BIOGRAPHICAL SKETCH

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NAME: Aaron Wayne McGee

eRA COMMONS USER NAME (credential, e.g., agency login): awmcgee

POSITION TITLE: Associate Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Colorado at Boulder	B.A.	1990-1995	MCD Biology
University of California – San Francisco	Ph.D.	1995-2001	Neuroscience
University of California – San Francisco		2002	Neuroscience
Yale University School of Medicine		2003-2008	Neuroscience

A. Personal Statement

My lab investigates how specific genes govern the capacity for experience-dependent changes in cortical circuitry that impact behaviour. My long-term goal is to devise strategies to reactivate developmental plasticity selectively within the central nervous system (CNS) to promote compensatory modifications within neural circuitry that mitigate symptoms in patients suffering with developmental visual disorders such as amblyopia and central visual impairment. In pursuit of this goal, my lab studies how experience alters circuitry in visual cortex with a combination of mouse genetics, quantitative behavioural assays, electrophysiology, and chronic *in vivo* imaging of neuronal structure and activity.

Over the past decade, the major focus of my research has been elucidating how the nogo-66 receptor 1 (NGR1/RTN4R) protein contributes both to closing the critical period for ocular dominance plasticity and recovery of acuity following early visual deprivation. We have performed a comprehensive genetic dissection of experience-dependent visual plasticity.

1. Stephany CE, Chan LLH, Parivash SN, Dorton HM, Piechowicz, Qiu S, **McGee AW**. Plasticity of binocularity and visual acuity are differentially limited by nogo receptor. *J Neurosci.*, 2014 34(35):11631-11640. PMID: 25164659
2. Priebe NJ, **McGee AW**. Mouse vision as a gateway for understanding how experience shapes neural circuits. *Frontiers in Neural Circuits* 2014 Oct 2; 8(123) PMID: 25324730
3. Stephany CÉ, Ma X, Dorton HM, Wu J, Solomon AM, Frantz MG, Qiu S, **McGee AW**. Distinct Circuits for Recovery of Eye Dominance and Acuity in Murine Amblyopia. *Curr Biol.* 2018 Jun 18;28(12):1914-1923. PMID: 29887305
4. Frantz MG, Crouse EC, Sokhadze G, Ikrar T, Stephany CÉ, Nguyen C, Xu X, **McGee AW**. Layer 4 Gates Plasticity in Visual Cortex Independent of a Canonical Microcircuit. *Curr Biol*., 2020. PMID: 32589913 (in press)

B. Positions and Honors

Positions and Employment

1995-2001 Graduate student. University of California San Francisco (UCSF) Advisor: David S. Bredt.
2001-2002 Postdoctoral Associate. UCSF, Advisor: David S. Bredt
2003-2008 Postdoctoral Fellow. Yale University School of Medicine, Dept. of Neurology Advisor: Stephen M. Strittmatter
2009-2016 Assistant Professor of Pediatrics, Neuroscience Program, The Saban Research Institute, Children's Hospital Los Angeles and Keck School of Medicine, University of Southern California
2016-2019 Assistant Professor. Department of Anatomical Sciences and Neurobiology. University of Louisville School of Medicine
2019- Associate Professor. Department of Anatomical Sciences and Neurobiology. University of Louisville School of Medicine

Professional Memberships

2004-present Member, Society for Neuroscience

Honors and Awards

1995-2000 Howard Hughes Medical Institute Predoctoral Fellowship
2006-2007 Postdoctoral Fellowship, The Kavli Institute for Neuroscience at Yale
2006-2011 Burroughs Wellcome Fund Career Award in the Biomedical Sciences
2008-2010 Research Development Career Award, Children's Hospital Los Angeles

C. Contribution to Science

Biochemical and structural characterization of synaptic scaffolding proteins

During my training as a graduate student at UCSF, the composition of the excitatory synapse was largely unknown. I explored whether neurons assemble this post-synaptic specialization through the regulated interaction of abundant scaffolding proteins like PSD-95. I drew upon preceding work of invertebrate geneticists studying mutations in homologues of PSD-95 and employed a battery of techniques spanning molecular biology, biochemistry, and structural biology, to determine the structure of two conserved domains in the protein, the SH3 and GK domains. In subsequent work, I extended the structural model of this family of membrane-associated guanylate kinase (MAGUKs) scaffolding proteins to a family of distantly related of proteins, the beta subunit of the voltage-gated calcium channel.

1. **McGee AW**, Bredt DS. Identification of an intramolecular interaction between the SH3 and guanylate kinase domains of PSD-95. *J. Biol. Chem*. 1999, 274(25):17431-6. PMID: 10364172
2. **McGee AW**, Topinka JR, Hashimoto K, Petralia RS, Kakizawa S, Kauer F, Aguilera-Moreno A, Wenthold RJ, Kano M, Bredt DS. PSD-93 knock-out mice reveal that neuronal MAGUKs are not required for development or function of parallel fiber synapses in cerebellum. *J. Neurosci*. 2001, 21(9):3085-91. PMID: 11312293
3. **McGee AW**, Dakoji SR, Olsen O, Bredt DS, Lim WA, Prehoda KE. Structure of the SH3-guanylate kinase module from PSD-95 suggests a mechanism for regulated assembly of MAGUK scaffolding proteins. *Molecular Cell* 2001, 8(6):1291-301. PMID: 11779504
4. **McGee AW**, Nunziato DA, Maltez JM, Prehoda KE, Pitt GS, Bredt DS. Calcium channel function regulated by the SH3-GK module in beta subunits. *Neuron* 2004, 42(1):89-99. PMID: 15066267

Identified genes required to close developmental critical periods for plasticity

As a postdoctoral fellow, my original plan was to apply my training as a molecular biologist to identify genes and signaling pathways inhibiting recovery from traumatic CNS injury. At the time, the Strittmatter lab had just reported that both the Nogo-A gene (*nogo-a*/*rtn4a*) and associated Nogo Receptor 1 (*ngr1*/*rtn4r*) genes limited regeneration of injured axons and recovery from spinal cord injury (SCI). However, as the results of *in vitro* and *in vivo* assays used to study axon outgrowth did not register with the rapid though quite modest recovery from SCI in these mutant mice, I suspected the functional recovery after SCI in *ngr1* mutant mice was more likely a consequence of plasticity within the remaining intact neural circuitry.

To test the hypothesis that *ngr1* restricts plasticity in the uninjured adult CNS, I collaborated with Prof. Nigel Daw to investigate whether *ngr1* limits plasticity within the visual system. We identified *ngr1* as the first gene required to close the developmental critical period for ocular dominance (OD) plasticity, a prominent model of experience-dependent cortical plasticity. Determining how *ngr1* restricts visual plasticity is the primary focus of my lab.

1. **McGee AW**, Strittmatter SM. The Nogo-66 receptor: focusing myelin inhibition of axon regeneration. *Trends Neurosci*. 2003 Apr;26(4):193-8. PMID: 12689770
2. **McGee AW**, Yang Y, Fischer QS, Daw NW, Strittmatter SM. Experience-driven plasticity of visual cortex limited by myelin and nogo receptor. *Science* 2005, 309:2222-2226. PMID: 16195464
3. Cafferty WB, **McGee AW**, Strittmatter SM. Axonal growth therapeutics: regeneration or sprouting or plasticity? *Trends Neurosci*. 2008 May;31(5):215-20 PMID: 18395807

Identified circuits gating plasticity for binocularity and acuity

To investigate how *ngr1* governs plasticity in the visual system, I generated and validated a conditional allele ('floxed') for *ngr1*. My lab discovered that the constitutive *ngr1* mutants spontaneously recover normal eye dominance and acuity with the restoration of binocular vision. We then pursued a genetic dissection strategy in combination with electrophysiology *in vivo* and behavioural assays of acuity to determine where *ngr1* is required to limit plasticity for eye dominance and acuity. Surprisingly, *ngr1* operates in cortical neurons to restrict plasticity of eye dominance, but in thalamus to limit recovery of acuity. Turning to electrophysiology with acute slices of visual cortex *in vitro*, we demonstrated that monocular deprivation (MD) and return of binocular vision following MD have reciprocal effects on inhibitory cortical circuits as well. Deprivation is associated with cortical disinhibition while recovery after deprivation augments cortical inhibition. These findings that binocularity and acuity can recover from deprivation independently and have opposing effects on cortical circuits contributes to revising long-standing models of the relationship between binocularity and acuity.

1. Stephany CE, Chan LLH, Parivash SN, Dorton HM, Piechowicz, Qiu S, **McGee AW**. Plasticity of binocularity and visual acuity are differentially limited by nogo receptor. *J Neurosci.* 2014 34(35):11631-11640. PMID: 25164659
2. Stephany CE, Ikrar T, Nguyen C, Xu X, **McGee AW.** Nogo receptor 1 confines a disinhibitory microcircuit to the critical period in visual cortex. *J Neurosci.* 2016, 36(43):11006-11012. PMID: 27798181
3. Stephany CÉ, Ma X, Dorton HM, Wu J, Solomon AM, Frantz MG, Qiu S, **McGee AW**. Distinct Circuits for Recovery of Eye Dominance and Acuity in Murine Amblyopia. *Curr Biol.* 2018 Jun 18;28(12):1914-1923. PMID: 29887305
5. Frantz MG, Crouse EC, Sokhadze G, Ikrar T, Stephany CÉ, Nguyen C, Xu X, **McGee AW**. Layer 4 Gates Plasticity in Visual Cortex Independent of a Canonical Microcircuit. *Curr Biol*., 2020. PMID: 32589913 (in press)

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/myncbi/browse/collection/47715438/

D. Research Support

Active Research Support

1EY027407 (McGee, Trachtenberg, Xu, Multi-PI) 06/1/17-05/31/21
NIH/NEI
'Disinhibition and Experience-Dependent Visual Plasticity'
This project investigates how brief monocular deprivation drives laminar plasticity within visual cortex, as well as how this plasticity is restricted to the critical period. Although experiments of this project also exploit the plasticity phenotype of *ngr1* mutant mice, there is no overlap with experiments in the current proposal that examine the progression of recovery of OD and acuity following extended monocular deprivation. For my component, this project provides resources sufficient animal costs and a technician to investigate the laminar progression of OD plasticity with brief MD.

Completed Research Support

1R21NS077288 (McGee, PI) 08/1/11-7/31/13
NIH/NINDS
'Regulation of Anatomical Plasticity and Perceptual Learning by NgR1'This project examines the role of a gene that regulates cortical plasticity, NgR1, in determining the rate of perceptual learning in a whisker-dependent task, the gap cross assay, as well as if this learning is associated with specific alterations to dendritic spine dynamics in barrel cortex.

1R01EY021580 (McGee, PI) 5/1/12-4/30/17
NIH/NEI
'Deciphering Inhibition of Visual Plasticity by NgR1'
This project investigates how NgR1 functions within inhibitory cortical circuitry to close the critical period for ocular dominance plasticity in the developing visual system.
The proposed research is the competitive renewal for this grant