BIOGRAPHICAL SKETCH

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NAME: John F. Disterhoft

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POSITION TITLE: Magerstadt Memorial Professor of Physiology

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
Loras College, Dubuque, IA	B.A.	06/1966	Psychology
Fordham University	M.A.	06/1968	Psychology
Fordham University	Ph.D.	01/1971	Psychology
California Institute of Technology, Pasadena, CA	Postdoctoral	09/1970 - 03/1973	Neurobiology

A. Personal Statement

John Disterhoft has extensive research experience investigating the neural mechanisms of learning in young and aging animals and in the learning deficits associated with aging and Alzheimer's Disease. The portion of his research program investigating slow outward currents during learning in aging has received two consecutive MERIT award designations from the National Institute on Aging. The competing renewal of his research program to investigate the synaptic changes occurring in aging hippocampus using cutting edge molecular and 2P imaging approaches was recently renewed. The other portion of his research program involves studying the activity of many single neurons in conscious animals during learning and memory consolidation. Dr. Disterhoft directs the Northwestern University NIA funded predoctoral and postdoctoral training program on Mechanisms of Aging and Dementia, is Associate Director of the Northwestern University Alzheimer's Disease Center and is Executive Director of the Northwestern University Behavioral Phenotyping Core. He possess a combination of scientific, administrative and extensive mentoring experience that qualifies him to serve as a faculty mentor. Dr. Disterhoft has mentored more than 20 graduate students and 25 postdoctoral fellows during his scientific career.

B. Positions and Honors

Assistant Professor of Anatomy, Northwestern University Medical School 1973-1978
Associate Professor of Cell Biology and Anatomy, Northwestern Univ. Medical School 1978-1990
Research Investigator, Lab. of Biophysics, NINCDS, MBL, Woods Hole, MA 1984-1986
Professor of Cell and Molecular Biology, Northwestern University Medical School 1990-2001
Professor of Psychology, Northwestern University 1994-
Professor of Physiology, Northwestern University Medical School 2001-
Ernest J. and Hattie H. Magerstadt Memorial Research Professor, 2006-
Department of Physiology, Feinberg Medical School, Northwestern University
Associate Director, Northwestern University Alzheimer's Disease Center 2010-
Director, Northwestern University Interdepartmental Neuroscience Program (NUIN) 2006-2011
Fellow, American Association for the Advancement of Science 1992
Fellow, American Psychological Society 1993
MERIT Award, National Institute on Aging 1999-2009; 2010-2020
Fellow, American Psychological Association 2004
Secretary to Neuroscience Section, AAAS 2009-2012

Editorial Board, American Psychologist	2010-
Editorial Board, Neurobiology of Learning and Memory	2004-
Editorial Advisory Board, Trends in Neuroscience	2003-2011
Behavioral Neuroscience (Editorial Board, 1992-, Editor, 2002-2008)	1992-
Editorial Board, Behavioral and Neural Biology	1985-91
Editor, North America, Neuroscience Research Communications	1997-2000
Site Visitor and Ad Hoc Study Section Member, NIA, NIH	1986-
Cognitive and Functional Neuroscience Subcommittee, NIMH (Chairperson, 1994-97)	1991-97
Neurobiology of Learning and Memory Study Section (LAM), CSR, NIH	2007-2011

C. Contribution to Science

1. Single neuron recording in vivo during learning to functionally characterize circuits mediating learning and memory storage in the brain. These experiments have been done during classical conditioning of food rewards and eyeblink conditioning in rats and rabbits. They have been important in characterizing how sensory system processing is heightened to a conditioned stimulus during learning; how information flows within the the hippocampus and associated temporal lobe structures that occurs during acquisition and after consolidation of conditioned responses; and that posterior prefrontal cortex neurons change very early during learning and that prelimbic prefrontal cortex neurons show dramatic firing rate increases that serve to link the conditioned and unconditioned stimuli after memory consolidation has occurred.
   a. Disterhoft, J.F. and Olds, J. Differential development of conditioned unit changes in thalamus and cortex of rat. J. Neurophysiology, 1972, 35, 665-679.
   b. Ward, R.L., Flores, L. and Disterhoft, J.F. Infragranular barrel cortex activity is enhanced with learning. J. Neurophysiology, 2012, 108, 1278-1287. PMCID:PMC3544956
   c. Hattori, S., Yoon, Y., Disterhoft, J.F. and Weiss, C. Functional reorganization of a prefrontal cortical network mediating consolidation of trace eyeblink conditioning. J. Neuroscience, 2014, 34, 1432-1445. PMCID: PMC3898299
   d. Hattori, S., Chen, L., Weiss, C. and Disterhoft, J.F. Robust hippocampal responsivity during retrieval of consolidated associative memory. Hippocampus, 2015, 25, 655-669. PMCID:PMC4412761

2. Neuronal intrinsic excitability is altered during learning, a mechanism for increasing neuron firing during learning. My laboratory was the first to demonstrate with ex vivo brain slice biophysical recordings that hippocampal neurons show increased excitability after learning by reducing outward calcium-activated potassium currents. We have subsequently demonstrated that such intrinsic excitability increases are conditioning-specific, occurring after learning but not when animals receive training trials but don't learn and not after unpaired control conditions. We have also demonstrated that these intrinsic excitability changes are not permanent in the hippocampus but have a time course appropriate for involvement in acquisition and supporting initial consolidation of learned memories. Finally, these excitability changes occur following learning of several hippocampus-dependent learning tasks including trace eyeblink conditioning, spatial water maze learning and trace fear conditioning.
   a. Disterhoft, J.F., Coulter, D.A. and Alkon, D.L. Conditioning-specific membrane changes of rabbit hippocampal neurons measured in vitro. Proceedings of the National Academy of Sciences, USA, 1986, 83, 2733-2737.
   b. Moyer, J.R., Jr., Thompson, L.T. and Disterhoft, J.F. Trace eyeblink conditioning increases CA1 excitability in a transient and learning-specific manner. Journal of Neuroscience, 1996, 16, 5536-5546.
   c. Oh, M.M., McKay, B.M., Power, J.M. and Disterhoft, J.F. Learning-related postburst afterhyperpolarization reduction in CA1 pyramidal neurons is mediated by protein kinase A. PNAS, 2009,106,1620-1625. PMCID:PMC2635792
   d. McKay, B.M., Oh, M.M. and Disterhoft, J.F. Learning increases intrinsic excitability of hippocampal interneurons. J. Neuroscience, 2013, 33, 5499-5506. PMCID: PMC3678545

3. Aging associated cognitive impairments are associated with altered intrinsic excitability in neurons. My laboratory group has extended our examination of intrinsic excitability changes that occur during

learning in young adult animals into aging animals. We have shown that cognitive deficits in aging are associated with reduced intrinsic excitability of CA1 hippocampal neurons at baseline and the inability of hippocampal neurons to appropriately reduce the size of outward potassium currents during learning. Conversely, we have recently shown that CA3 pyramidal neurons show increased excitability with aging. We are continuing to explore the neuronal mechanisms that contribute to these functional alterations and reduced ability for learning.

a. Moyer, J.R., Jr., Power, J.M., Thompson, L.T. and Disterhoft, J.F. Increased excitability of aged rabbit CA1 neurons after trace eyeblink conditioning. Journal of Neuroscience, 2000, 20, 5476-5482. PMID:10884331
b. Disterhoft, J.F. and Oh, M.M. Learning, Aging, and Intrinsic Neuronal Plasticity. Trends in Neurosciences, 2006, 29, 587-599. PMID:17517042
c. Oh, M.M., Oliveira, F., Waters, J. and Disterhoft, J.F. Altered calcium metabolism in aging CA1 hippocampal pyramidal neurons. J. Neuroscience, 2013, 33, 7905-7911. PMCID: PMC3679661.
d. Simkin, D., Hattori, S., Ybarra, N., Musial, T.F., Buss, E.W., Richter, H., Oh, M.M., Nicholson, D.A., Disterhoft, J.F. Aging-related hyperexcitability in CA3 pyramidal neurons is mediated by enhanced A-type K+ channel function and expression. Journal of Neuroscience, 2015, 35, 13206-13218. PMCID: In Process

4. Enhancement of learning in animal models. My colleagues and I have done extensive experiments to determine pharmacological compounds that enhance learning in young and especially in aging animals. These experiments have generally used drugs that we have shown to enhance intrinsic excitability and thus enhance the ability of young and aging animals to learn and remember.
   a. Deyo, R.A., Straube, K. and Disterhoft, J.F. Nimodipine facilitates associative learning in aging rabbits. Science, 1989, 243, 809-811.
   b. Thompson, L.T., Moskal, J.R. and Disterhoft, J.F. Hippocampus-dependent learning facilitated by a monoclonal antibody or D-cycloserine. Nature, 1992, 359, 638-641.
   c. Oh, M.M., Power, J.M., Thompson, L.T. and Disterhoft, J.F. Metrifonate increases neuronal excitability in CA1 pyramidal neurons from both young and aging rabbit hippocampus. Journal of Neuroscience, 1999, 19, 1814-1823.
   d. Weiss, C., Preston, A.R., Oh, M.M., Schwarz, R.D., Welty, D. and Disterhoft, J.F. The M1 muscarinic agonist CI-1017 facilitates trace eyeblink conditioning in aging rabbits and increases the excitability of CA1 pyramidal neurons. Journal of Neuroscience, 2000, 20, 783-790.

5. Temporal learning depends upon forebrain structures, including the hippocampus, in humans and animals. Our laboratory has demonstrated with lesion-behavioral techniques that trace conditioning, a temporal learning task in which the conditioned stimulus is separated from the unconditioned stimulus by a time interval, depends upon the hippocampus and, subsequently, other forebrain regions for successful acquisition. We have translated these animal lesion and behavioral experiments to humans, and have demonstrated with imaging and behavioral approaches that temporal learning tasks depend upon the hippocampus in humans as well as in experimental animals.
   a. Moyer, J.R., Deyo, R.A. and Disterhoft, J.F. Hippocampal lesions impair trace eye-blink conditioning in rabbits. Behavioral Neuroscience, 1990, 104, 243-252. PMID:2346619
   b. Disterhoft, J.F., Carrillo, M.C., Fortier, C.B., Gabrieli, J.D.E., Knuttinen, M-G., McGlinchey-Berroth, R., Preston, A. and Weiss, C. Impact of temporal lobe amnesia, aging and awareness on human eyeblink conditioning. In, Neuropsychology of Memory (3rd Edition) edited by L. Squire and D. Schacter. New York: Guilford, 2002, 97-113.
   c. Cheng, D.T., Disterhoft, J.F., Power, J.M., Ellis, D.A., Desmond, J.E. Neural substrates underlying human delay and trace eyeblink conditioning. Proceedings of the National Academy of Sciences (USA), 2008, 105, 8108-8113. PMCID:PMC2430367
   d. Weiss, C. and Disterhoft, J.F. The impact of hippocampal lesions on trace eyeblink conditioning and forebrain-cerebellar interactions. Behavioral Neuroscience, 2015, 129, 512-522.

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/myncbi/collections/bibliography/40445148/

D. Research Support

Active

R37 AG008796 (MERIT Award) (Disterhoft) 03/01/1990 – 01/31/2020
NIH/NIA
Slow Outward Currents and Learning in Aging Hippocampus
The goals of this project are to investigate hippocampal mechanisms of learning, and of age-related deficits in learning with a combination of behavioral and biophysical techniques.
Role: Principal Investigator

RF1 AG017139-15 (Disterhoft, J.F. & Nicholson, D.A, MPI) 05/15/2016 - 4/30/21
NIH/NIA
Synaptic Substrates of Age-Dependent Memory Deficits
The goals of this project are to continue investigating the synaptic mechanisms of age-related deficits in learning with a combination of unbiased quantitative electron microscopic, behavioral and electrophysiological techniques applied to the CA1 region of the hippocampus.
Role: Principal Investigator

P30 AG013854 (Mesulam) 07/01/2016-06/30/2021
NIH/NIA (this program will be renewed from 07/01/2016-06/30/2016 awaiting NOGA)
Alzheimer's Disease Core Center
The Alzheimer's Disease Core Center serves as the focus of clinical and basic research into Alzheimer's Disease, Primary Progressive Aphasia and Frontal Lobe Temporal Dementia at Feinberg School of Medicine. In addition, the ADCC serves to educate the public regarding these neurodegenerative diseases of aging. Dr. Disterhoft serves as the Associate Director, Chair of the Pilot Grants Program and a member of the ADCC Steering Committee.

T32 AG20506-11-15 (Disterhoft) 05/01/2002-04/30/2017
NIH/NIA
Mechanisms of Aging and Dementia Training Program
A postdoctoral and predoctoral training program from a multi-disciplinary group of investigators whose work focuses on the mechanisms of aging and dementia, in particular Alzheimer's Disease.
Role: Principal Investigator

5 R01 DC011855-03 (Richter) 03/01/2012 – 02/28/2017
NIH/NIDCD
Understanding the Benefits of Infrared Nerve Stimulators for Neural Interfaces
The long-term objective of the proposed experiments is to design and build safe optical neural prostheses with significantly improved spatial selectivity, here increased spatial selectivity for spiral ganglion cell stimulation. As a consequence, it is expected that cochlear implants will provide significantly more independent perceptual channels to the implant user that can be used in parallel and thus improve speech recognition in noisy listening environments and provide music appreciation.
Role: Co-Investigator

R01MH103211 (Hansel) 04/01/2014 – 03/31/2017
NINDS/University of Chicago
Intrinsic Plasticity and Information Storage in Cerebellar Purkinje Cells
We will do behavioral (delay and trace eyeblink conditioning) on transgenic mice that Dr. Hansel will develop and supply to us. We will then transport the trained mice to the University of Chicago for biophysical and cellular imaging experiments to be carried out in Dr. Hansel's laboratory.
Role: Subaward PI

RF1 AG017139-15 (Disterhoft, J.F. & Nicholson, D.A, MPT) 05/15/2016 - 4/30/21
NIH/NIA
Synaptic Substrates of Age-Dependent Memory Deficits

Administrative Supplement for additional equipment 07/01/2016-04/30/2017 $76,450

R37 AG008796 (MERIT Award) (Disterhoft, J.F., PI) 03/01/1990 – 01/31/2020
NIH/NIA
Slow Outward Currents and Learning in Aging Hippocampus

Administrative Supplement to Explore Lateral Entorhinal Cortex as a Region Important for Alzheimer's Disease 09/01/2016-08/31/2017 $156,443 Total Costs

F31 AG055331-01 (Lin, C. PI; Disterhoft, J.F., Sponsor) 09/01/2016 – 08/31/2019

Pending

R25GM121231 1-5 (Disterhoft, P.I.) 07/01/17-06/30/22 (Impact Score of 20, likely to be funded)
Northwestern University Interdepartmental Neuroscience Postbaccalaureate Research Education Program

The advancement of biomedical research critically relies on training the next generation of scientists. The goal of the Northwestern University Interdepartmental Neuroscience Postbaccalaureate Research Education Program is to recruit trainees from diverse, underrepresented groups and prepare them for a successful transition into graduate school and to help guarantee their success in obtaining the PhD degree. The program features core research, communication skills, and coursework components, but also provides access to a broad range of opportunities within the neurosciences PhD and affiliated institutional training (T32) programs, allowing for individualized experiences that will foster scientific and professional growth.

T32 AG020506 16-20 (Disterhoft, J.F., PI) 05/01/17 – 04/30/22
NIH/NIA
Predoctoral and Postdoctoral Training in Mechanisms of Aging and Dementia.

Goal: Funding for a training program for predoctoral and postdoctoral scholars mentored by a multidisciplinary group of investigators whose work focuses on the mechanisms of aging and dementia, including Alzheimer's Disease, Parkinson's Disease and Amyotrophic Lateral Sclerosis, with approaches spanning molecular, cellular, systems, behavioral, neuropsychological and clinical neuroscience.

1R01AG050492-01 (Klein, PI; MPI, Disterhoft, Co-PI) 4/1/15 – 3/31/20 (not funded, will be resubmitted)
NIH/NIA
Sporadic Alzheimer's Disease modeled with diabetes and high cholesterol in rabbit