

# Introduction

 Our early sensory experiences and ability to explore our environment shapes our brain, perceptions and behavior

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- 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:  $9.75 \times 2.5 \times 2.5 \text{ m}$ ). (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.  $12 - 44^{\circ}\text{C}$ ; 4-100% humidity), day/night length and sun/moon light

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

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## 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

## **Preliminary Results**

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

**Table 1.** Description of the intracortical microsimulation experimental outcomes. 10 sites were stimulated at a depth of 1,200  $\mu$ m 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.



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

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# 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 ( $0.02-0.05 \mu$ l) 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

1. Halley, Andrew C., et al. "Distributed motor control of limb movements in rat motor and somatosensory cortex: the sensorimotor amalgam revisited." *Cerebral Cortex* 30.12 (2020): 6296-6312.

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

We would like to thank the Krubitzer Lab of Evolutionary Neurobiology at the UC Davis Center for Neuroscience