

Cerebellum, autism, and sensitive periods

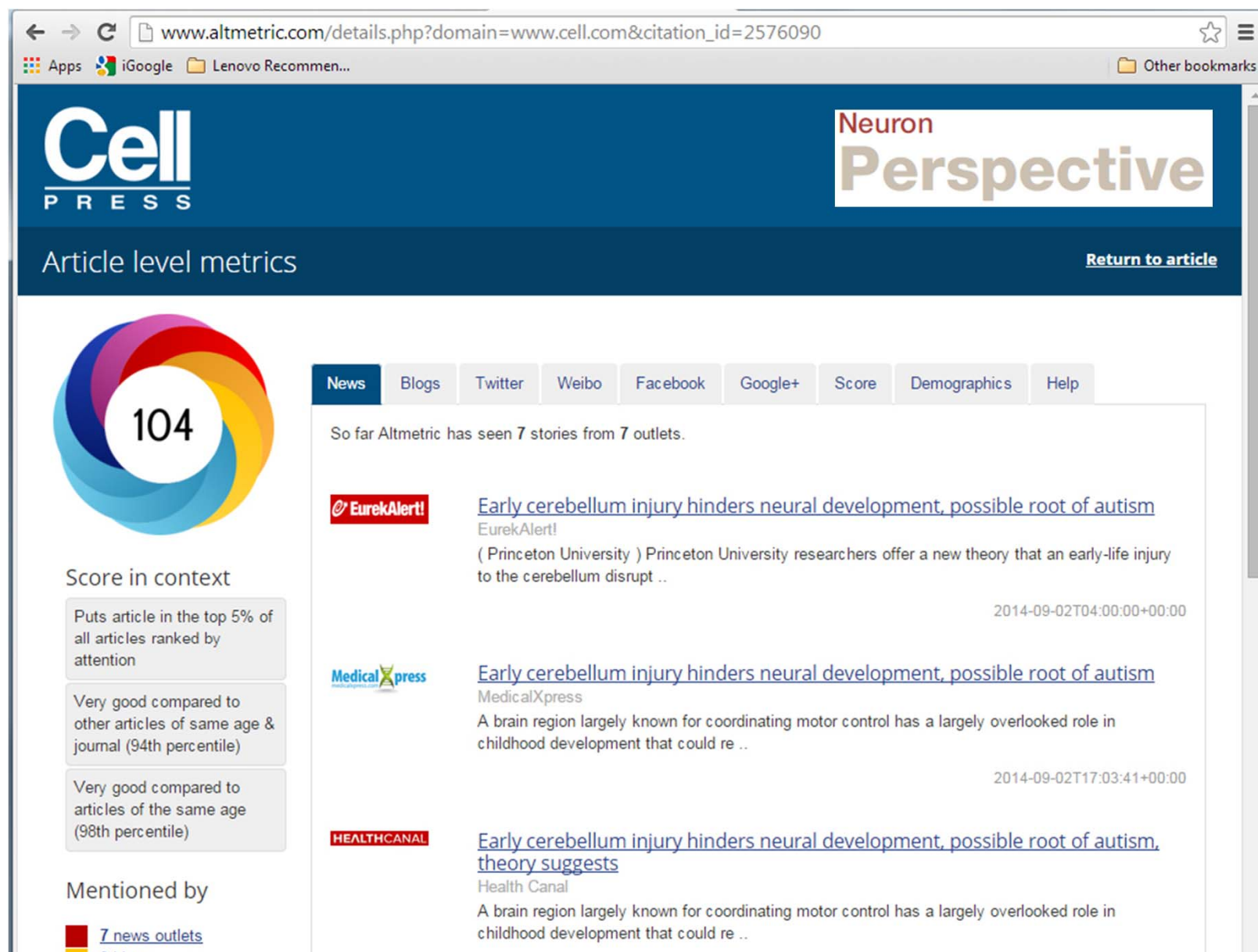
Sam Wang, Aleksandra Badura and Tom Pisano



The Cerebellum, Sensitive Periods, and Autism

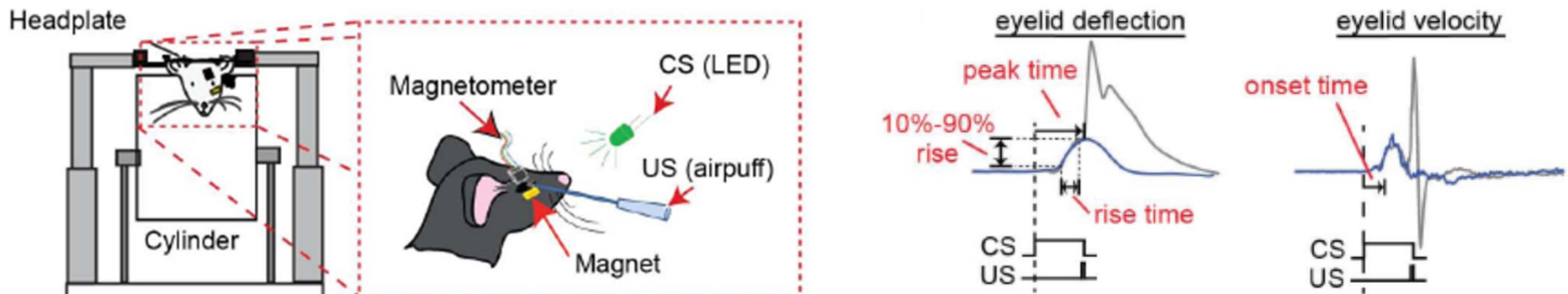
Samuel S.-H. Wang,^{1,*} Alexander D. Kloth,¹ and Aleksandra Badura¹

Neuron 83, August 6, 2014



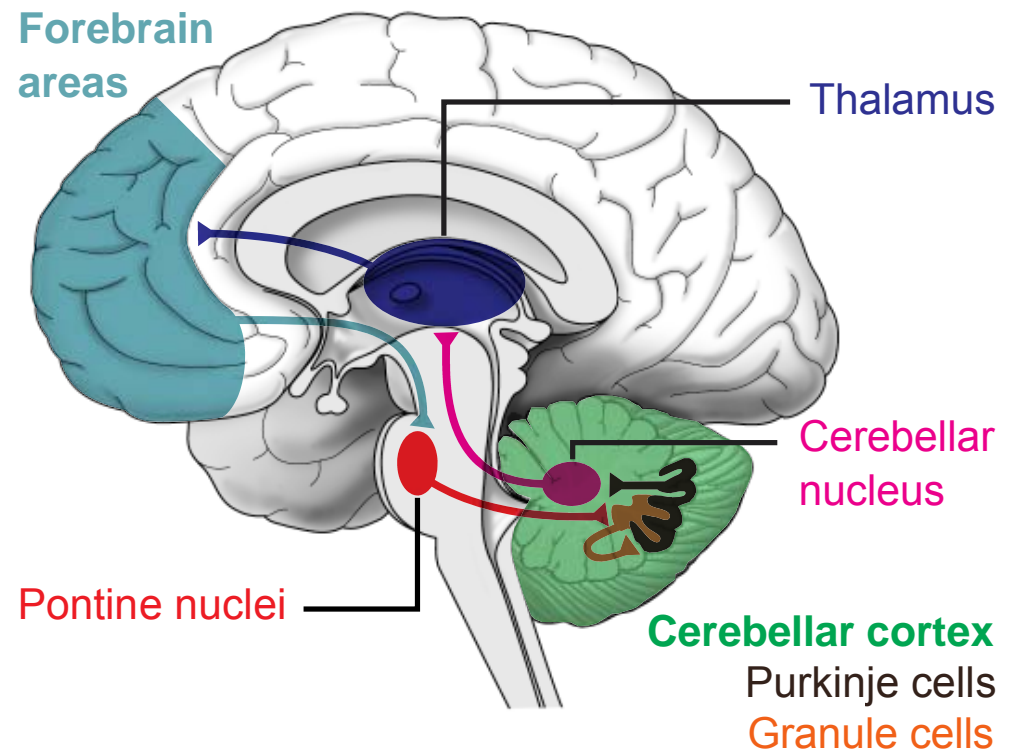
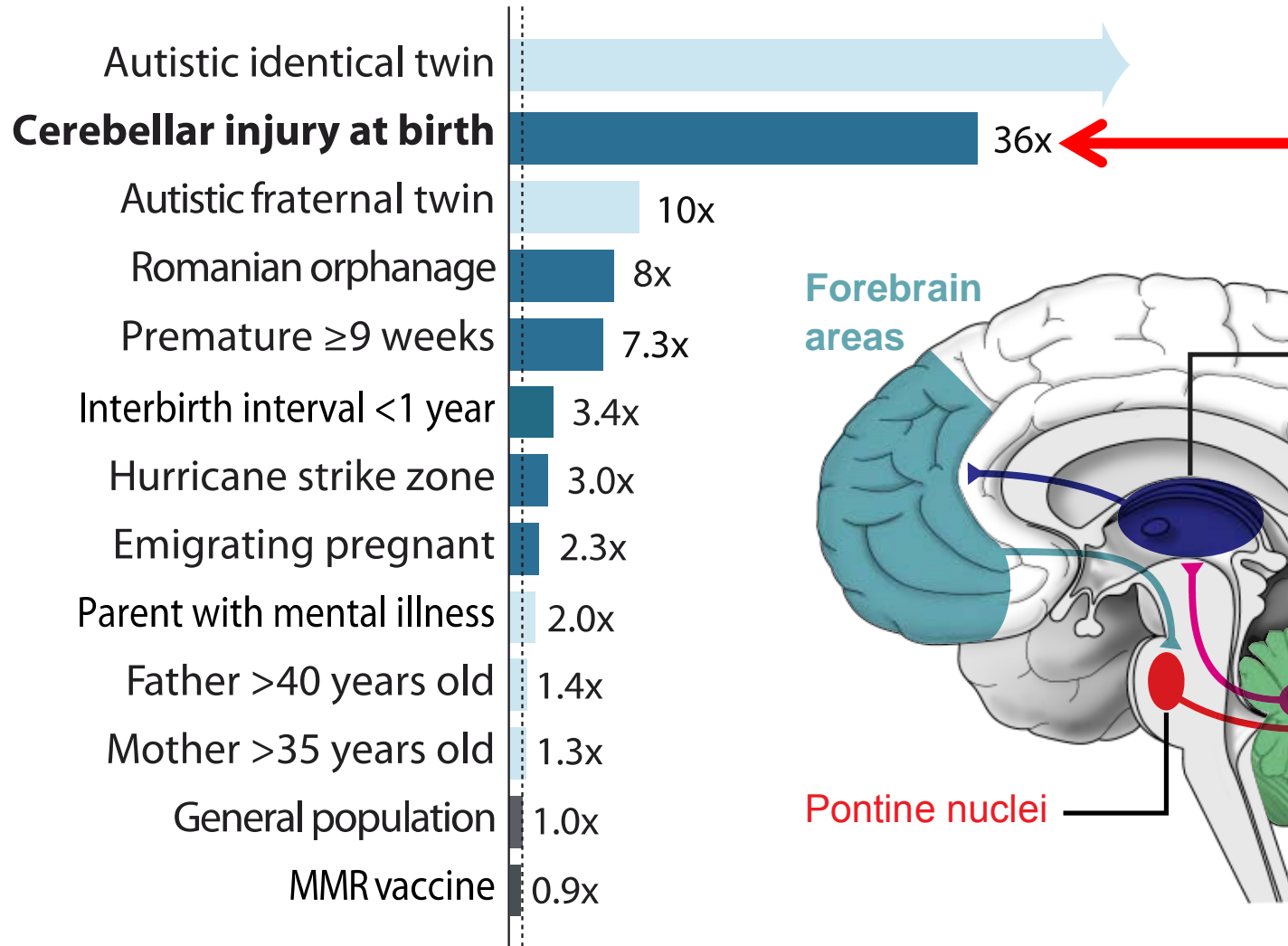
Many mouse autism models show cerebellar learning deficits

MOUSE MODEL	ASD-like?	LEARNING	PERFORMANCE			GENE EXPRESSION	
		Probability	Amplitude	Peak time	Rise time	Olivocerebellar	Mossy fiber
<i>Mecp2</i> ^{R308/Y}	yes	unchanged	decrease	later	slower	PC, IO	GoC, GrC
<i>Shank3</i> ^{+/ΔC}	yes	decrease	decrease	earlier	faster	PC	GrC
<i>L7-Tsc1</i>	yes	decrease	decrease	unchanged	unchanged	PC	none
<i>Cntnap2</i> ^{-/-}	yes	decrease	unchanged	unchanged	unchanged	PC, DCN, IO	none
<i>patDp</i> ^{+/+}	yes	decrease	unchanged	unchanged	unchanged	PC, DCN, IO	none
<i>Cntnap2</i> ^{+/-}	no	unchanged	unchanged	unchanged	unchanged	none	none



Piochon, Kloth et al. (2014) *Nature Communications*
Kloth et al. in review

Why cerebellum?

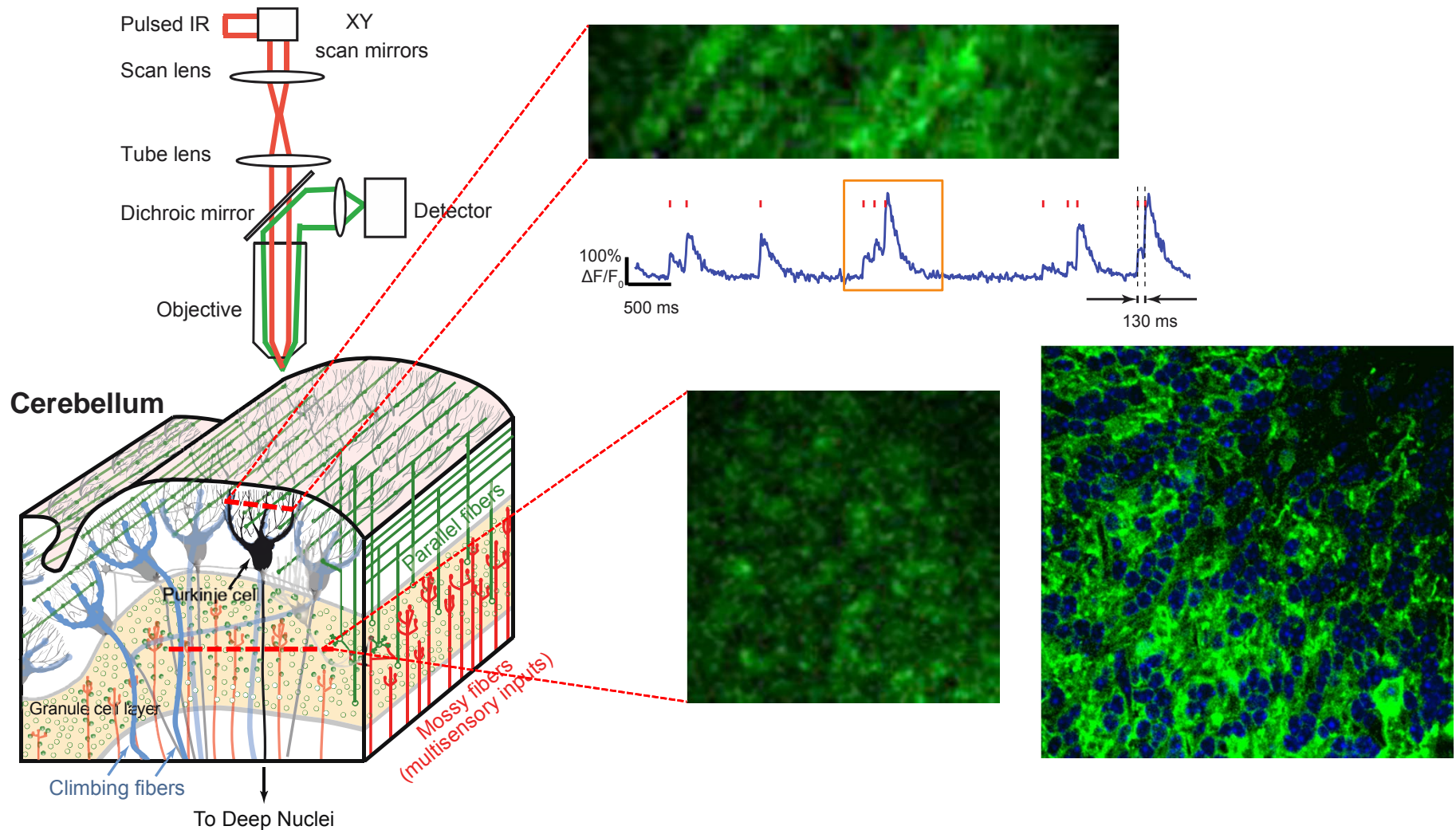


Tests for cerebellar roles in cognitive and social behavior

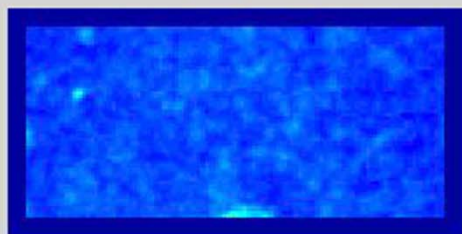
1. Cellular imaging of cerebellar network activity
2. Subregion-specific perturbations
3. Transsynaptic pathway tracing
4. Developmental shaping of distant brain circuits

Multisensory processing in the cerebellum

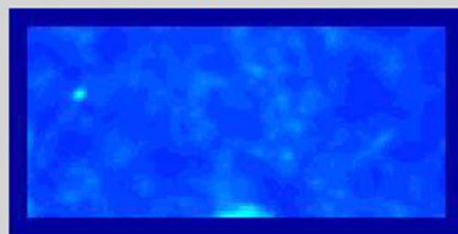
2-photon microscope



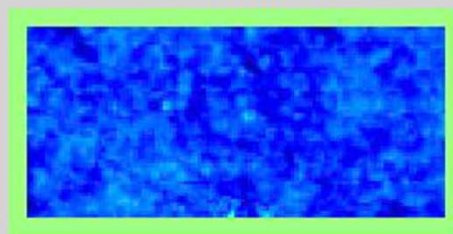
Raw data



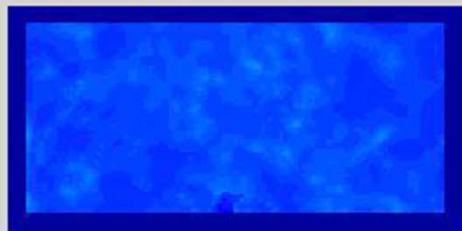
Timestep 1
Denoised



Residual 4x



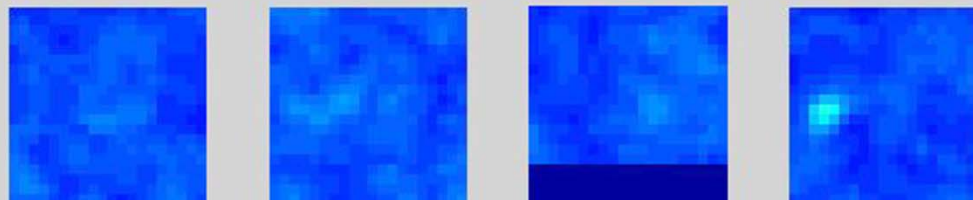
Background
synchronized activity



Representative spatial components



Raw data patches

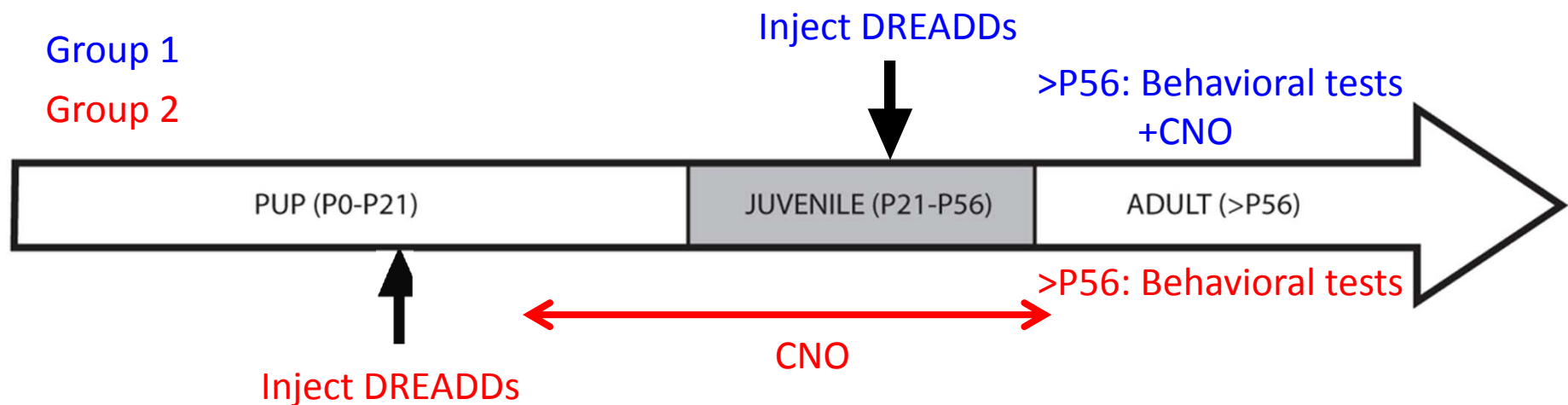
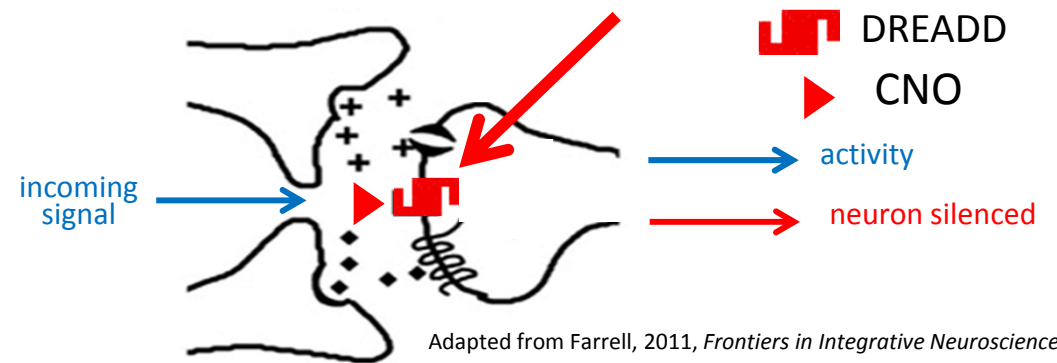


What cerebellar regions keep cognitive development on track?

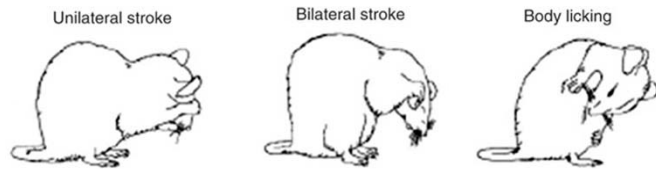


DREADDs - Designer Receptors

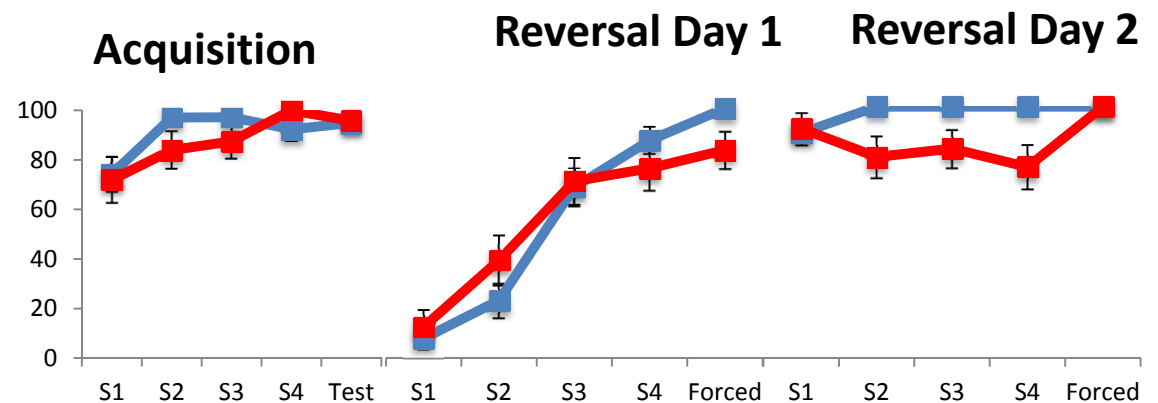
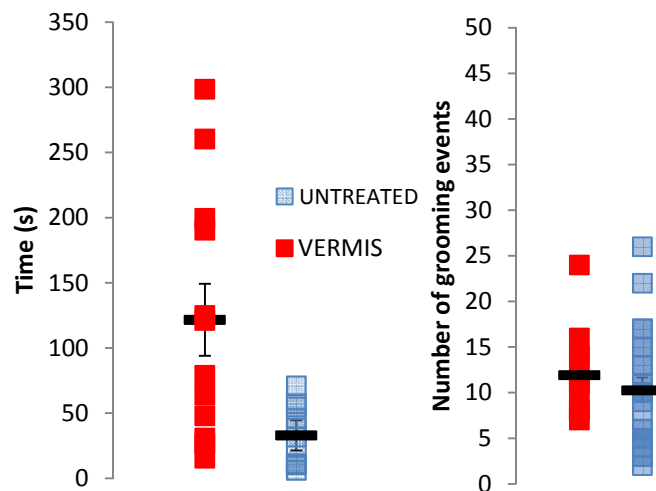
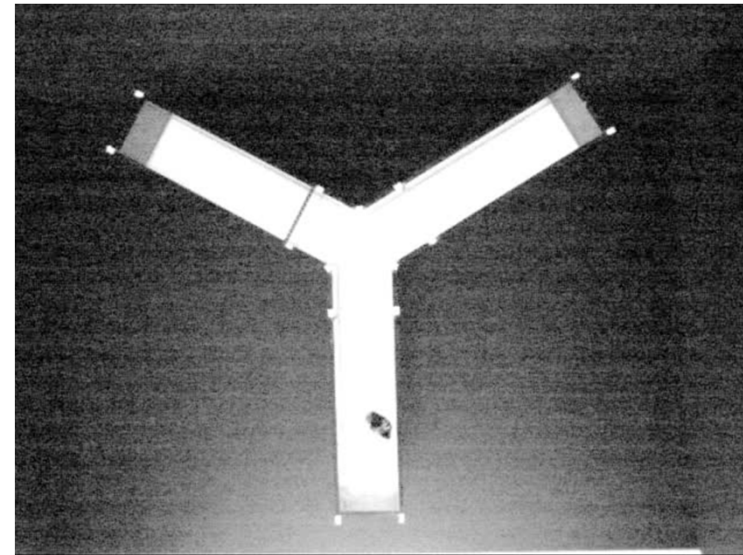
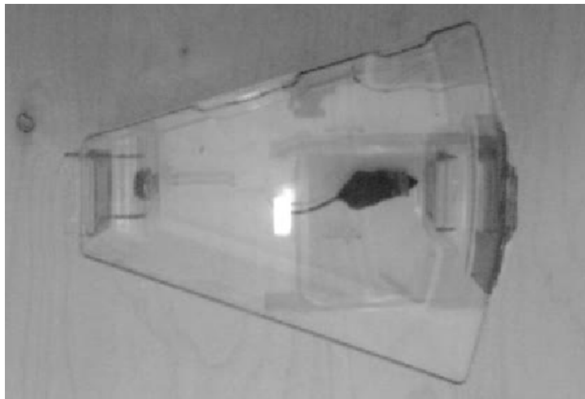
Exclusively Activated by Designer Drugs



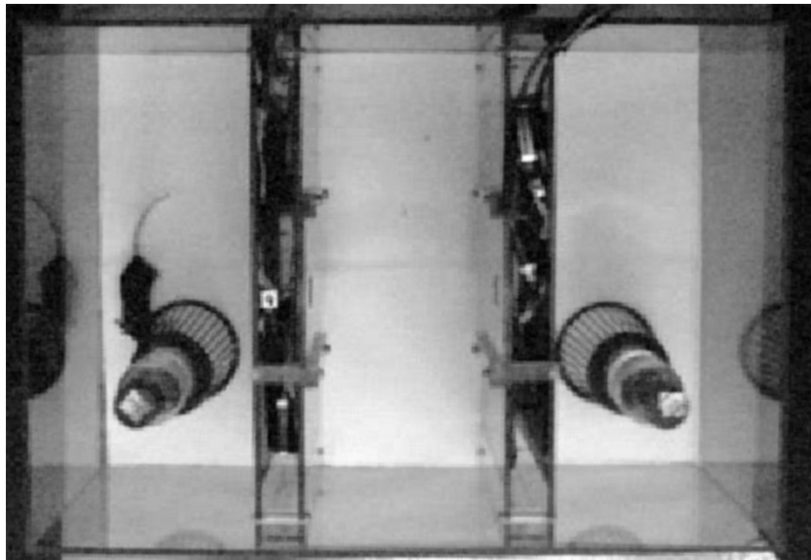
Stereotyped Behavior: Grooming and Y-maze Reversal



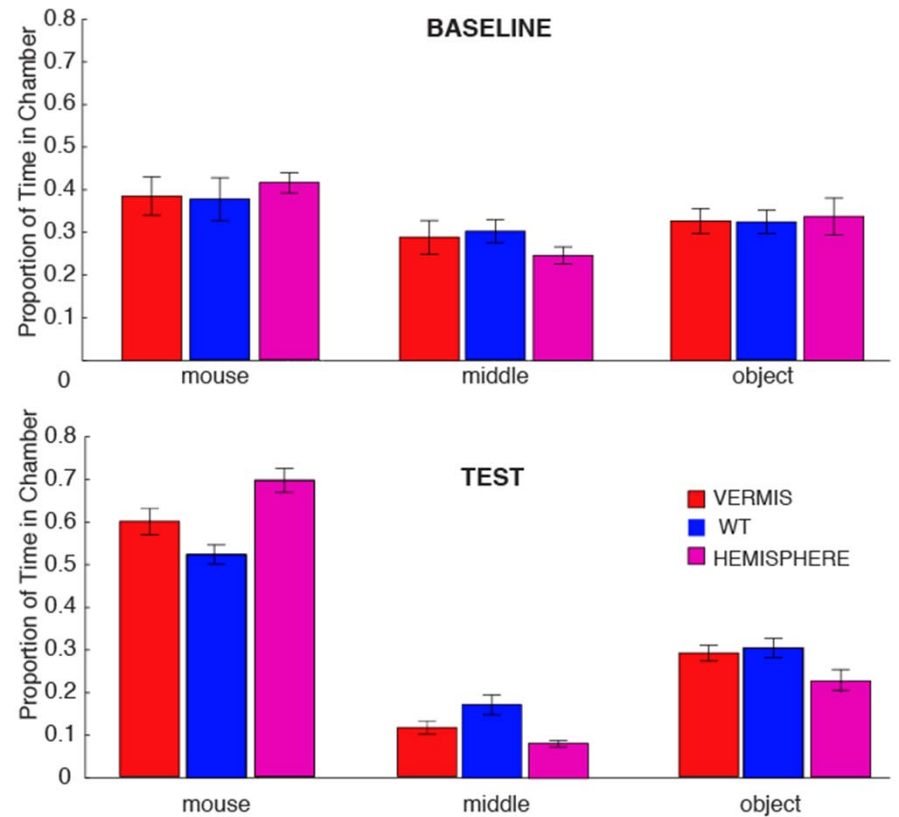
Wild-Type Grooming Components, adapted from Kalueff et al, 2007



Sociability: Three-Chamber Test



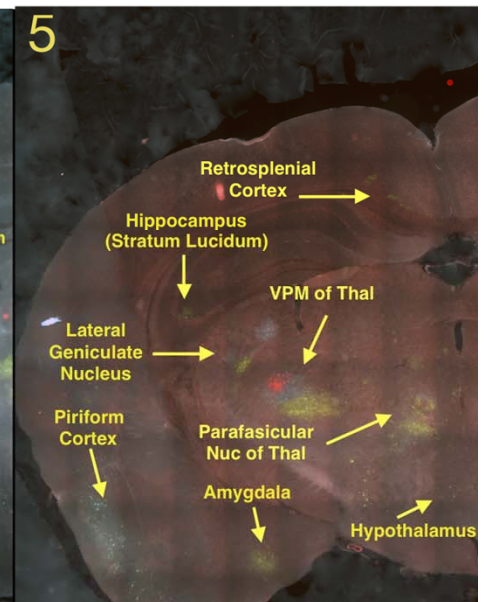
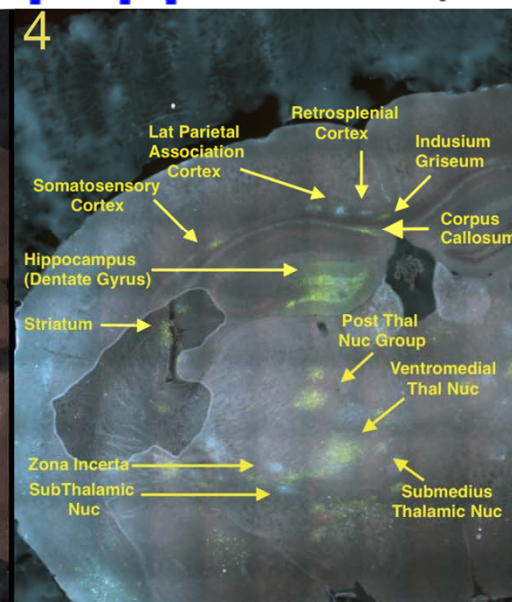
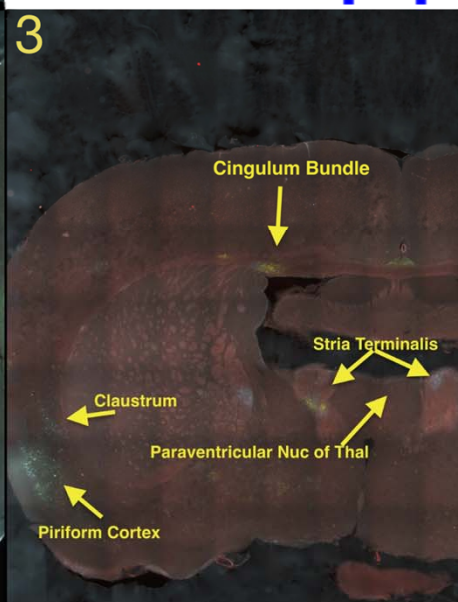
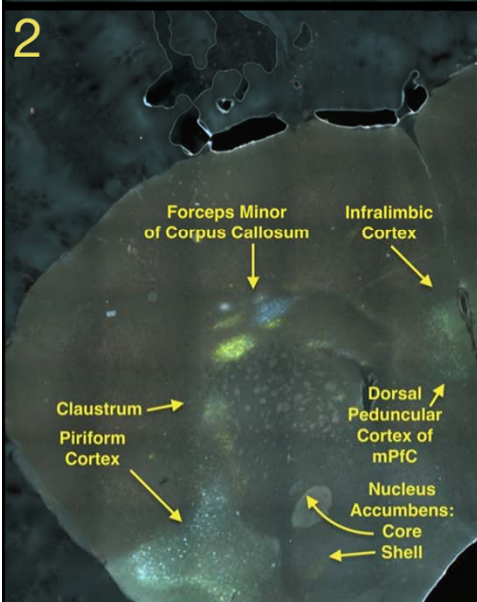
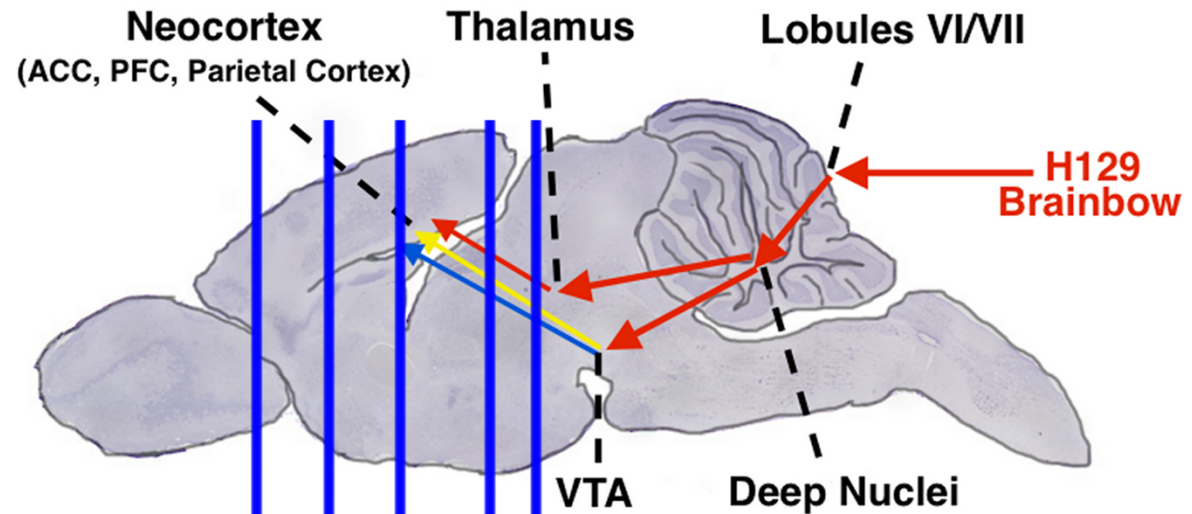
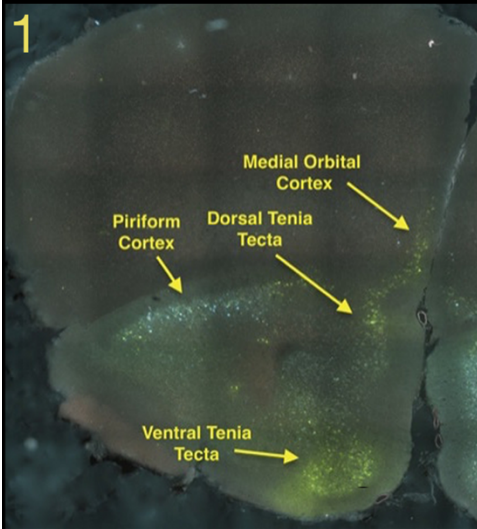
Captured Still Image from Video Recording:
Lobule Vermis-Injected Mouse Social Chamber Test



Tests for cerebellar roles in cognitive and social behavior

1. Cellular imaging of cerebellar network activity
2. Subregion-specific perturbations
3. **Transsynaptic pathway tracing**
4. **Developmental shaping of distant brain circuits**

Tracing strategy



Clearing techniques

ARTICLE

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Structural and molecular interrogation of intact biological systems

Kwanghun Chung^{1,2}, Jenelle Wallace¹, Sung-Yon Kim¹, Sandhiya Kalyanasundaram², Aaron S. Andalman^{1,2}, Thomas J. Davidson^{1,2}, Julie J. Mirzabekov¹, Kelly A. Zalocusky^{1,2}, Joanna Mattis¹, Aleksandra K. Denisin¹, Sally Pak¹, Hannah Bernstein¹, Charu Ramakrishnan¹, Logan Grosenick¹, Viviana Gradinaru² & Karl Deisseroth^{1,2,3,4}

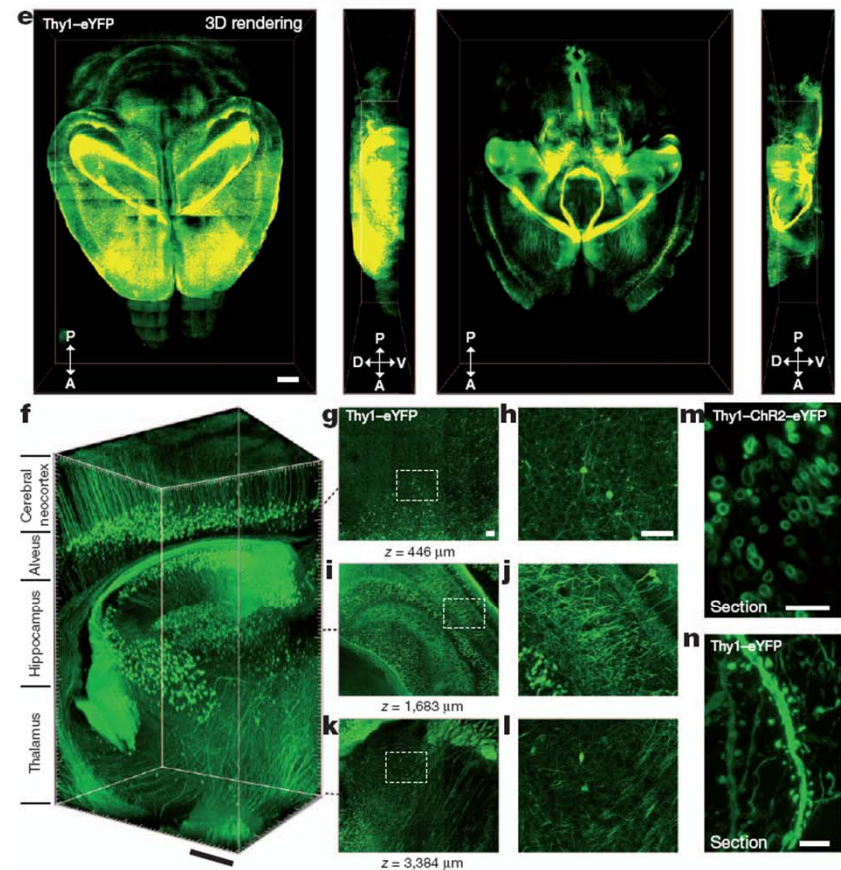
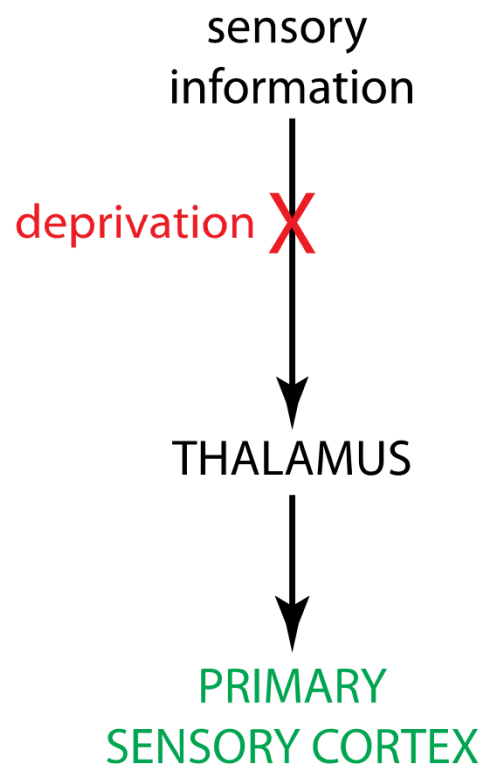
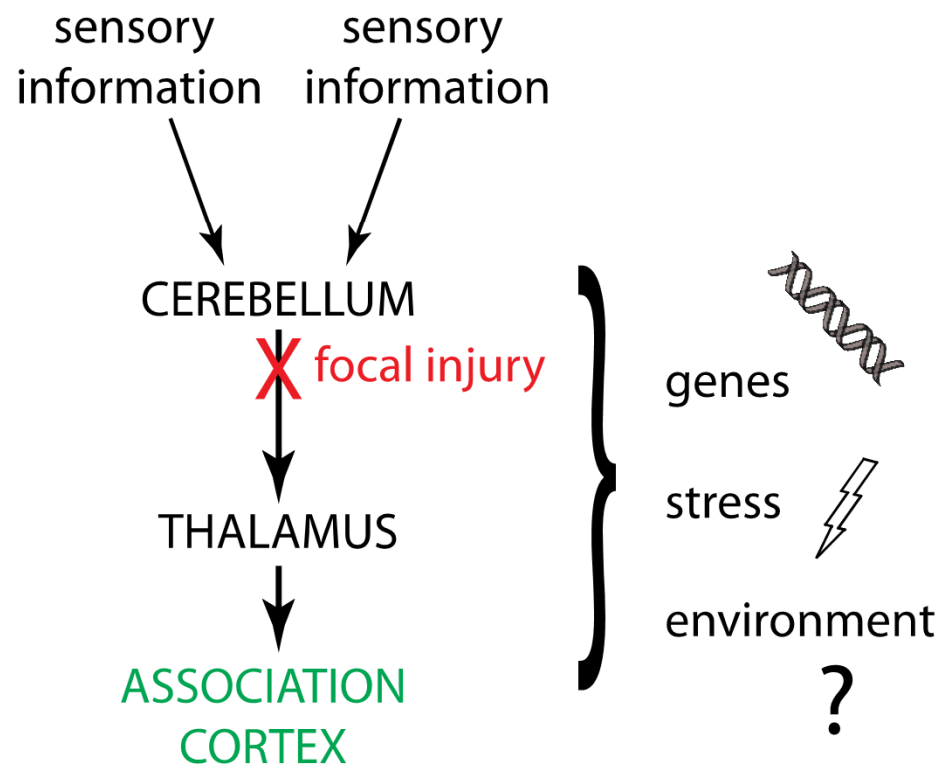


Figure 2 | Intact adult mouse brain imaging. Imaging was performed in

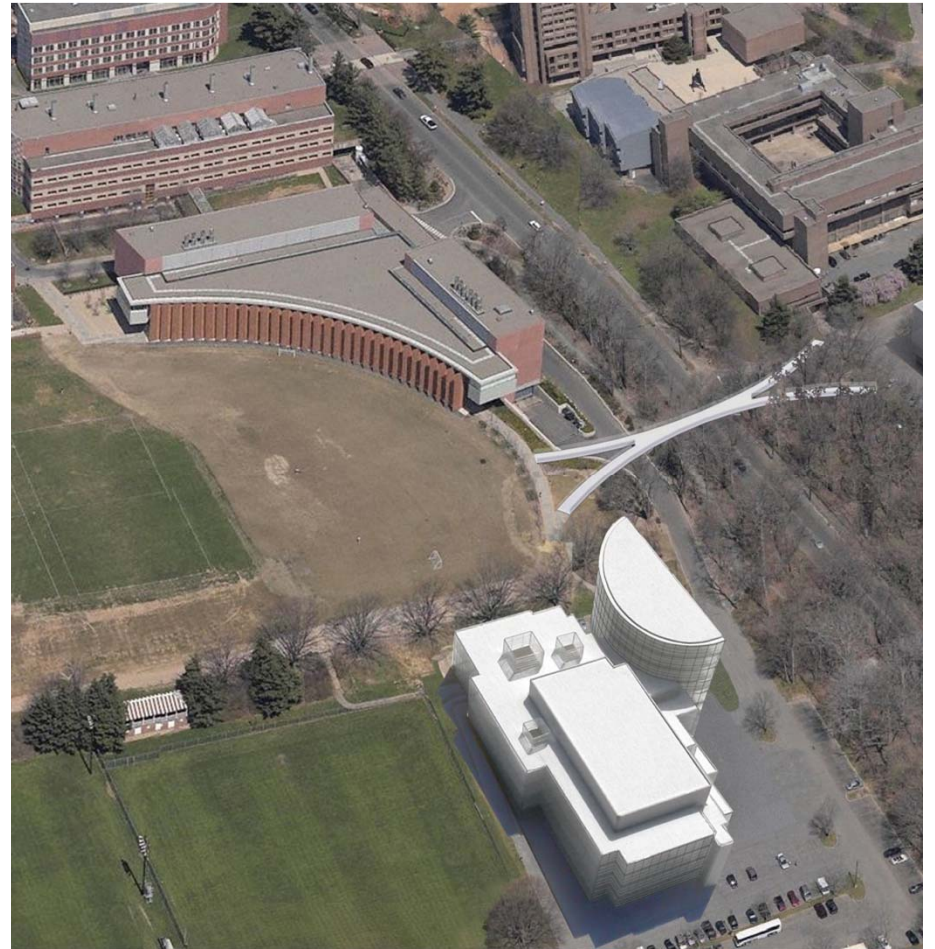
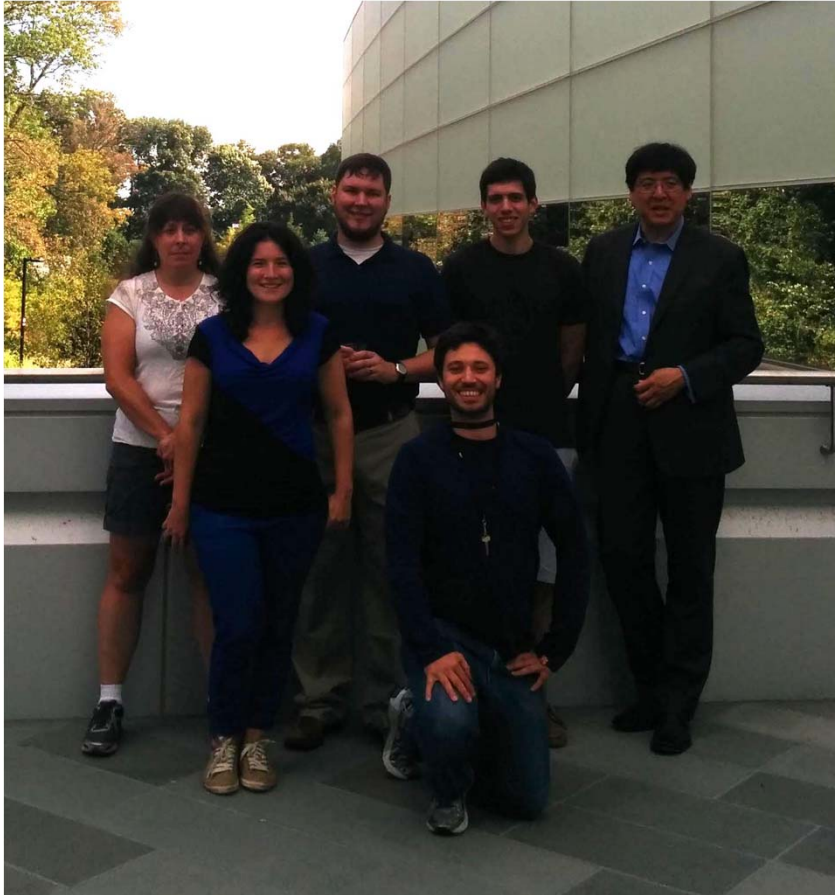
HUBEL AND WIESEL



DEVELOPMENTAL DIASCHISIS



Wang laboratory



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