BIOGRAPHICAL SKETCH

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NAME: Myongsoo Matthew Oh

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

POSITION TITLE: Research Assistant 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 Maryland, College Park, MD	B.S.	05/1993	Psychology
Northwestern University, Evanston, IL	Ph.D.	04/2002	Neuroscience
Feinberg School of Medicine, Northwestern University, Chicago, IL	Postdoctoral	12/2008	Physiology

A. Personal Statement

My research over the past 15+ years have been focused on my interest in identifying why learning becomes progressively more difficult with normal aging, and if the age-related cognitive deficits can be reversed and/or prevented. With these broad goals in mind, I have been studying the cellular properties of principle neurons of the hippocampus as an animal ages and after an animal has learned a task that involves the hippocampus. Thus far, my colleagues and I have identified that (1) CA1 hippocampal pyramidal neurons (the principle output neurons of the hippocampus) become more excitable (that is, they are able to fire more action potentials) following successful learning on various hippocampus dependent tasks and in different species (e.g., water maze learning: Oh et al., 2003, *J Neurophysiol*); (2) the learning dependent excitability change of CA1 pyramidal neurons is mediated in part by activity of protein kinase A (Oh et al., 2009, *PNAS*); (3) the learning-dependent excitability change may be a generalized cellular mechanism used by all neuron types, as hippocampal interneurons also undergo learning dependent increase in excitability after successful learning (McKay, Oh & Disterhoft, 2013, *J Neurosci*); and (4) the same population of hippocampal pyramidal neurons becomes less excitable with normal aging (e.g., Oh et al., 2006, *Neurosci*; Power et al., 2002, *J Neurosci*). More importantly, we have tested a key component of the 'Calcium Hypothesis of Normal Aging' by using calcium-imaging with two-photon laser scanning microscopy (2PLSM) technique to directly measure the resting concentration of free calcium and the endogenous calcium buffer capacity of CA1 pyramidal neurons, and showed that, contrary to popular belief, the resting free calcium level is reduced while the calcium buffer capacity is enhanced in CA1 pyramidal neurons from aged rats (Oh et al., 2013, *J Neurosci*). In addition, we demonstrated that reducing the excitability of hippocampal neurons (via increasing the postburst afterhyperpolarization) in young adults impaired their learning ability that partially resembled the behavioral of normal aging subjects (McKay, Oh, et al., 2012, *J Neurophysiol*). Thus, it is our working hypothesis that the reduced excitability level of the hippocampal pyramidal neurons with normal aging is a cause of the learning deficits observed in the aging population. We are currently using state of the art calcium imaging and glutamate uncaging techniques to further characterize the changes in the hippocampal pyramidal neurons following learning and with normal aging. By systematically examining these cellular changes that occur following successful learning and with normal aging, a goal is to identify potential pharmacological targets to ameliorate and/or reverse the normal aging-related cognitive deficits. In addition, given that incidence of Alzheimer's disease increases with age, it is another goal of our research to translate our findings and approach to identify the cellular changes that occur in this debilitating condition. Therefore, I have been developing my skills (e.g., behavior, behavioral pharmacology, electrophysiology, and 2PLSM imaging) to answer the questions laid out in the proposed research program.

1. **Oh MM**, Oliveira FA, Waters J, Disterhoft JF (2013) Altered calcium metabolism in aging CA1 hippocampal pyramidal neurons. Journal of Neuroscience 33:7905-7911
2. **Oh MM**, Gamelli AE, Wu WW, Sametsky E, Disterhoft (2003) Watermaze learning enhances excitability of CA1 pyramidal neurons. Journal of Neurophysiology 90:2171-2179
3. **Oh MM**, McKay BM, Power JM, Disterhoft JF (2009) Learning-related postburst afterhyperpolarization reduction in CA1 pyramidal neurons is mediated by protein kinase A. PNAS 106:1620-1625
4. **McKay BM*, Oh MM***, Galvez R, Burgdorf J, Kroes RA, Weiss C, Adelman JP, Moskal JR, Disterhoft JF (2012) Increasing SK2 channel activity impairs associative learning. Journal of Neurophysiology 108: 863-870 ***Co-First Author**.

B. Positions and Honors

Positions

1993 – 1995 Special Volunteer, Laboratory of Adaptive Systems (LAS), NINDS, NIH. Advisors: Daniel Alkon and Bernard Schreurs
1995 Summer Intern, LAS, NINDS, NIH. Advisors: Daniel Alkon and Bernard Schreurs
2002 – 2008 Postdoctoral Fellow, Department of Physiology, Feinberg School of Medicine (FSM), Northwestern University, Chicago, IL. Advisor: John Disterhoft
2009 – 2010 Research Associate, Department of Physiology, FSM, Northwestern University, Chicago, IL
2010 – Research Assistant Professor, Department of Physiology, FSM, Northwestern University, Chicago, IL

Other Experiences and Other Professional Activities

1992 – 1993 Undergraduate Teaching Assistant, University of Maryland, College Park, MD
1997 Teaching Assistant, Northwestern University, Evanston, IL

1997 – Member, Society for Neuroscience
1997 – Member, American Association for the Advancement of Science

2006 – Ad hoc reviewer for the journals: Developmental Neurobiology; Learning and Memory; Neurobiology of Aging; Neurobiology of Learning and Memory; Neuropsychopharmacology; Neuroscience; Neuroscience Letters
2009 – Grant reviewer for the Alzheimer's Association

Invited Lectures, Seminars and Colloquia

Aug 2002 3rd NUIN Postdoc Day. Institute for Neuroscience, FSM, Northwestern University, Chicago, IL
July 2003 The Annual Meeting of the General Motor Control Mechanisms and Disease Training Program: Motor Day. Institute for Neuroscience, FSM, Northwestern University, Chicago, IL
July 2009 Northwestern University's Neurobiology of Information Storage Training Program's Annual Retreat, Lake Geneva, WI
Nov 2009 Conference on Neurocognition: From Early Development to Aging, Singapore
Sept 2010 Northwestern University's Interdepartmental Neuroscience Program's Annual Retreat, Oak Brook, IL
Oct 2010 Invited Lecturer for Proseminar in Biological Psychology, University of Wisconsin at Milwaukee, Milwaukee, IL
Nov 2010 Nanosymposium on Associative Learning and Fear Conditioning, Society for Neuroscience Annual Meeting, San Diego, CA

Honors and Awards

1991 – 1992 Dean's List, Academic Semester Honors, University of Maryland, College Park, MD
1993 Zoology Department Award for Teaching, University of Maryland, College Park, MD
1995 Summer Internship, NINDS, NIH, Bethesda, MD
1998 – 2001 University Scholar, Northwestern University, Evanston, IL
1999 – 2001 NIMH/NIH Individual Predoctoral National Research Service Award, (MH11737)
2002 Best Presentation, 3rd NUIN Postdoc Day, Institute for Neuroscience, FSM, Northwestern University, Chicago, IL
2002 – 2004 NINDS/NIH Institutional Postdoctoral National Research Service Award, (NS41234)

C. Contribution to Science

1. At present, the postburst afterhyperpolarization (AHP) is known to be due to mainly a calcium-dependent outward potassium conductance comprised of activity of apamin-sensitive SK channels for the medium AHP and activity of yet to be identified slow AHP channel(s). However, when I began my scientific career, there was great debate and doubt about the existence of an apamin-sensitive AHP in CA1 pyramidal neurons. Therefore, one of my early studies addressed this issue by systematically testing the effect of apamin on the biophysical properties of CA1 pyramidal neurons from young adult rabbit hippocampal slices. I found that there is a dose-dependent effect of apamin on the medium postburst AHP and spike-frequency adaptation (accommodation) (Oh et al., 2000). Furthermore, increasing the activity of the apamin-sensitive medium AHP with NS309 reduced the excitability of hippocampal neurons and severely impaired acquisition of the hippocampus-dependent trace eyeblink conditioning in young adult rats that partially resembled the behavioral of normal aging subjects (McKay, Oh, et al., 2012). Recently, we demonstrated that the apamin-sensitive medium AHP is reduced not only in pyramidal neurons, but also in interneurons located in the stratum oriens of dorsal CA1 region to increase the excitability of these interneurons following trace eyeblink conditioning in young adult rats and mice (McKay et al., 2013). Therefore, the highly doubted apamin-sensitive medium AHP of late 1990's, have been shown to be a potential cellular mechanism used by all neuron types to undergo learning-dependent intrinsic excitability change. I served as the primary investigator or co-investigator in all of these studies.
    a. **Oh MM**, Power JM, Thompson LT, Disterhoft JF (2000) Apamin increases neuronal excitability of CA1 pyramidal neurons from rabbit hippocampus. Neuroscience Research Comm 27:135-142
    b. **McKay BM*, Oh MM***, Galvez R, Burgdorf J, Kroes RA, Weiss C, Adelman JP, Moskal JR, Disterhoft JF (2012) Increasing SK2 channel activity impairs associative learning. Journal of Neurophysiology 108: 863-870 ***Co-First Author**.
    c. McKay BM, **Oh MM**, Disterhoft JF (2013) Learning increases intrinsic excitability of hippocampal interneurons. Journal of Neuroscience 33:5499-5506

2. In the late 1990's, the transient learning-dependent increase in hippocampal neuronal excitability, due to reduced postburst AHP (e.g., Moyer et al., 1996; Thompson et al., 1996), had been considered to be a 'rabbit' phenomenon following a specific temporal learning task, the eyeblink condition task. These findings were not embraced because they did not use the dominant scientific animal model (rodents: rats and mice) using the widely used behavioral tasks; either fear conditioning or water maze training. Therefore, I was determined to demonstrate that the learning-dependent postburst AHP modulation was applicable across species and across behavioral tasks. In a series of experiments using both current- and voltage-clamp recording methods, we demonstrated that the postburst AHP and currents that underlie it are reduced in CA1 pyramidal neurons from young adult rats that successful learned the spatial water maze task and not in those animals that were yoke-controls nor in those that failed to learn (Oh et al., 2003). Then we demonstrated that the postburst AHP is reduced in CA1 pyramidal neurons and interneurons from young adult rats and mice that learned the trace eyeblink conditioning task (McKay et al., 2013). Importantly, we demonstrated that protein kinase A activity mediates the learning-dependent postburst AHP reduction (Oh et al., 2009). Therefore, we hypothesize that the postburst AHP is a cellular mechanism that is modulated by learning various tasks and in different species.
    a. **Oh MM**, Gamelli AE, Wu WW, Sametsky E, Disterhoft (2003) Watermaze learning enhances excitability of CA1 pyramidal neurons. Journal of Neurophysiology 90:2171-2179
    b. **Oh MM**, McKay BM, Power JM, Disterhoft JF (2009) Learning-related postburst afterhyperpolarization reduction in CA1 pyramidal neurons is mediated by protein kinase A. PNAS 106:1620-1625
    c. McKay BM, **Oh MM**, Disterhoft JF (2013) Learning increases intrinsic excitability of hippocampal interneurons. Journal of Neuroscience 33:5499-5506

3. In addition to the learning-related changes in the postburst AHP, I have focused my efforts in identifying the aging-related changes in the postburst AHP in CA1 pyramidal neurons as a cellular mechanism that underlies the normal aging-related cognitive deficits. First, we demonstrated that the currents that underlie the postburst AHP are enlarged in CA1 pyramidal neurons from aged animals (Power et al., 2002). We also demonstrated that aging-related learning deficits can be ameliorated with pharmacological compounds that reduces the postburst AHP in CA1 pyramidal neurons from aged animal (reviewed in Oh et al., 2010). Then we demonstrated that increasing the medium, apamin-sensitive AHP in young adults partially mimics the

aging-related learning deficits (McKay, Oh, et al., 2012). However, the slow AHP cannot directly examined, because the channel identity has yet to be discovered. Therefore, we decided to examine the aging-related changes in calcium handling in CA1 pyramidal neurons using 2PLSM calcium imaging experiments. Until our 2PLSM calcium imaging experiments, most scientists (including us) believed that the resting free calcium concentration is enlarged while the calcium buffer capacity is reduced in CA1 pyramidal neurons, based on circumstantial evidence used to formulate the 'Calcium Hypothesis of Normal Aging' proposed in the 1980's and 1990's. So it was surprising when our systematic evaluation of the calcium dynamics revealed that the resting free calcium is reduced while the calcium buffer capacity is enhanced in CA1 pyramidal neurons from aged rats (Oh et al., 2013). The enhanced calcium buffer capacity allows the aged CA1 neuron to accommodate the calcium accumulation to a few (~3) action potentials; however, it is overwhelmed with a train of action potentials that normally evoke a postburst AHP. This recent finding has opened a new venue of research to identify the source(s) of the enhanced calcium buffer with normal aging. In addition to the 2PLSM calcium imaging study, we discovered that the surface expression, and not total levels, of L-type voltage-gated calcium channels is enhanced on CA1 neurons from aged animals (Nunez-Santana et al., 2014). Thus, these findings have shed new light and focus on studying aging-related intrinsic excitability changes that may underlie aging-related cognitive deficits. These findings also strongly implicate the need for high-resolution functional (2PLSM imaging) and structural (channel composition) studies to characterize the aging-related changes that occur at the cellular level, so that potential therapeutic targets to reverse and/or prevent the aging-related cognitive deficits can be identified.

a. Power JM, Wu WW, Sametsky E, **Oh MM**, Disterhoft JF (2002) Age related enhancement of the sIAHP in CA1 pyramidal neurons in vitro. Journal of Neuroscience 22:7234-43
b. **Oh MM**, Oliveira FA, Disterhoft JF (2010) Learning and aging related changes in intrinsic neuronal excitability. Frontiers in Aging Neuroscience doi:10.3389/neuro.24.002.2010
c. **Oh MM**, Oliveira FA, Waters J, Disterhoft JF (2013) Altered calcium metabolism in aging CA1 hippocampal pyramidal neurons. Journal of Neuroscience 33:7905-7911
d. Nunez-Santana FL, **Oh MM**, Antion MD, Lee A, Hell JW, Disterhoft JF (2014) Surface L-type Ca2+ channel expression levels are increased in aged hippocampus. Aging Cell 13:111-120

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/myongsoo.oh.1/bibliograpahy/40448263/public/?sort=date&direction=ascending

D. Research Support

Active

RF1 AG017139 (Disterhoft) 05/15/2016 – 04/30/2021
Synaptic Substrates of Age-Dependent Memory Deficits
The goals of this project are to identify potential link between functional biophysical properties and the proteomic properties at dendritic spines of CA1 hippocampal pyramidal neurons that may underlie the aging-related learning and memory deficits. This project will use cutting edge methods to assess functional (multiphoton (2P) glutamate uncaging and 2P calcium imaging) and proteomic (immunogold field emission scanning electron microscopy and immunofluorescence array tomography) properties from behaviorally characterized young adult and aged rats.
Role: Co-Investigator

Completed

F31 MH011737 (Oh) 01/01/1999 – 12/31/2001
Cholinergic Modulation of Learning and CA1 Excitability
The goals of this project are to identify the role of cholinergic modulation on CA1 pyramidal neurons from behaviorally naïve and trained young adult and aged animals.
Role: Principle Investigator