Quantifying How Early Environment Shapes Connectivity and Organization of Corticospinal Tract: Impact & Methodology

UC DAVIS HEALTH | SCHOOL OF MEDICINE

Center for Neuroscience, University of California Davis;
University of California Davis School of Medicine

Gabriel Urreola, Fernando Gomez, Leah Krubitzer

Introduction

- Our early sensory experiences and ability to explore our environment shapes our brain, perceptions and behavior
- Active exploration provides kinematic and sensory feedback which drives movement that are distributed in neural networks
- Deprivation and unnatural environments effect fine motor precision, manual dexterity, bilateral coordination, balance and motor limb coordination.
- On the contrary, naturalistic environments are key for cognitive function, stress regulation, and motor development
- Our study looks to quantify functional brain organization, motor cortex connectivity, corticospinal tract connectivity and use statistical analysis to correlate/predict neural or behavioral phenotypes that are demonstrated by the environment

Control/Hypothesis

- **Control Group:** Norwegian Brown (NB) rats raised from birth in standard laboratory housing [Lab (L) rats]
- **Experimental Group**: NB rats raised in super-enriched, semi-natural environments in outdoor field pends (3000 times larger than standard housing) [Field Pen (FP) rats]
- **Hypothesis:** Environmental and behavioral differences will correlate with differences in intrinsic connections of M1, specifically the corticospinal tract

Figure 1. (A) Aerial view of field pens (B) Depiction of field pens near Putah Creek Riparian Reserve Field (Dimensions: 9.75 x 2.5 x 2.5 m). (C) View inside the field pends and the rats nest box (D) View inside the nest boxes where the rats typically sleep (E-G) Depictions of the rats maneuvering around the field pen, performing complex movements and behaviors. These field pens are open to natural weather (e.g. 12 – 44°C; 4–100% humidity), day/night length and sun/moon light

Design/Methodology

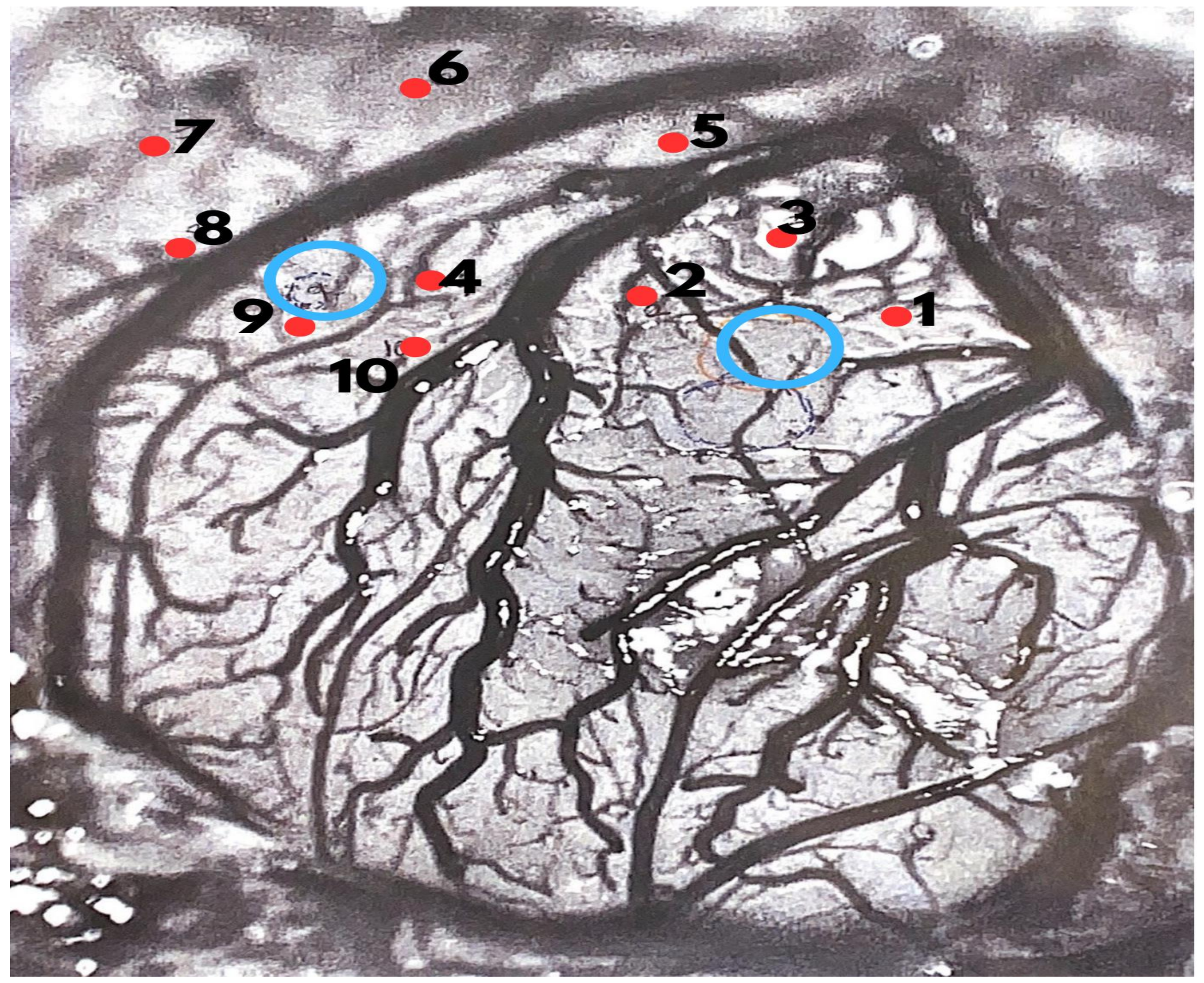

Figure 2. Annotated pictures of a rat brain during a survival surgery – post craniotomy and durotomy. (A) Red Circles: Sites of Intracortical Stimulation (B) Blue circles: Injection Sites of Neuroanatomical tracers

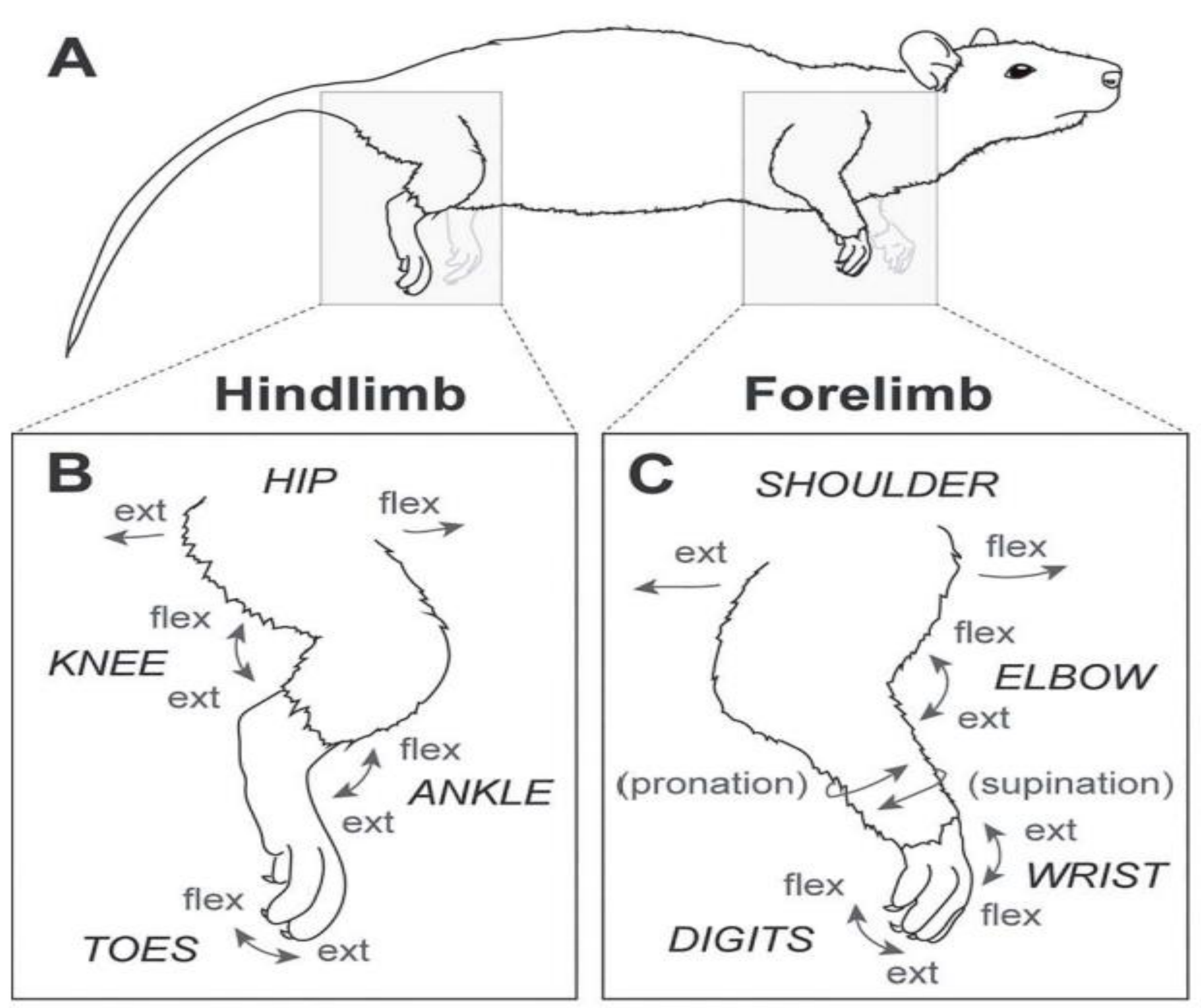

Figure 3. Visual Representation of Forelimb and Hindlimb movements which were evoked during ICMS mapping. Data Source: (Drew et al, 2020)

Preliminary Results

Intracortical Microsimulation Brain Map								
Site #	Depth (µm)	Voltage (mA)	Evoked Movements	Hindlimb	Forelimb	Torso	Head/Face	Tail
1	1,200	300	• Ankle Movement • Toe Movement	X				
2	1,200	300	• Leg Movement • Arm Movement • Tail Movement • Torso Movement	X	X	X		X
3	1,200		• Hip Flexion	X				
4	1,200	500	NCM					
5	1,200	300	• Arm Movement • Leg Movement • Torso Movement	X	X	X		
6	1,200	300	• Whisker Movement				X	
7	1,200	500	• Whisker Movement • Torso Movement			X	X	
8	1,200	300	• Shoulder Abduction • Wrist Extension		X			
9	1,200	300	• Elbow Flexion		X			
10	1,200	300	• Elbow Flexion		X			

Table 1. Description of the intracortical microsimulation experimental outcomes. 10 sites were stimulated at a depth of 1,200 µm with evoked responses resulting from voltages ranging from 300 – 500 mA. Examples of evoked Movements are visually represented in Figure 3. and during the experiment encompassed movements in the hindlimb, forelimb, torso, head/face and tail.

Design/Analysis

1.) Motor Maps will be generated via Intracortical Microsimulation (ICMS), generating functional movement representation in M1 & allow for precision of neuroanatomical tracers and connections
2.) Small volumes (0.02-0.05 µl) of fast neuroanatomical transport tracers (Fluro-ruby (FR) or Cholera Toxin B (CTB) will be injected in desired motor representations via survival surgery
3.) After retrograde transport of the tracers (6-8 days) the spinal Cord will be sectioned horizontally and mounted for fluorescent microscopy
4.) Retrogradely labeled cells of the corticospinal tract will be plotted using X/Y stage encoding and the connections will be quantified

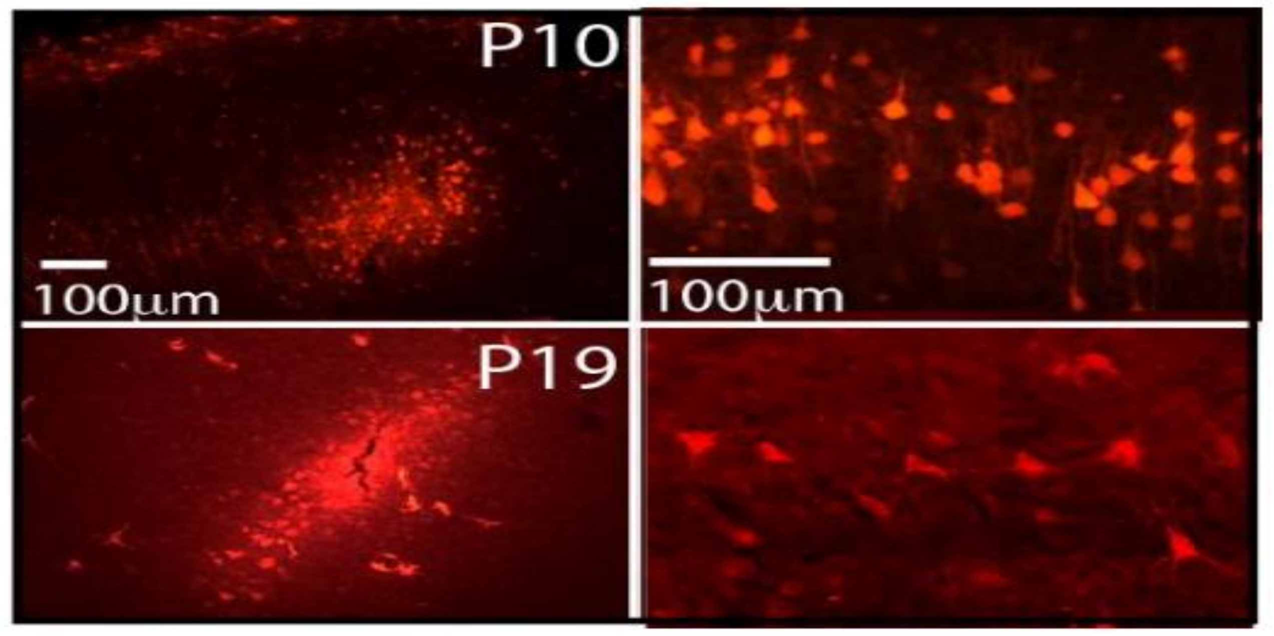

Figure 4. Examples of injections and cells retrogradely labeled with Fluoro-ruby

Conclusions/Further Study

- We are the first to rear rats in housing 3,000 times larger than standard housing providing insight into how environmental design can impact future studies in neuroscience
- We expect FP rats to evoke more complex, multi-joint movements of the hindlimb/tail, more evoked synergies of the hindlimb and forelimb over a large region of cortex, and novel evoked synergies.
- We expect corticospinal axons from forelimb, hindlimb and tail representations in cortex will project over a larger number of spinal segments in FP rats compared to L rats.
- Our study provides insight into how early environment effects neurodevelopment and organization – highlighting the potential need for early environmental interventions in patients with congenital neurological disease and children in underserved communities

References

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2. Seelke, Adele MH, et al. "Individual differences in cortical connections of somatosensory cortex are associated with parental rearing style in prairie voles (Microtus ochrogaster)." *Journal of Comparative Neurology* 524.3 (2016): 564-577.

Acknowledgements

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