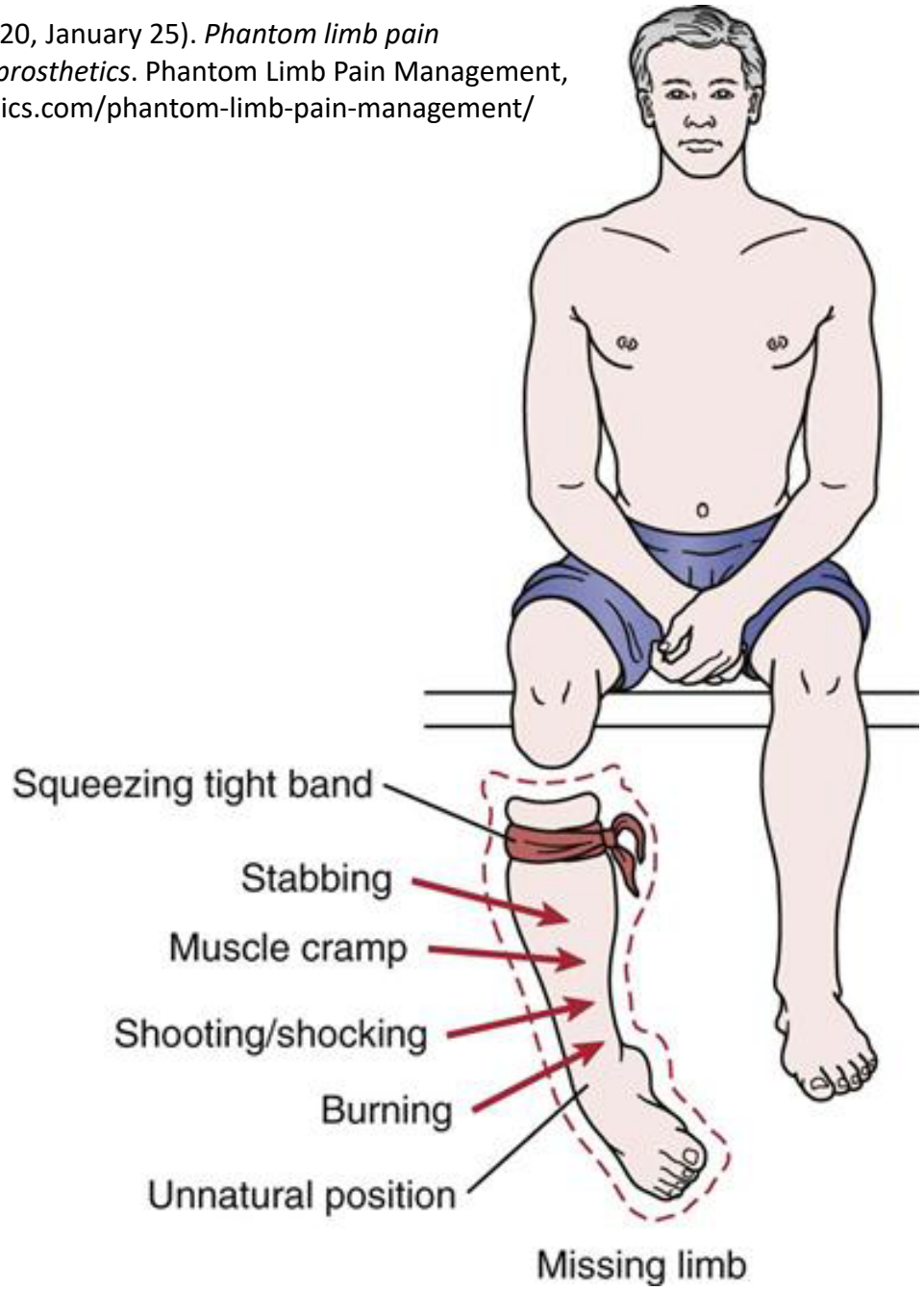


www.mayoclinic.org

Phantom Limb Pain

Purple Prosthetics. (2020, January 25). *Phantom limb pain management - purple prosthetics*. Phantom Limb Pain Management, https://purpleprosthetics.com/phantom-limb-pain-management/

Neuromatrix Representation	Mismatch in sense of self created by the brain leads to pain
Pain Flashback	Reexperience of either the pain from surgery or trauma
Proprioceptive memory	After limb loss, the last position of the limb is remembered and expressed as pain
Cortical remapping	Neurons that once responded to the lost limb respond to inputs from another part of the body



Treatments and Aids for Phantom Limb Pain

Pharmaceuticals

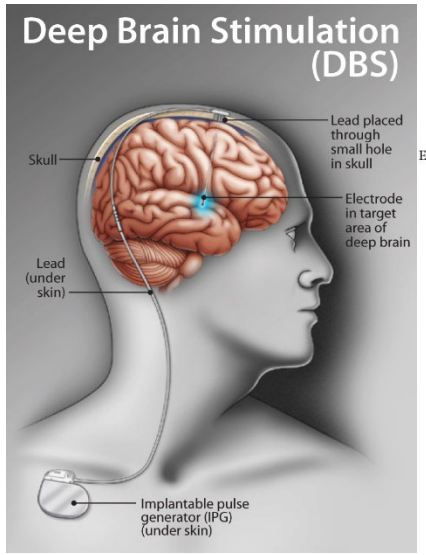
Deep Brain Stimulation (DBS)

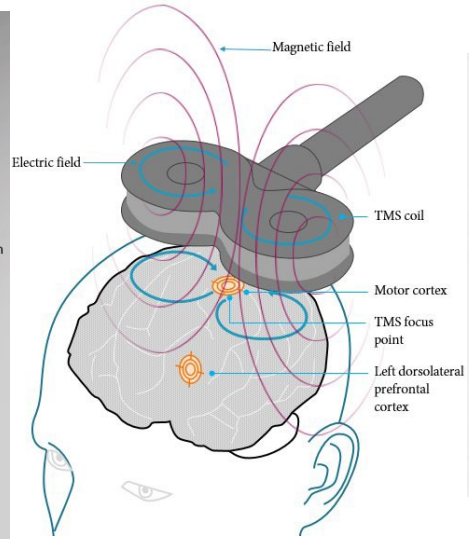
Repetitive transcranial magnetic stimulation (rTMS)

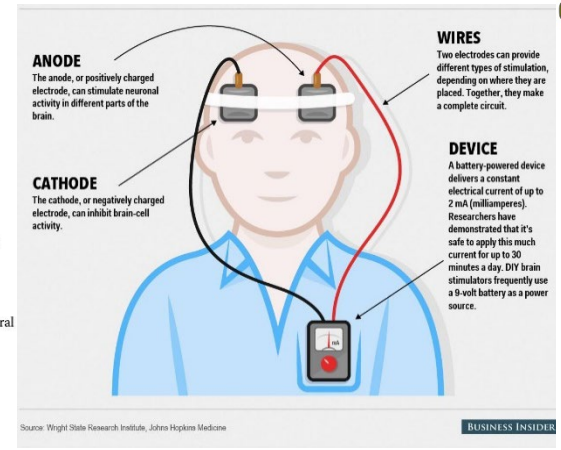
Transcranial direct current stimulation (tDCS)

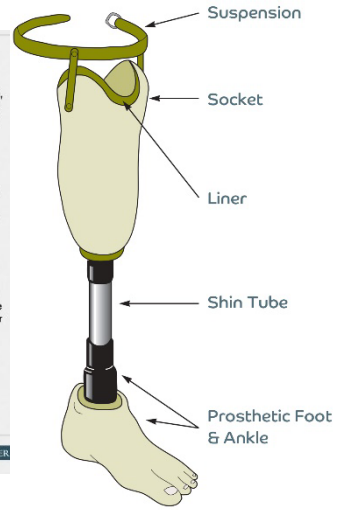
Prosthetics

Behavioral Therapies









U.S. Department of Health and Human Services. (2022, July 18). *Opioids*. National Institutes of Health. https://nida.nih.gov/research-topics/opioids

Raju, S. E., & Boehm, N. L. (2022, February 6). *Deep Brain stimulation*. The Defeating Epilepsy Foundation, https://www.defeatingepilepsy.org/treatment-for-epilepsy/deep-brain-stimulation/

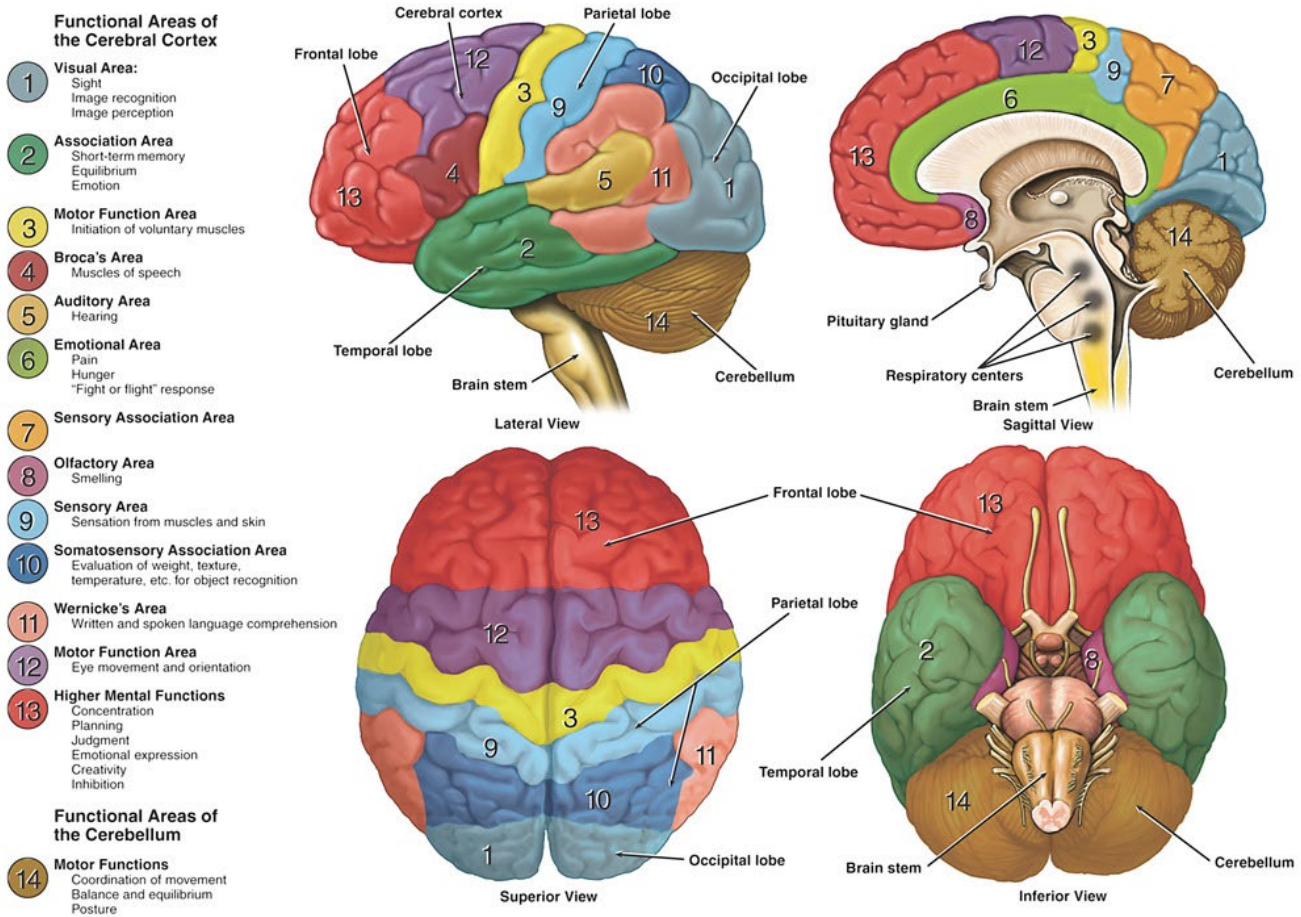
Fitzgerald, P., Cassidy, T., & Rege, S. (2022, June 30). *Transcranial magnetic stimulation for Depression - review of the evidence*. Psych Scene Hub. https://psychscenehub.com/psychinsights/transcranial-magnetic-stimulation-for-depression/

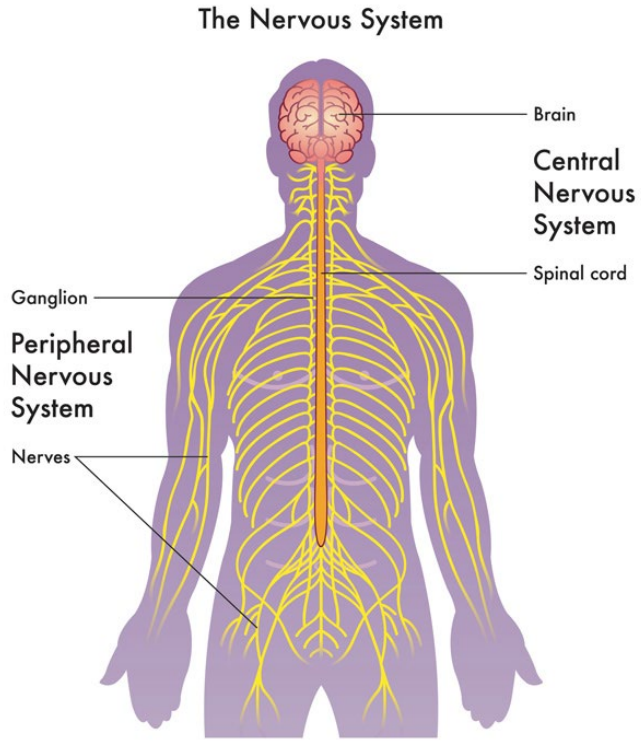
Loria, K. (2014, August 5). *Brain hacking is having incredible effects and it's just getting started*. Business Insider. https://www.businessinsider.com/brain-hacking-will-make-us-smarter-and-more-productive-2014-7

Blatchford. (2019, October 10). *Standard Features of a Below Knee Prosthesis* https://www.blatchford.co.uk/prosthetics/information-for-amputees/understanding-prosthetics/below-knee-prosthesis/

Baun, K. (2020, September 14). *Graded motor imagery: Mirror therapy explanation and steps*. Redefining Possibility https://www.armdynamics.com/upper-limb-library/mirror-therapy-explanation-steps

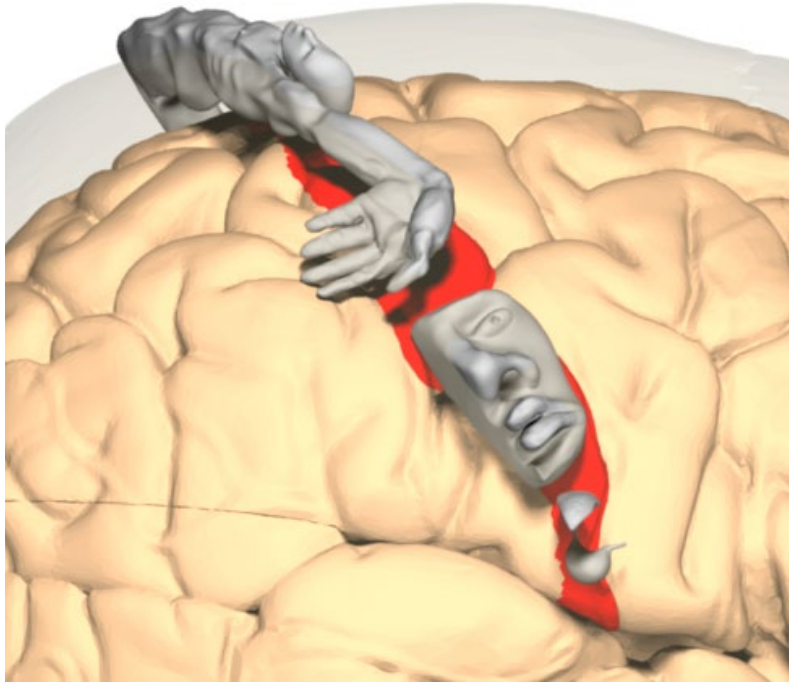
Neuroanatomy Basics



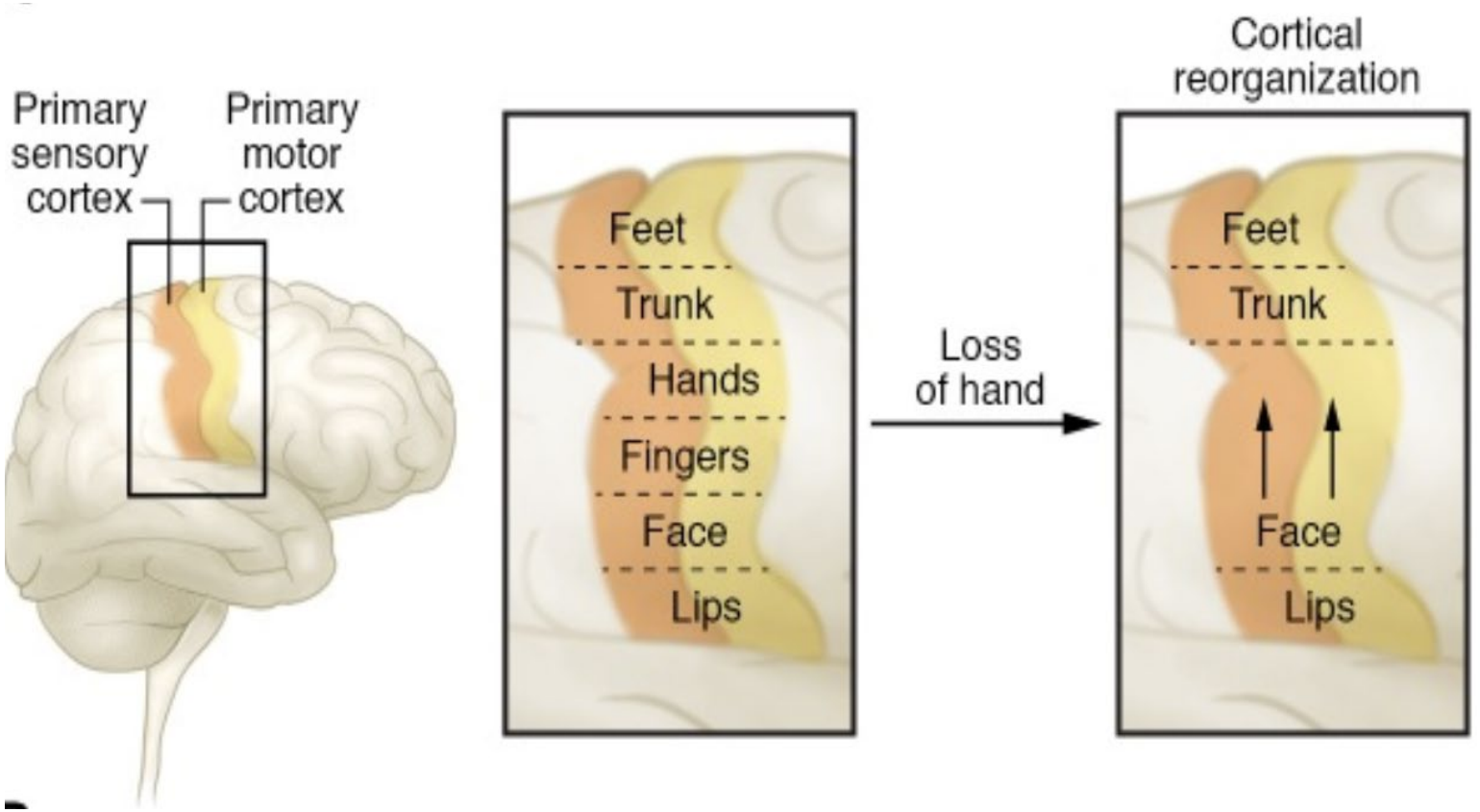


https://dana.org/article/neuroanatomy-the-basics/

Cortical Reorganization that follows amputation is a leading theory underlying Phantom Limb Pain and non-painful Sensation



Homunculus overlaid on Primary Somatosenory Cortex (Red)

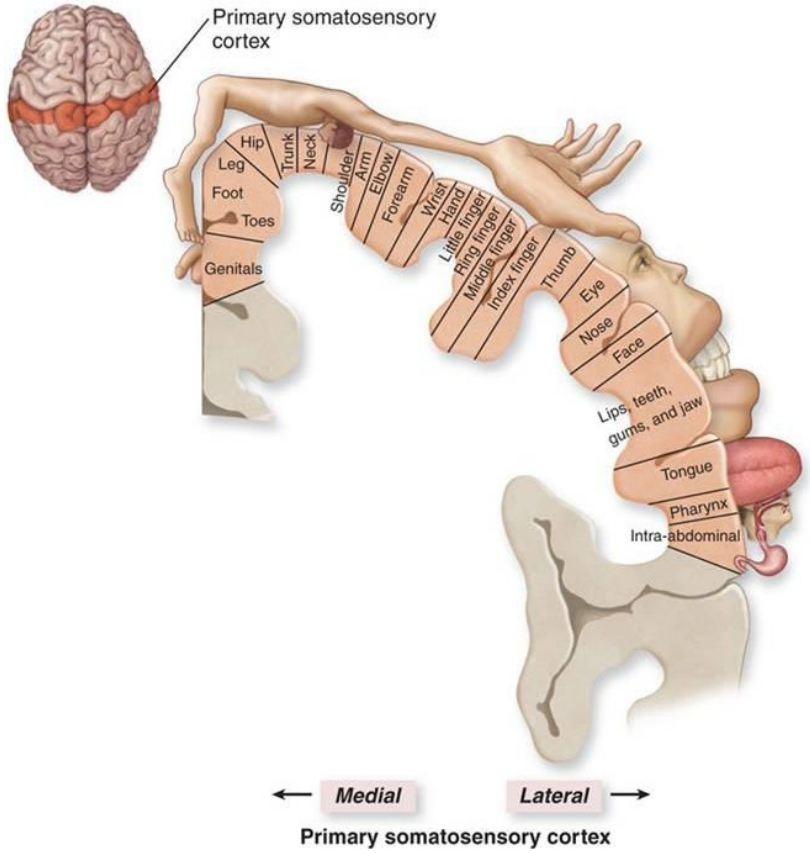


Collins, K.L., Russell, H.G., Schumacher, P.J., Robinson-Freeman, K/E., O-Conor, E.C., Gibney, K.D., Yambem, O., Dykes, R.W., Waters, R. S., & Tsao, J. W. (2018). A review of current theories and treatments for phantom limb pain. Journal of Clinical Investigation. 128:6, 2168–2176. https://doi.org/10.1172/JCI94003.

Why are rats a useful model?

Primary Somatosensory Cortex (S1)

- Processes sensory input
- Contains a somatotopic map of the body surface
- Barrel cortex (rodent, layer IV)
  - Forepaw barrel subfield (FBS)
- Laminar
- Cortical column - basic functional unit



https://www.studyblue.com/notes/note/n/brain--cranial-nerves/deck/1242177

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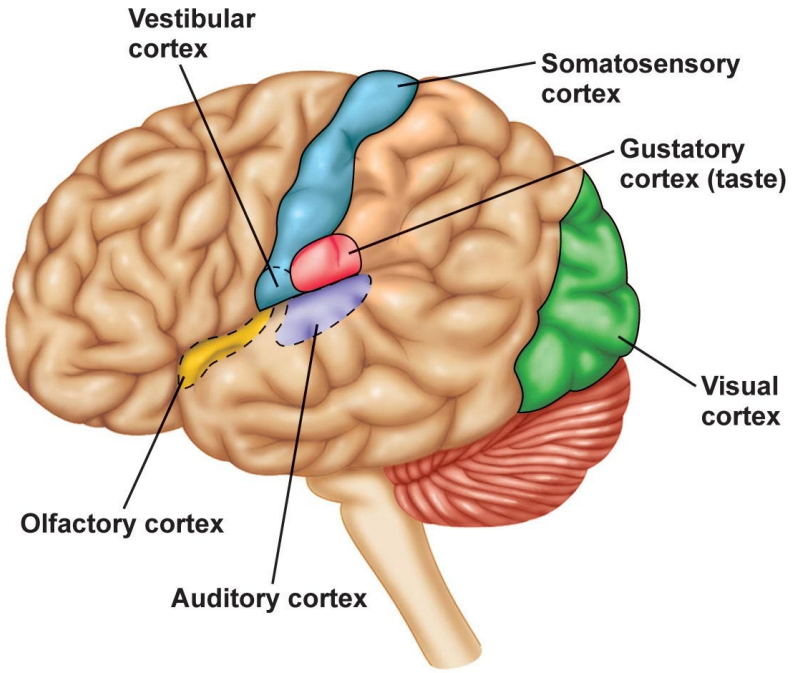
Human



2011 Pearson Education:
https://fuzzyscience.wikispaces.com/Somatosensory+Cortex

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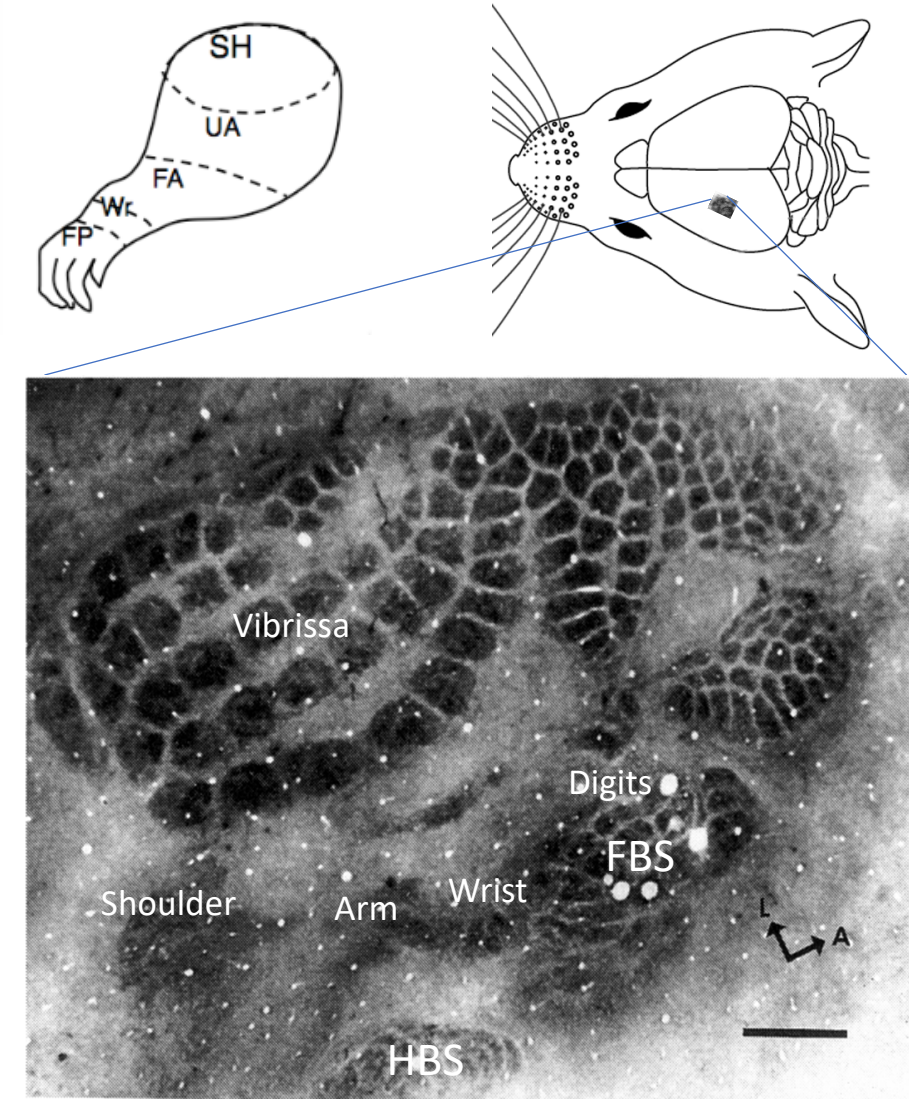

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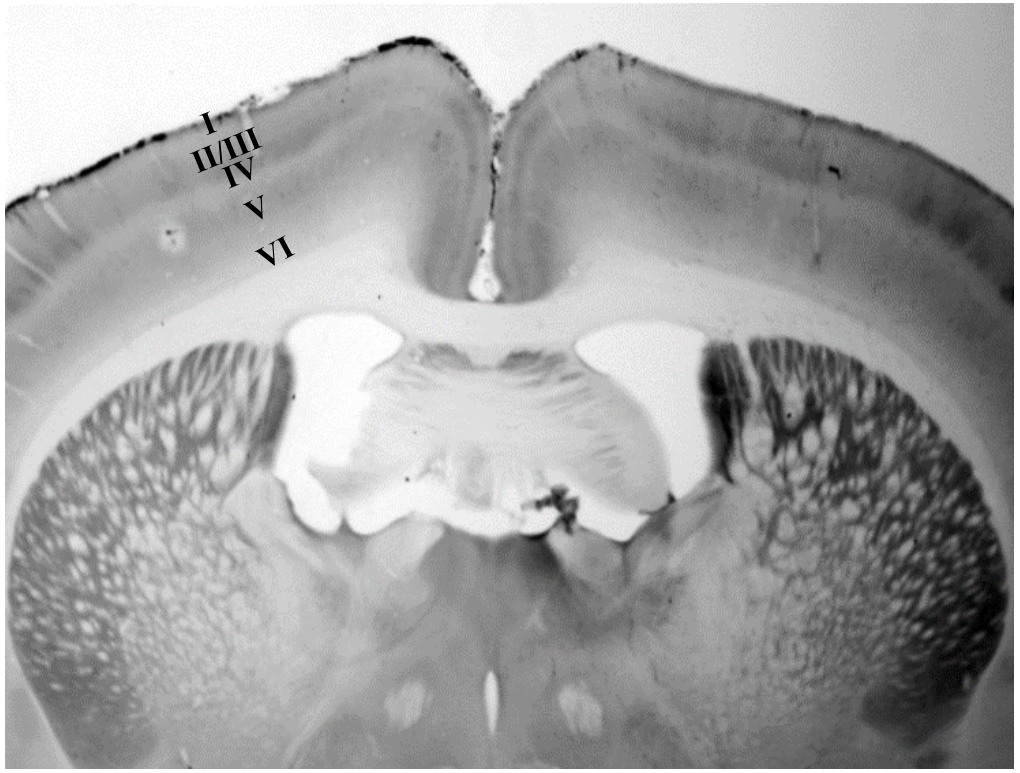

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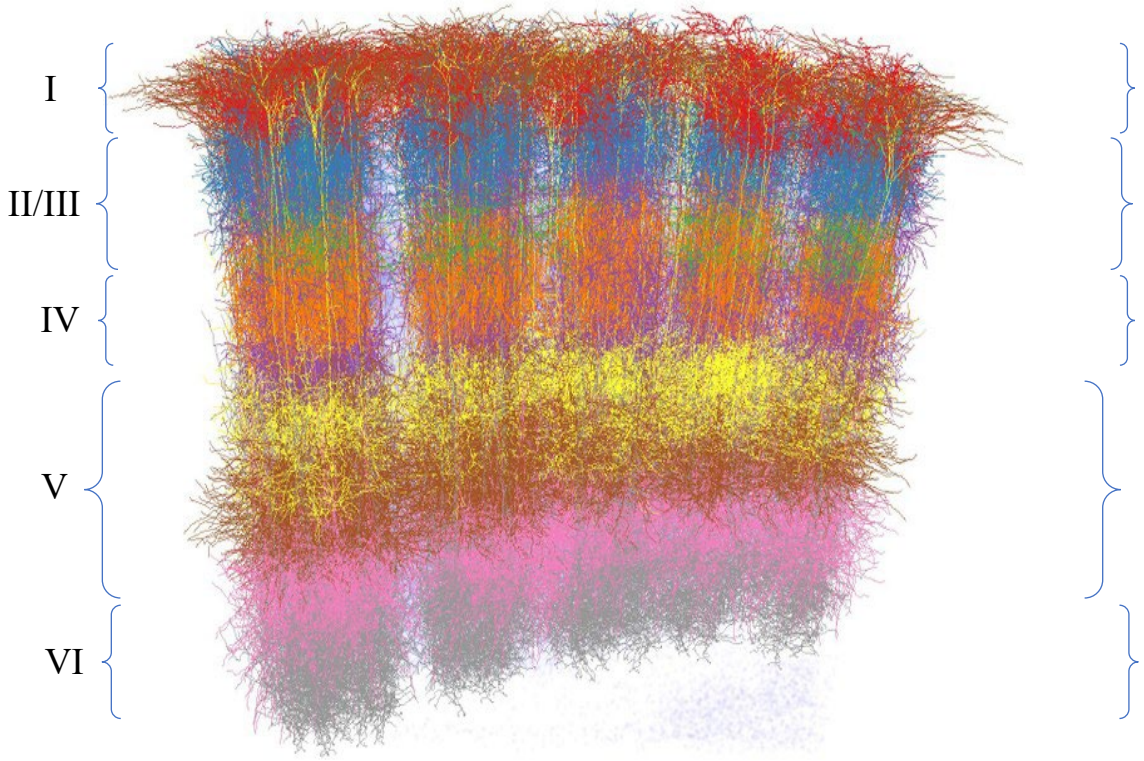
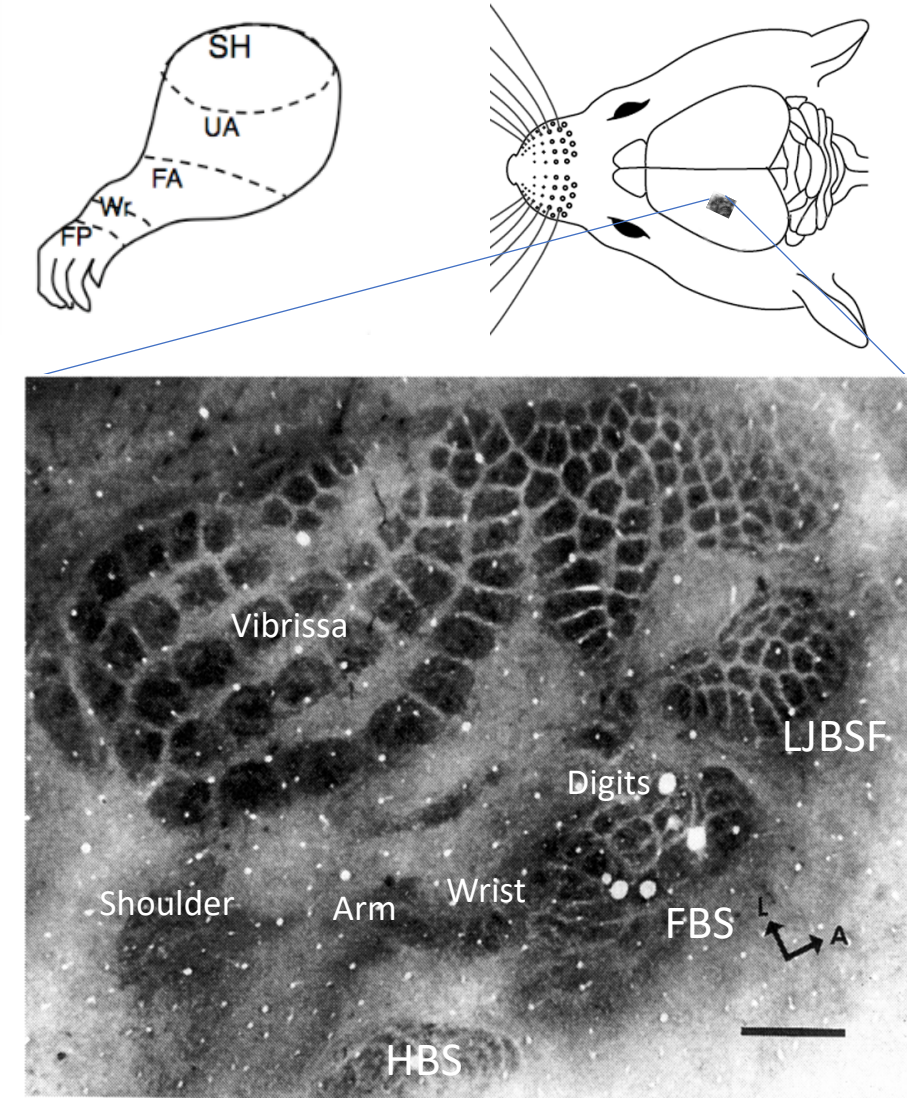
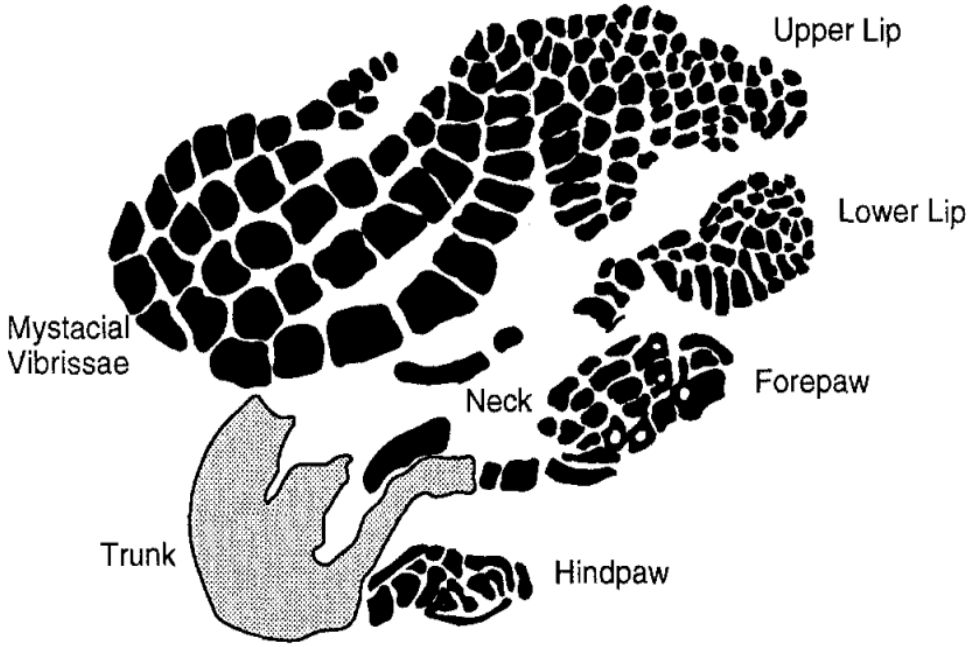


Cell-type-specific 3D reconstruction of five neighboring barrel columns in rat vibrissal cortex, Marcel Oberlaender et al.

Forepaw and Lower Jaw Barrel Subfields are Adjacent in Rat

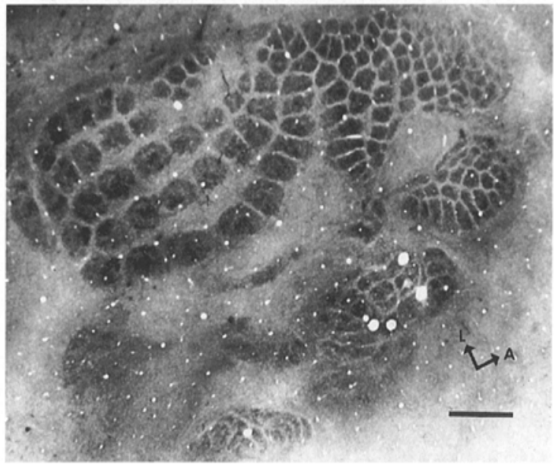


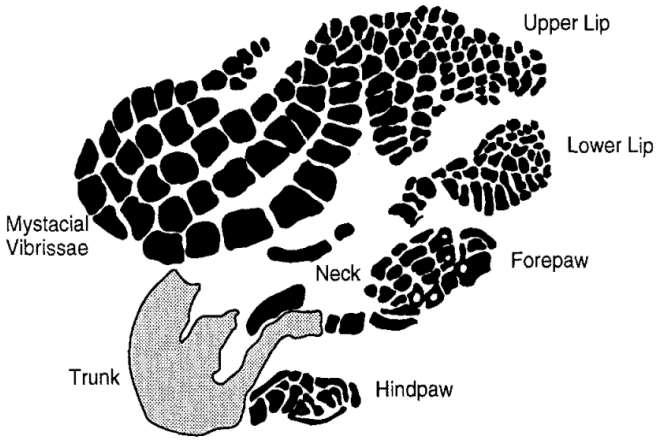
FBS = forepaw barrel subfield
LJBSF = lower jaw barrel subfield
HBS = hindpaw barrel subfield

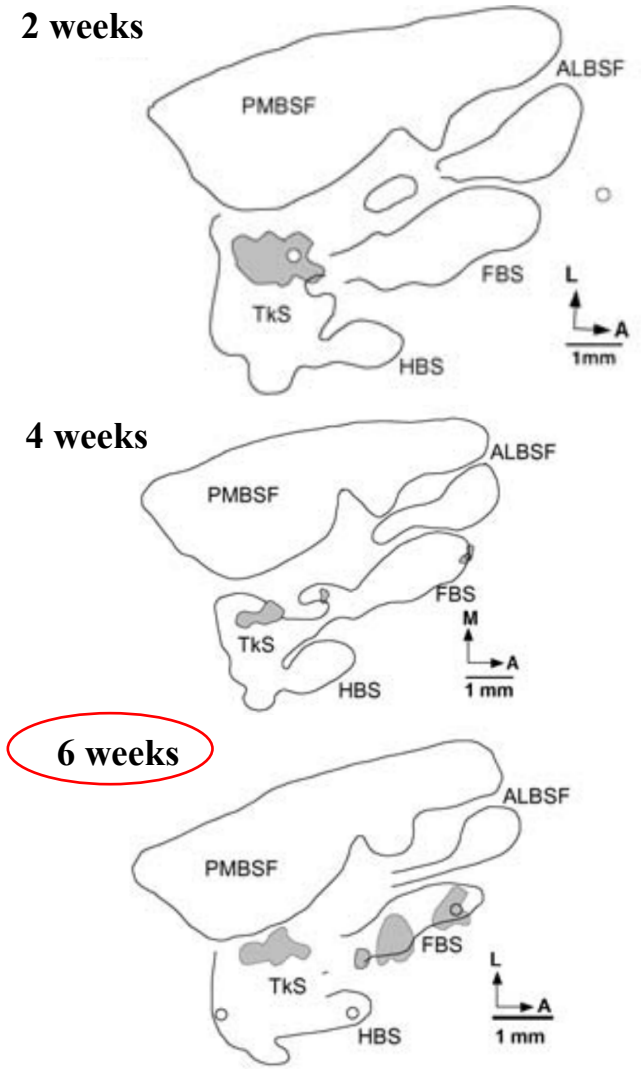


Pearson, P., Li, C. & Waters, R. *Exp Brain Res*, *128,* 315–331 (1999). https://doi.org/10.1007/s002210050852

Cortical Reorganization Follows Forelimb Amputation in Rat







Delayed Reorganization

Occurs 6 weeks following large-scale deafferentation by forelimb amputation

Pearson, P., Li, C. & Waters, R. Effects of large-scale limb deafferentation on the morphological and physiological organization of the forepaw barrel subfield (FBS) in somatosensory cortex (SI) in adult and neonatal rats. *Exp Brain Res*, *128,* 315–331 (1999). https://doi.org/10.1007/s002210050852

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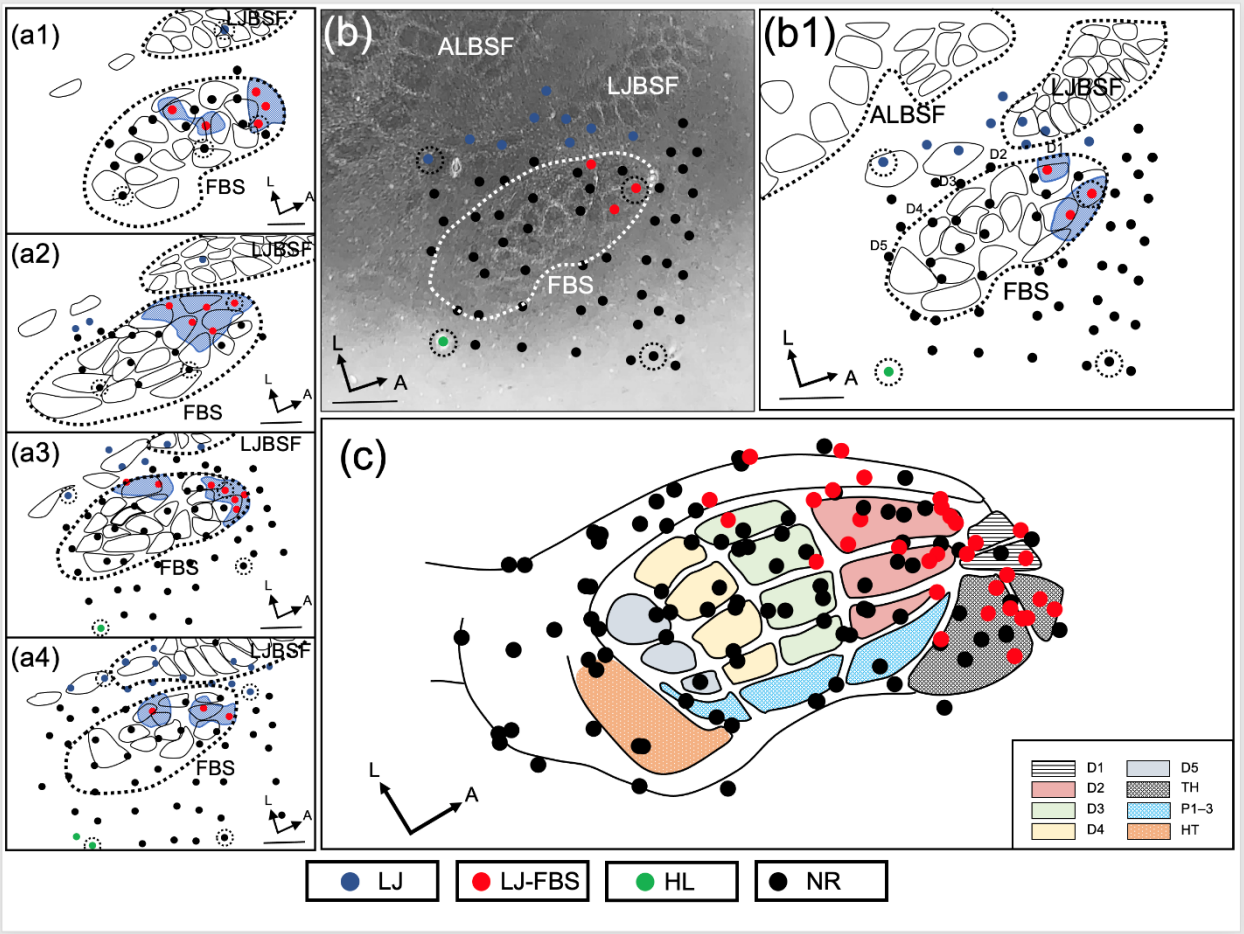
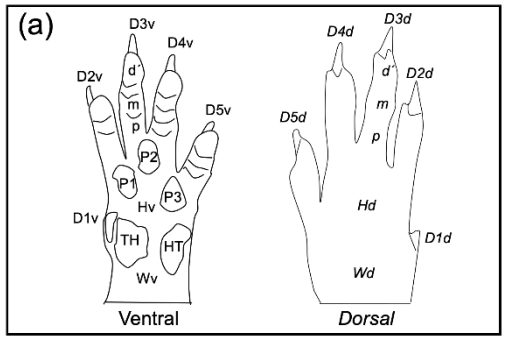


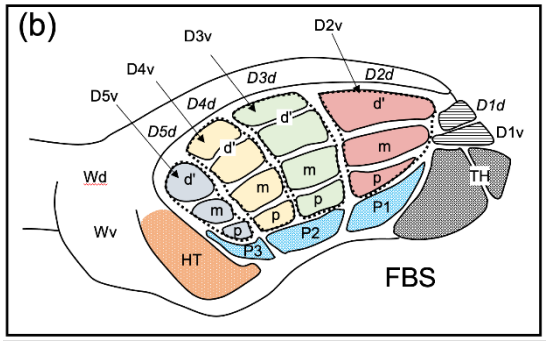
LJ = lower jaw
LJ-FBS = lower jaw - forepaw barrel subfield
HL = hindlimb
NR = no response

Rapid Reorganization

Occurs immediately following deafferentation by

- Forelimb amputation
- Brachial plexus nerve cut
- Brachial plexus anesthesia





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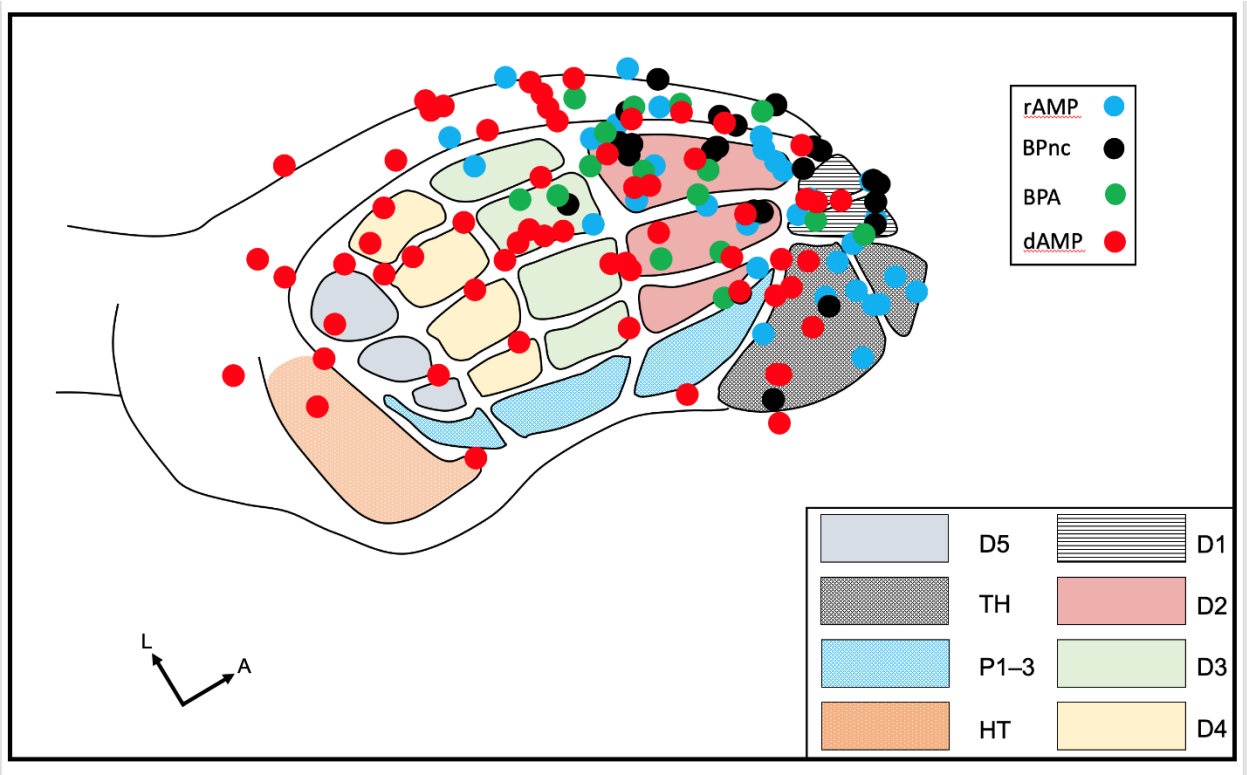
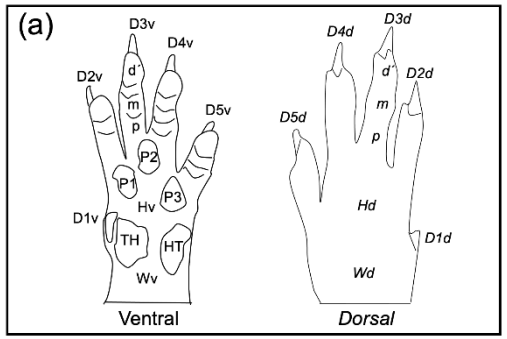


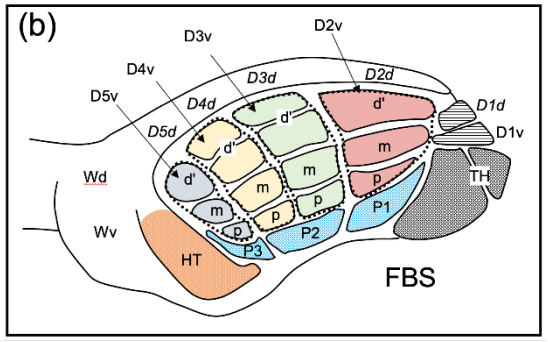
Delayed Reorganization spans entire FBS

Rapid Reorganization

is confined to anterior FBS

- Forelimb amputation (rAMP)
- Brachial plexus nerve cut (BPnc)
- Brachial plexus anesthesia (BPA)



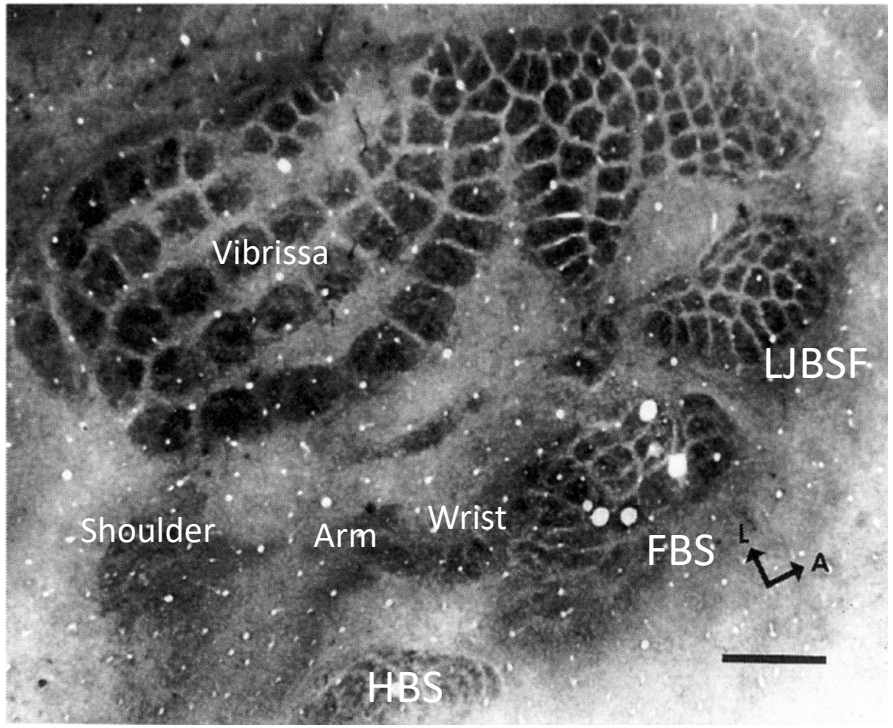


FBS = forepaw barrel subfield

Anatomical connections and GABAergic mechanisms may explain Rapid and Delayed reorganization

Cortical-Cortical Projections → Rapid Reorganization

Sub-cortical Projections → Delayed Reorganization



Preliminary findings in intact rat

- LJBSF projects to anterior FBS
- Removal of GABAergic inhibition ($GABA_A$) unmasks previously unexpressed lower jaw input in anterior FBS
- Ventral posteromedial (VPM) nucleus of thalamus projects to lower jaw

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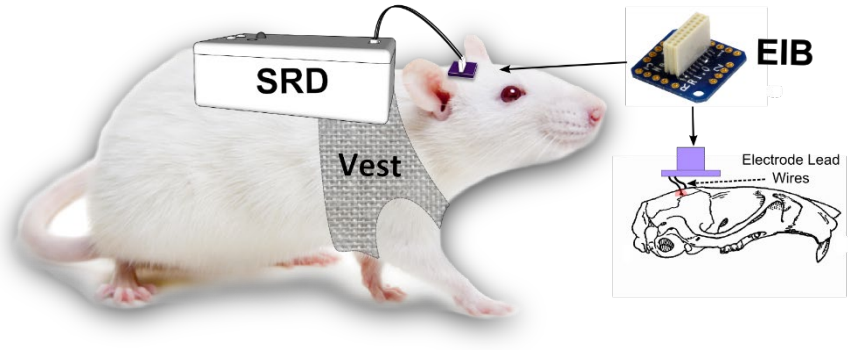

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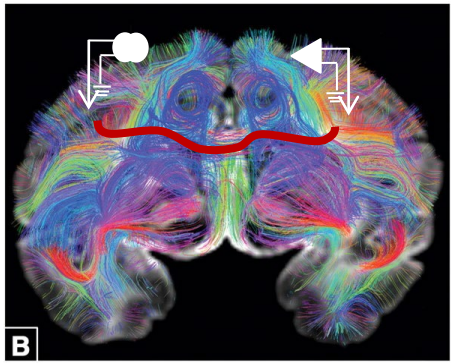

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- induce cortical remodeling in patients suffering from stroke

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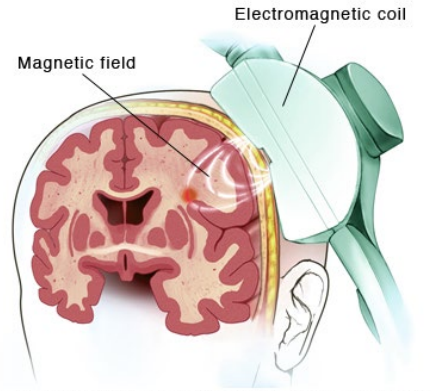
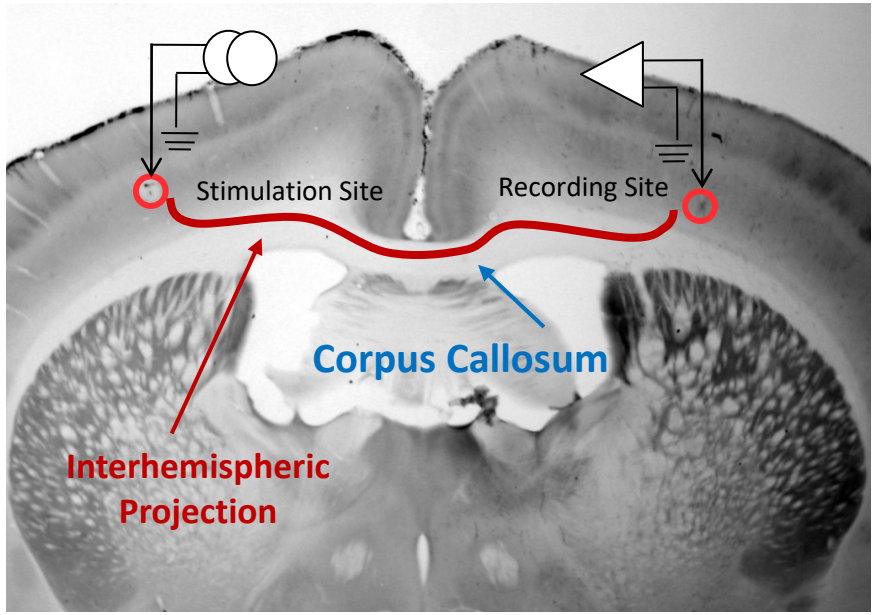


www.mayoclinic.org

Repetitive Intracortical Microstimulation Induces Ipsilateral Response



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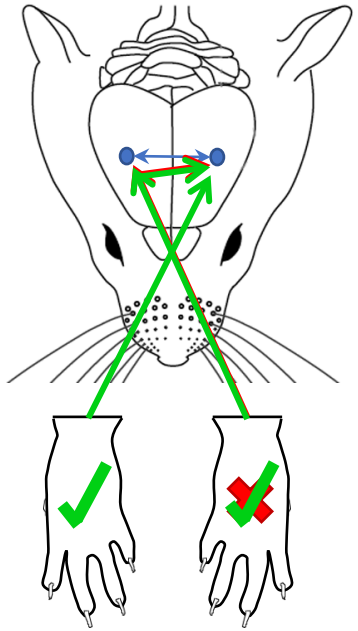


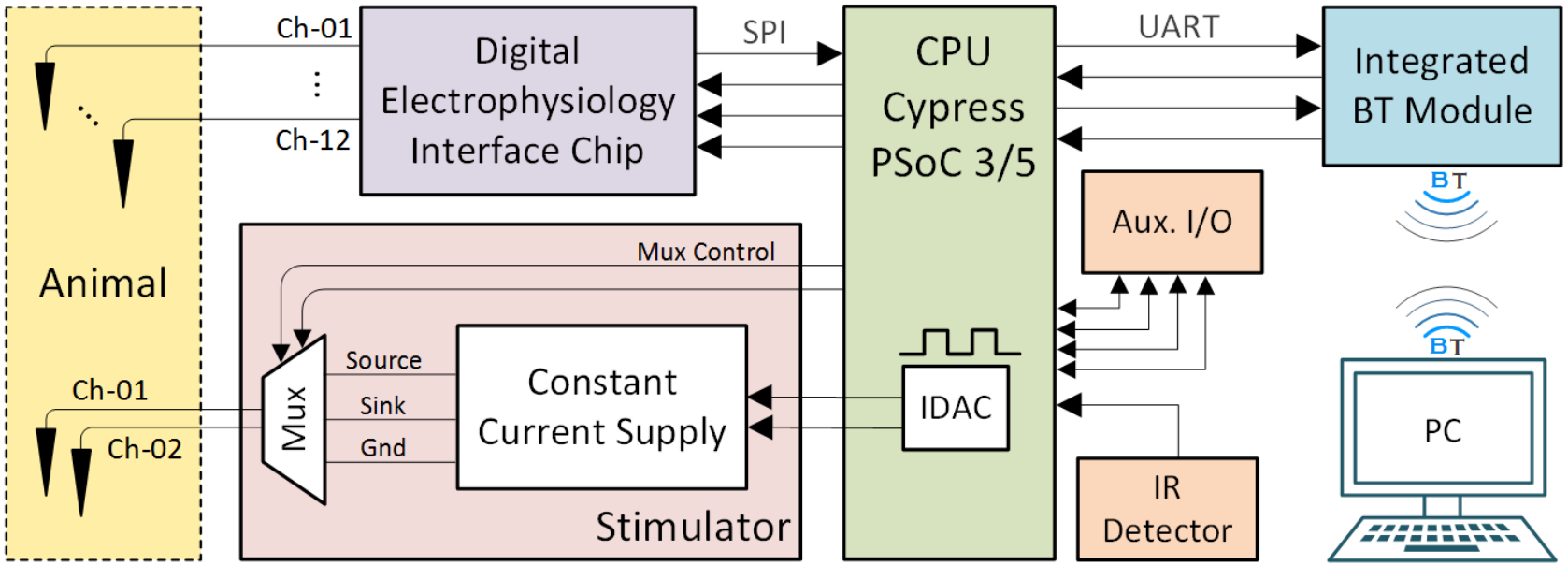
Post-stimulation (~30 min)

Pre-stimulation

DeCosta-Fortune TM, Ramshur JT, Li CX, de Jongh Curry A, Pellicer-Morata V, Wang L, Waters RS. Repetitive microstimulation in rat primary somatosensory cortex (SI) strengthens the connection between homotopic sites in the opposite SI and leads to expression of previously ineffective input from the ipsilateral forelimb. Brain Res. 2020

Following repetitive intracortical microstimulation in one hemisphere, response is evoked in both hemispheres

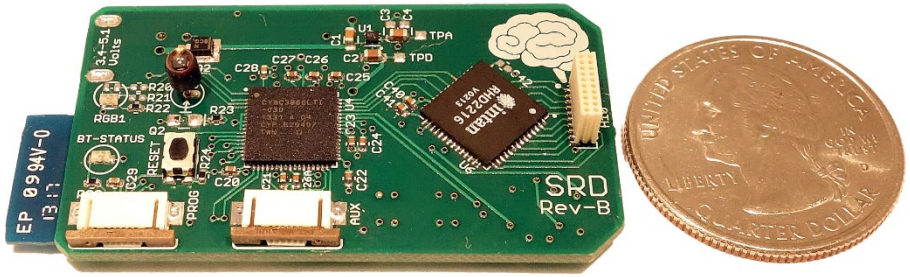
Stimulation and Recording Device for Rat

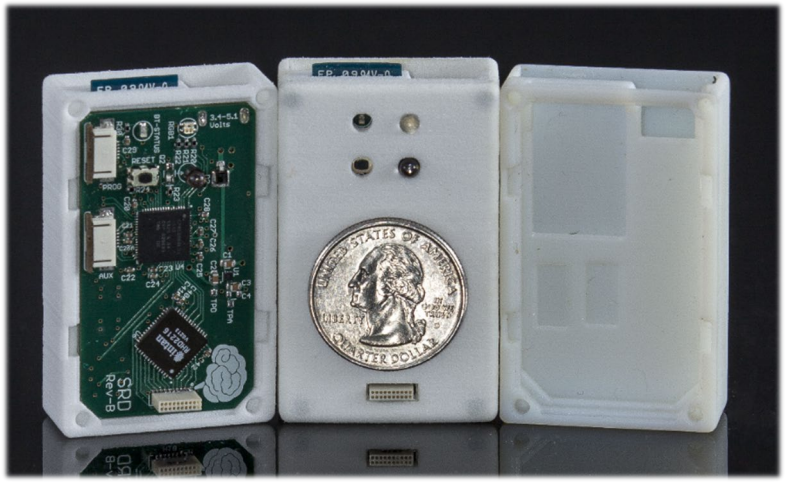


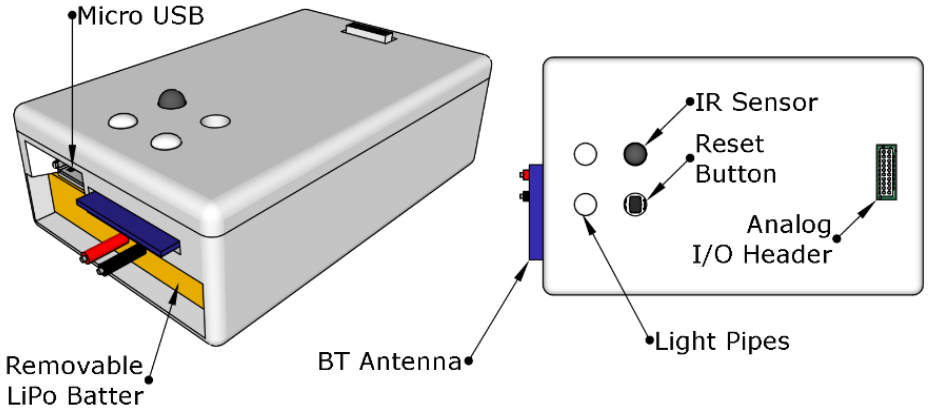
High level overview illustrating system signal and communication connections.

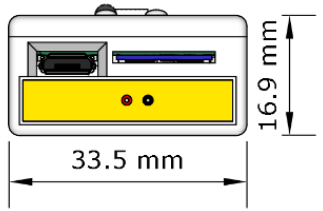
Brain-Computer Interface

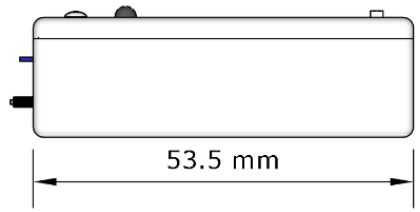
- Open-source code
- Off-the-shelf components



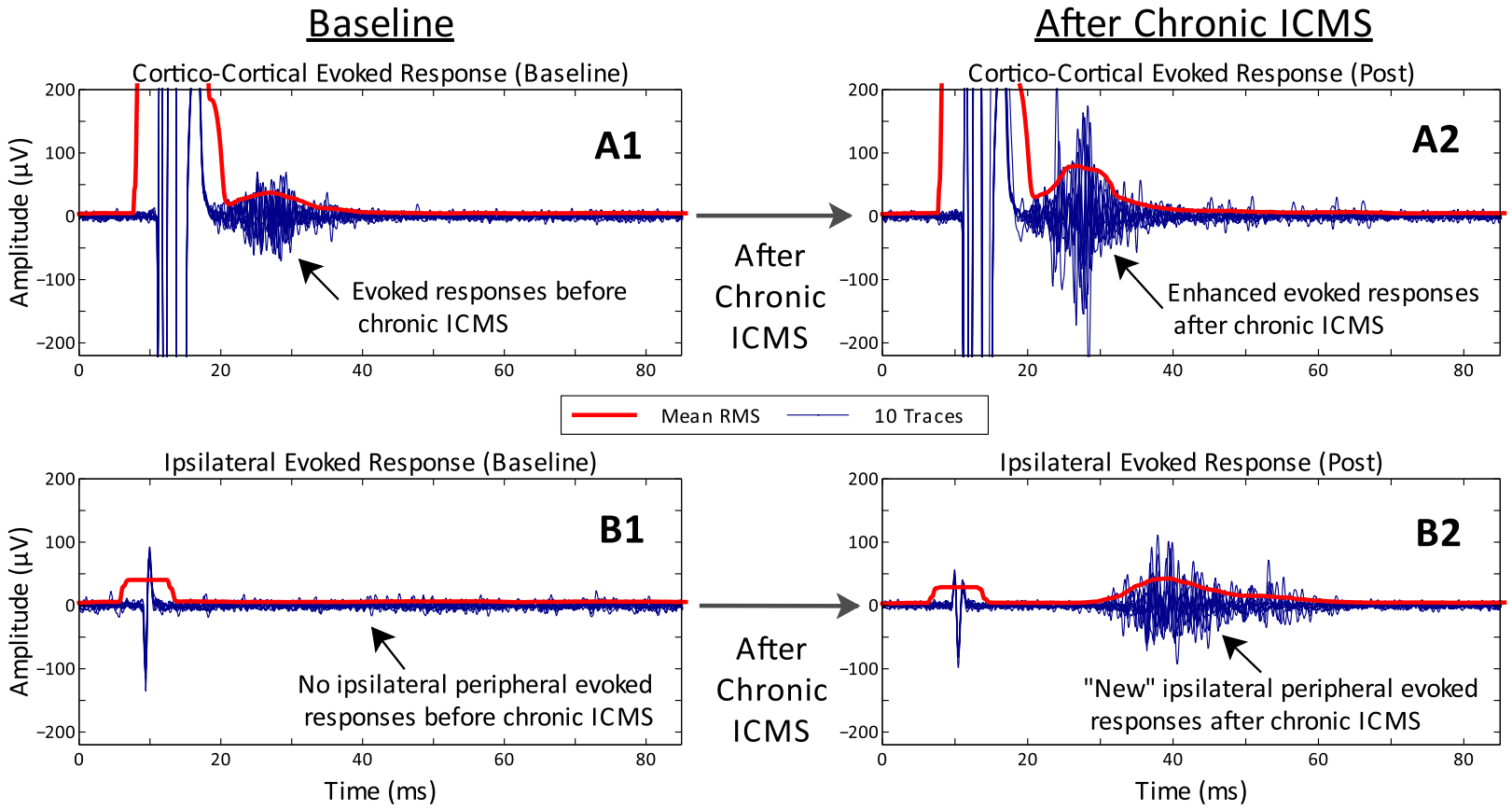


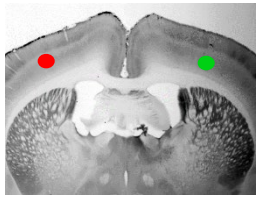






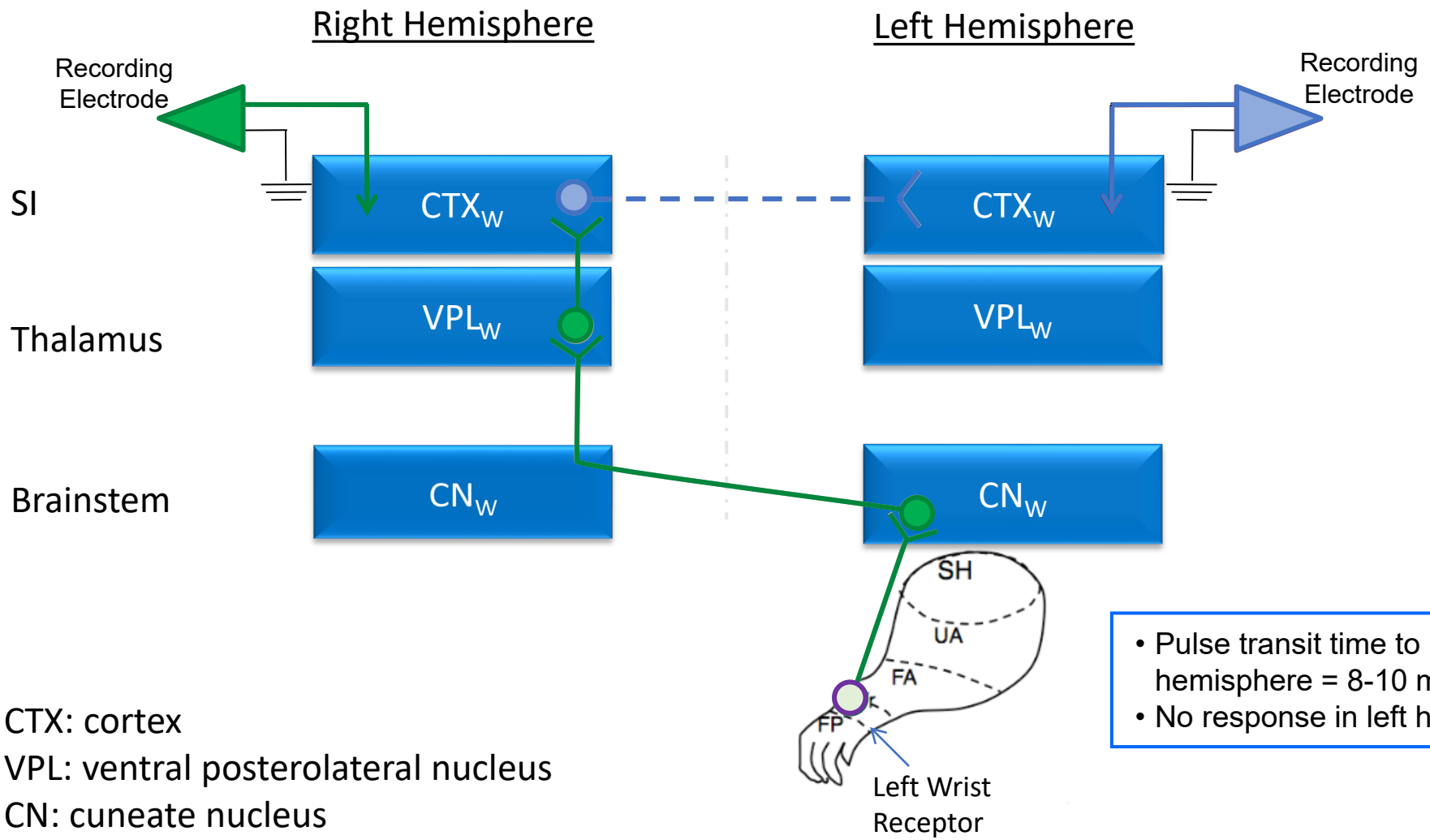
Repetitive Intracortical Microstimulation Induces Ipsilateral Response





Ramshur JT, Morshed BI, de Jongh Curry AL, Waters RS. Telemetry-controlled simultaneous stimulation-and-recording device (SRD) to study interhemispheric cortical circuits in rat primary somatosensory (SI) cortex. BMC Biomed Eng. 2019

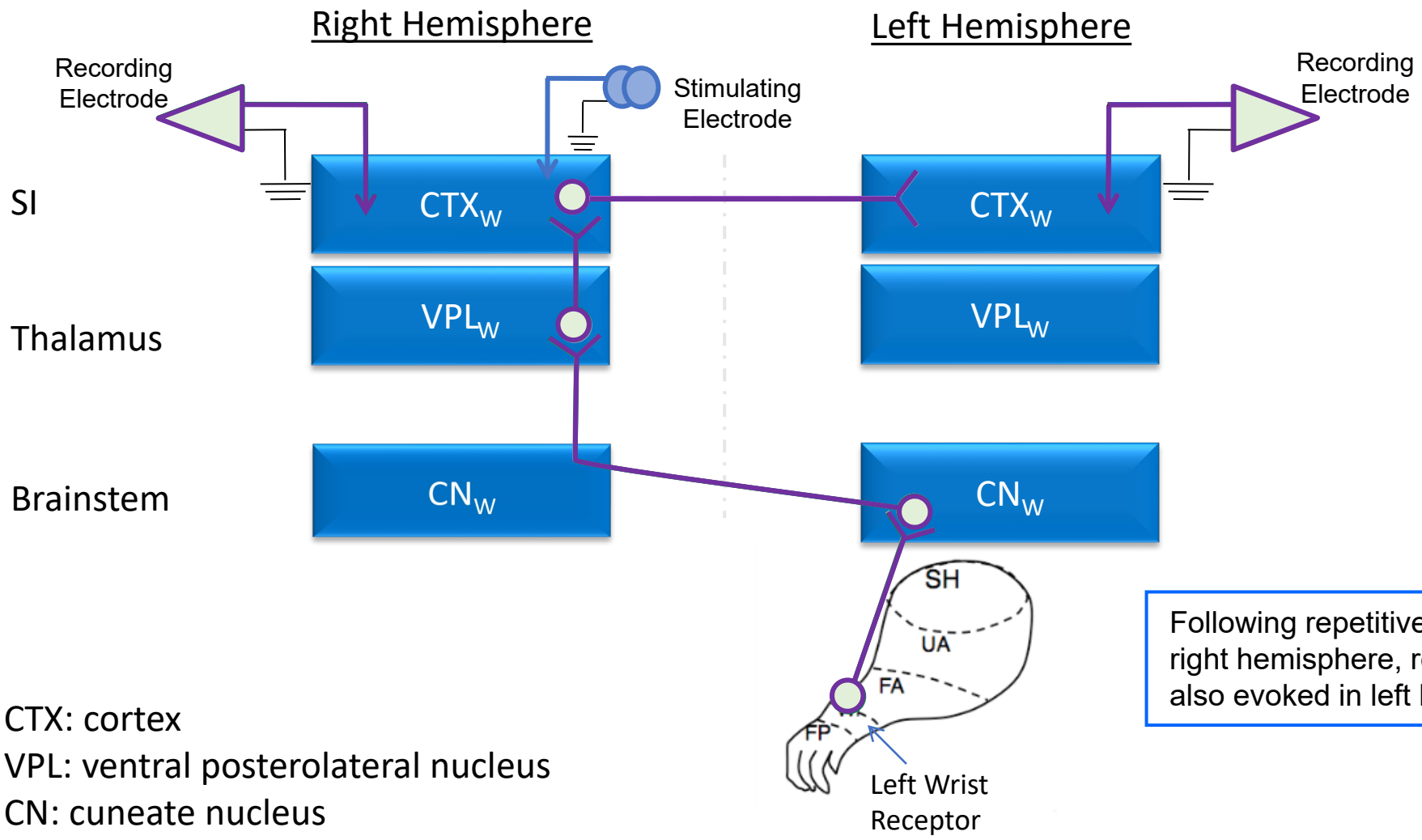
Sensory pathway



- Pulse transit time to right hemisphere = 8-10 ms
- No response in left hemisphere

CTX: cortex
VPL: ventral posterolateral nucleus
CN: cuneate nucleus
W: wrist

Sensory pathway

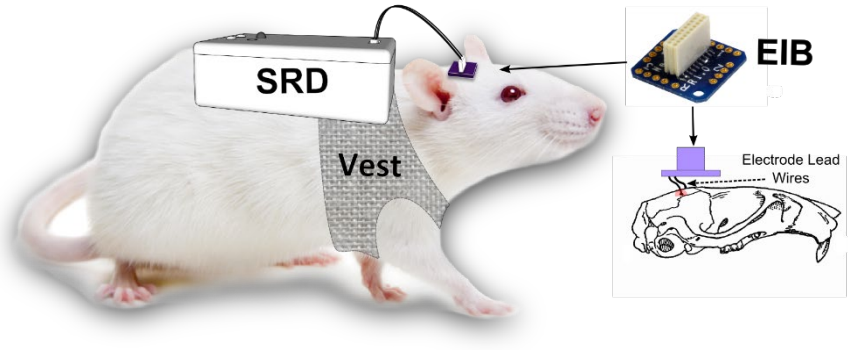


Following repetitive stimulation in right hemisphere, response is also evoked in left hemisphere

CTX: cortex
VPL: ventral posterolateral nucleus
CN: cuneate nucleus
W: wrist

http://www.disneylandpostcards.com/images/Mickey-Mouse.png

Summary



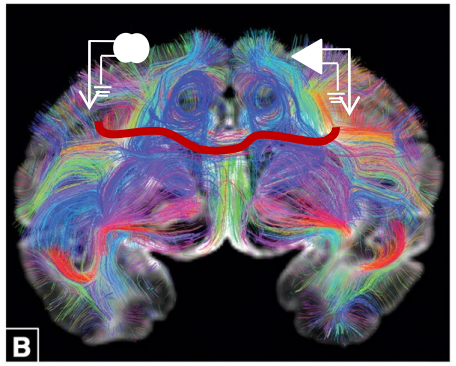
Telemetry-controlled simultaneous stimulation-and-recording device (SRD)

Clinical problems

- 1.7 million amputees in US, 70% suffer from phantom limb pain
- 6.8 million stroke survivors in US

Interhemispheric Pathway

- Repetitive intracortical microstimulation affects homotopic site in opposite hemisphere:
  - Increases neuronal firing rates
  - Leads to functional changes (new inputs/outputs)

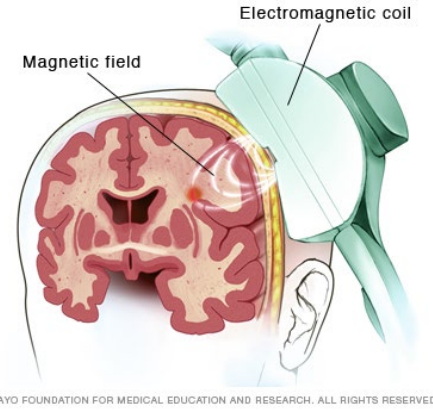


Schmahmann J D et al. Brain 2007;130:630-653

Repetitive intracortical microstimulation may

- prevent maladaptive cortical reorganization following limb amputation
- induce cortical remodeling in patients suffering from stroke

Transcranial Magnetic Stimulation



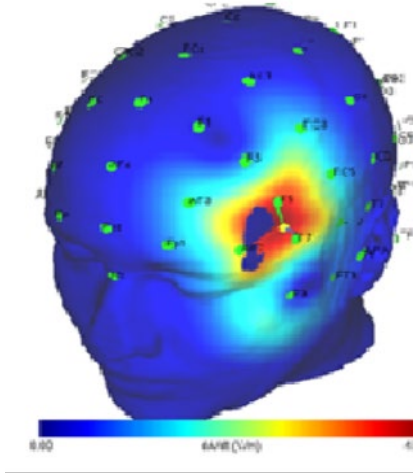
www.mayoclinic.org

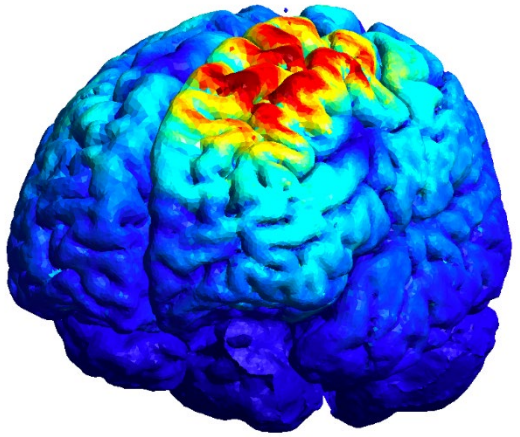
Konakanchi D, de Jongh Curry AL, Waters RS, Narayana S. **Focality of the Induced E-Field Is a Contributing Factor in the Choice of TMS Parameters: Evidence from a 3D Computational Model of the Human Brain**. Brain Sci. 2020

Transcranial Magnetic Stimulation

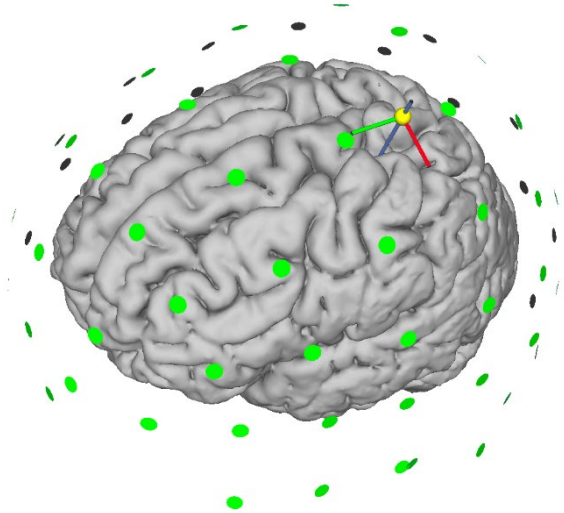
https://neurology.ufl.edu/divisions/epilepsy/neurodiagnostic-services/transcranial-magnetic-stimulation/

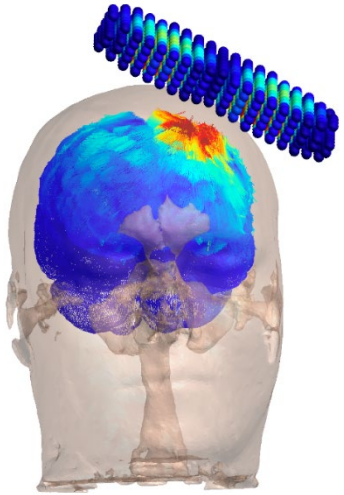
Transcranial Magnetic Stimulation Simulations





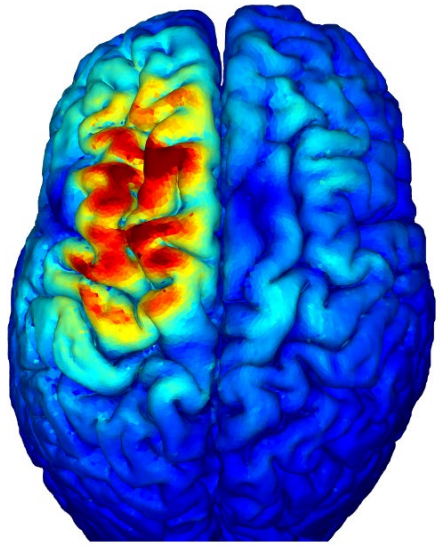
magnE

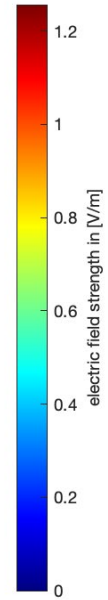




E

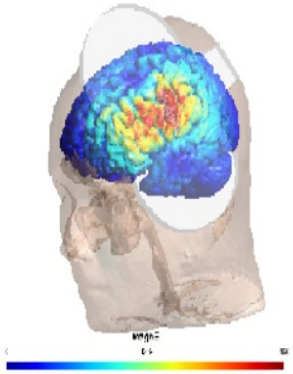
0 0.626 1.25



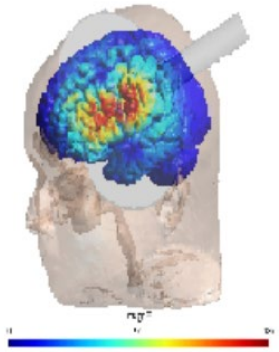


Transcranial Magnetic Stimulation Simulations – Different Coil Types

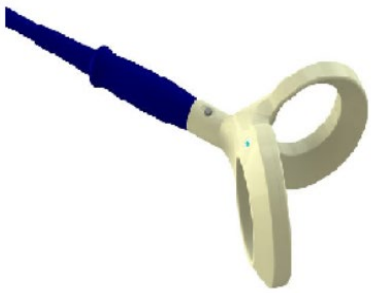
Magstim 70mm Fig.8

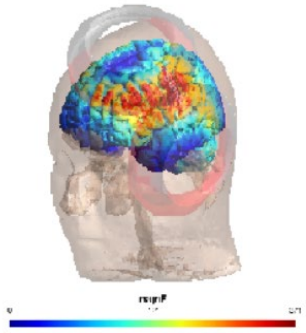


MagVenture MC B70

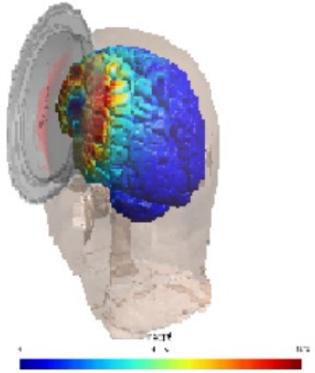


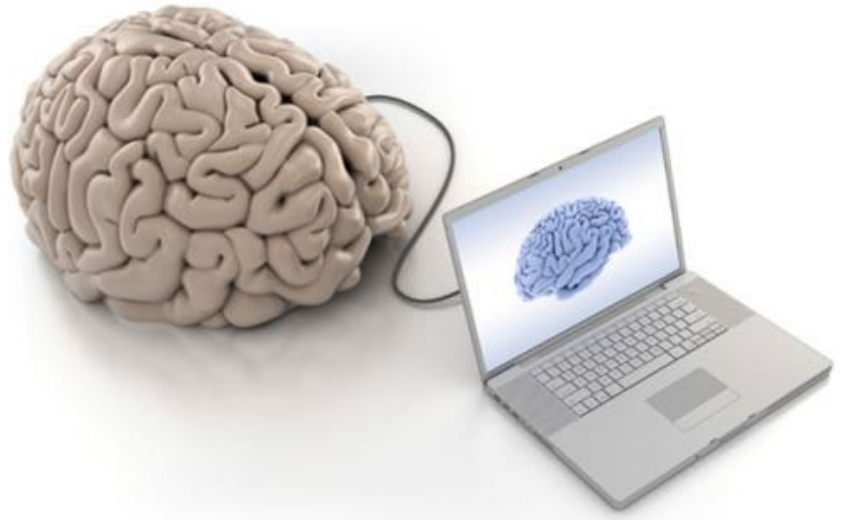
Magstim Double Cone Coil (DCC)





MagVenture MST Twin





Thank you!

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