SPONSORING SECTION:
Binocular Vision, Perception, & Pediatric Optometry

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SPEAKERS
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Benjamin Thompson, PhD  
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Tara Alvarez, PhD  
New Jersey Institute of Technology

MODERATOR
Tawna L. Roberts, OD, MS, FAAO  
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OVERVIEW:
Neural plasticity refers to the reorganization of neural pathways and synapses in the brain as the result of perceptual and motor learning experiences. Because most synaptic circuitry development is known to occur in the first few years of life, it was assumed that neural synapses were unalterable after his time – hence, the clinical dogma that vision anomalies such as amblyopia and oculomotor disorders were untreatable beyond early childhood. However, in recent years there have been major scientific breakthroughs to support clinical observations that neural plasticity continues beyond early childhood and even into adulthood. Using a cells to systems approach in this symposium, three leading scientists will present their cutting-edge research pertaining to neural plasticity of the visual system.
1. Introduction: Visual Neural Plasticity and its Clinical Importance
   (5 minutes)
   Tawna L. Roberts, OD, MS, FAAO
   University of Houston College of Optometry

2. Visual Plasticity beyond the Synapse: Activity-Dependent White Matter Changes
   (25 minutes)
   Dr. R. Douglas Fields, PhD
   Chief, Nervous System Development & Plasticity Section
   National Institutes of Health

   The cellular basis of learning, cognition and plasticity is traditionally considered the synapse, but new research is expanding, thinking beyond gray matter to consider white matter function in information processing and plasticity. Human brain imaging shows differences in white matter in association with environmental experience and learning. Our research has identified several cellular and molecular mechanisms regulating myelination by action potential firing in axons. Since myelination can increase conduction velocity by at least 50 times, activity-dependent regulation of myelination could modify the speed and synchrony of impulse conduction through neural circuits to improve performance of complex cognitive functions. Our recent findings in the visual system show that myelination and structure of the nod of Ranvier in optic nerve axons are dynamically regulated, with effects of visual acuity.

3. Influence of Perceptual Learning on Synaptic Changes in Mature Visual Cortex
   (25 minutes)
   Benjamin Thompson, PhD
   Associate Professor, School of Optometry and Vision Science, Univ. of Waterloo
   Associate Professor, Department of Optometry and Vision Science, The Univ. of Auckland

   Amblyopia has traditionally been thought of as an intractable problem in adulthood due to a lack of plasticity within the mature visual cortex. However, there is now growing evidence from studies using techniques such as binocular perceptual learning and non-invasive brain stimulation that plasticity can occur within the adult visual cortex to the extent that monocular and binocular visual function can be recovered in patients with amblyopia.

4. Neural Control Mechanisms of Vision Therapy in Convergence Insufficiency
   (25 minutes)
   Tara Alvarez, PhD
   Director of Vision and Neural Engineering Laboratory
   Professor, Biomedical Engineering New Jersey Institute Technology
   Associate Professor, Salus University

   Convergence insufficiency (CI) is a prevalent binocular vision disorder with symptoms that include double/blurred vision, eyestrain, and headaches when engaged in reading
or other near work that negatively impacts activities of daily living. CI is present in 4% of the population where approximately 27% of CI patients do not improve even with validated therapy. My talk will discuss data investigating two potential mechanisms causing CI, which may be improved via validated therapy by quantifying phoria adaptation, neural substrates using fMRI, and eye movement recordings.

5. Panel discussion and questions from the audience
(20 minutes)

Speaker Biographies or Biosketch

Douglas Fields, Ph.D.

R. Douglas Fields, Ph.D., has conducted research in the field of nervous system plasticity at the National Institutes of Health, NICHD since 1987, where he is currently Chief of the Nervous System Development and Plasticity Section. He received the PhD degree from UC San Diego and conducted postdoctoral research at Stanford University, Yale University, and the NIH on synaptic plasticity, myelination, and axon conduction using electron microscopy, live-cell imaging, and electrophysiology. Dr. Fields' long-standing interest is in how environmental experience and functional activity in the nervous system affect the developing structure and function of the nervous system. His current research emphasis is on neuron-glial interactions and in particular on regulation of myelination by impulse activity. In addition, his research explores synaptic plasticity (LTP, LTD, and homeostatic plasticity), and regulation of gene expression by specific patterns of action potentials. He was founding editor of the journal Neuron Glia Biology from 2004-2011, and he serves on the editorial board of Glia and several other journals. He also writes about neuroscience for Scientific American and other popular science magazines, and he is author of a recent book about glia written for the general audience, The Other Brain.
A. Personal Statement

I have been centrally involved in the development and initial testing of the binocular approach to treating amblyopia that forms the basis of this funding proposal. I have also collaborated closely and productively with the research team involved in this proposal and I have visited Zhongshan Ophthalmic Centre on multiple occasions. In related work, I was the first to show that non-invasive brain stimulation techniques could be applied to patients with amblyopia. This work not only opened up a new potential pathway for amblyopia therapy but also supported the hypothesis that suppressive interactions within the visual system play a key role in the vision loss experienced by individuals with amblyopia. It is these suppressive interactions that are targeted by the binocular therapy that forms the basis of the proposed study. I am currently leading a large, multicenter randomized clinical trial comparing binocular amblyopia treatment to a placebo in older children and adults. This trial will directly complement the proposed trial which is designed to compare binocular treatment to monocular treatment in children. Together, these two trials have the potential to provide the high quality evidence base required for the widespread international adoption of the binocular amblyopia treatment.

B. Positions and Honors

List in chronological order previous positions, concluding with the present position. List any honors. Include present membership on any Federal Government public advisory committee.

2002-2004  Queens University (Canada, UK Study Centre) – Lecturer
2004-2006  University of California Los Angeles (UCLA) (USA) - Postdoctoral Scholar
2006-2008  McGill University (Canada) – Postdoctoral Scholar
2008-2009  Lecturer, Department of Optometry and Vision Science, University of Auckland
2012-2013  Visiting Lecturer, Hong Kong Polytechnic University
2014- Associate Professor, Department of Optometry and Vision Science, University of Auckland
2014- Associate Professor, School of Optometry and Vision Science, University of Waterloo

Other Experience and Professional Memberships
- Health Research Council of New Zealand Grant Assessment Committee Member
- Elected member of the Program Committee for the Association for Research in Vision and Ophthalmology (ARVO) annual meeting.
- Steering Committee member Children with Hypoglycemia and their Later Development Study

Other Distinctions & Awards
- 2000 Medical Research Council Doctoral Studentship, UK.
- 2007 McGill Ophthalmology Department prize for best basic research.
- 2008 McGill Ophthalmology Department prize for best basic research.
- 2009 Marsden Fund (Royal Society of New Zealand) Fast Start Award
- 2009 Health Research Council of New Zealand Emerging Researcher Award
- 2010 Lloyd Morgan Lecturer, Department of Ophthalmology, Hospital for Sick Children/University of Toronto, Toronto, Canada
- 2011 University of Auckland Early Career Research Excellence Award
- 2012 Appointment to the Research Advisory Board of the Centre for Brain Research University of Auckland

C. Selected Peer-reviewed Publications

References relevant to the new treatment

Relevant references with the applicant

D. Research Support
List both selected ongoing and completed research projects for the past three years (Federal or non-Federally-supported). Begin with the projects that are most relevant to the research proposed in the application. Briefly indicate the overall goals of the projects and responsibilities of the key person identified on the Biographical Sketch. Do not include number of person months or direct costs.

Principle investigator: Health Research Council of New Zealand. “A randomized clinical trial of a new binocular treatment for amblyopia” 2013. The goal of this project is conduct a clinical trial comparing a new binocular treatment for amblyopia to a placebo in older children and adults. I have overall responsibility for all aspects of this multi-site, international clinical trial.
Principle investigator: University of Auckland Faculty Development Research Fund “A new portable, video-game based approach to recovering vision in patients with amblyopia”. 2012. This funding provides support for a postdoctoral fellow to support the set up the clinical trial described above.
Principle investigator: University of Auckland Early Career Research Excellence Award. “Enhancing brain plasticity to treat amblyopia”. 2011. The goal of this project was to assess the use of a binocular amvlyopia treatment in a home-based setting. I have overall responsibility for all aspects of the project.
Principle investigator: Health Research Council of New Zealand Emerging Researcher Grant. “Promoting neural plasticity to recover visual function in amblyopia”. 2010. The goal of this project was to investigate the potential use of non-invasive brain stimulation in the treatment of amblyopia. I had overall responsibility for all aspects of the project.
Principle Investigator: Marsden Fund Fast Start Award. “Teaching an old brain new tricks”. 2010. The goal of this project was to assess the use of selective reuptake inhibitors to boost plasticity in the normal and amblyopic visual cortex. I had overall responsibility for all aspects of the project.
Principle investigator: Neurological Foundation. “Evaluating alterations in Striate and Extrastriate Visual Brain Areas Using Structural and Functional Magnetic Resonance Imaging in Patients with Visual Loss”. 2010. The goal of this project is to use the visual
system as a model for exploring the effects of neurodegeneration, ischemia and compression on downstream cortical function. I have overall responsibility for all aspects of the project with a particular emphasis on the neuroimaging components of the work.

Principle investigator: Auckland UniServices gate Funding. Optokinetic nystagmus in young children”. 2012. The goal of this project is to produce a commercializable, fully automated device that can use optokinetic nystagmus to assess visual function in young children. I lead the vision science aspects of this project in collaboration with engineers at the University of Auckland.

Associate investigator: National Institutes of Health RO1. “Children with Hypoglycemia and their Later Development (The CHYLD Study).” The goal of this study is to assess the effect of neonatal hypoglycemia on later development. I lead the vision assessment components of this study.

Associate investigator: University of Auckland Cross Faculty Research Initiatives Fund. “The Auckland Face Simulator: A new tool for research in face perception”. The goal of this study is to use new advances in bioengineering to develop a face simulator for clinical and psychophysics research. I lead the vision science aspects of this study in collaboration with bioengineers and psychologists at the University of Auckland.
A. Personal Statement:

In the past 19 years, I have acquired the skill set to quantitatively measure eye movements with functional MRI in subjects with normal binocular vision and those with convergence insufficiency (CI). I have 45 peer-reviewed publications studying eye movements where 43 of those studies were on vergence eye movements. I recently completed a research project funded by an NSF CAREER award to incorporate fMRI research with my oculomotor expertise. This funding led to the first publication in 2010, to study vergence using fMRI in humans in collaboration with Dr. Biswal (co-investigator on this proposal). Thus far, my NSF CAREER award has lead to 25 peer reviewed publications. Six of those publications utilized fMRI. My CAREER award also funded the only publication to integrate fMRI with vergence eye movements and clinical measures studying patients with CI through office-based vergence and accommodative therapy. The results show promise in the small group we studied. This proposal would continue and extend those studies to quantitatively investigate whether CI is the result of a decreased ability to adapt vergence in near or far space or the decreased ability to reduce retinal disparity error.

Essilor international is currently and has a history of funding my research since 2003. The goal of the three Essilor grants I have received is to understand why some people are more likely to adapt to progressive additive lenses compared to others. This is a motor learning question which is synergistic but non-overlapping with the research of helping patients with convergence insufficiency reduce their visual symptoms. My current Essilor grant has a required enrollment of 80 subjects within a longitudinal design and data have been successfully analyzed on 61 subjects to date. The second Essilor grant was a successful study where we studied 65 subjects longitudinally (subject recruitment requirement was 60). My first grant from Essilor was a single session design where we successfully completed the data analysis on 61 subjects (subject recruitment requirement was 60).

Currently, I am funded through the NSF Major Research Instrumentation (MRI) grant. This grant purchased the Power Refractor 3 from PlusOptix and a Grand Seiko
Wide Open Field to measure accommodation dynamically and statically respectively. In addition, 2 papers have been accepted and three are in preparation funded from the PI's NSF MRI grant.

This present NIH proposal would give me the opportunity to learn from experienced NIH researchers (Drs. Biswal, Schor, and Scheiman) who have a history of successful R01 grants in imaging and clinical trials studying CI. As PI of this proposal, I am committed to ensure all aspects of the research plan are pursued and successfully completed. I have assembled a team of experts who will make progress in this area and develop innovative solutions to any challenges encountered. Quarterly meetings will be held among the researchers to discuss progress, data, interpretation of results and solutions to any difficulties. Weekly meetings will be held between with the PI and postdoctoral fellows (Drs. Kim and Taylor) to discuss progress and next steps. I currently have frequent meetings with Drs. Scheiman (clinical lead), Biswal (imaging lead), Bhavsur and Vicci (optometrists), and Dhar (statistician) to discuss this project. We have also published a collective paper. Dr. Schor and I have been collaborating since January 2013 and I recently visited him in Berkeley to discuss this proposal.

B. Positions and Honors. List in chronological order previous positions, concluding with your present position. List any honors. Include present membership on any Federal Government public advisory committee

Positions and Employment
Engineering Intern, Bell Laboratories, Holmdel, NJ, Summers 1990-1995
Teaching Assistant, Rutgers University, Piscataway, NJ, 1993
Graduate Assistant, Rutgers University, Piscataway, NJ, 1995 to 1998
Adjunct Professor, Fairleigh Dickinson University, Teaneck, NJ, Fall 2000
Member of Technical Staff, Bell Laboratories, Whippany, NJ, Aug 1998 till Aug 2001
Assistant Professor, New Jersey Institute of Technology, Newark, NJ, Aug 2001 till Jun 2006
Associate Professor, New Jersey Institute of Technology, Newark, NJ, Jun 2006 till 2013
Associate Professor, Salus University, Philadelphia, PA 2012 to present
Professor, New Jersey Institute of Technology Jun 2013 to present

Awards and Professional Activities
Invited Guest Editor with Dr. Bucci for Special Issue on Binocular Eye Movements for the Journal of Ophthalmology 2013
Symposium on Binocular Coordination within European Conference Eye Movement, Lund Sweden 2013
Editorial Board of Journal of Eye Movement Research January 2012 to present
Albert Dorman Outstanding Teaching Award 2010
Outstanding Women Scientist of NJ 2008
NORA founding members award for science 2008
Envision Conference functional MRI course (2 hours) 2008
Reviewer for Ophthalmology and Physiologic Optics 2005 to present; Experimental Brain Research 2008 to present; PLoS One 2010 to present. Brain Connectivity 2011 to present; Psychometrika 2011 to present; Journal of Eye
Movement Research 2009 to present, Vision Research 2012 to present; Brain 2011
NSF reviewer 2006 to present
CAREER Award from National Science Foundation 2005
Member of NJIT Institution Review Board 2005 to present
Sigma Xi: Research Honor Society 2002
Tau Beta Pi: Engineering Honor Society 1993
Eta Kappa Nu: EE Honor Society Golden Key Honor Society 1993
Shield and Key Award 1993
Garden State Scholarship 1990
President’s Medal 1990

C. **Selected peer-reviewed publications** (reverse chronological since 1998, of total 45 peer-reviewed papers published / in-press / accepted).

3. Alkan, Y., Biswal, B. B. **Alvarez T. L.** *(2011)* Differentiation between Vergence and Saccadic Functional Activity within the Human Frontal Eye Fields and Midbrain Revealed through fMRI PLoS One. 6(11), 25866

**Ten Additional Recent Publications of Importance to the Field (in chronological order)**

Changes in Phoria and Convergence Peak Velocity. PLoS One 6(6), e20883.

D. Research Support. List selected ongoing or completed (during the last three years) research projects (federal and non-federal support). Begin with the projects that are most relevant to the research proposed in this application. Briefly indicate the overall goals of the projects and your role (e.g. PI, Co-Investigator, Consultant) in the research project.

**ONGOING RESEARCH SUPPORT**

**T.L. Alvarez: Principal Investigator**

**National Institute of Health National Eye Institute** R01 EY02326
Functional Mechanism of Neural Control in Convergence Insufficiency
The goal of this grant is to study two potential mechanisms that may be stimulated the sustained reduction of visual symptoms from those with convergence insufficiency.

**T. L. Alvarez: Principal Investigator**

**National Science Foundation** CBET1228254
MRI: Development Neural and Visual Assessment Equipment
The goal of this grant is to develop new instrumentation to study vision function by integrating instruments that measure accommodation, visually evoked potential system with fMRI compatible eye movement system.

**T. L. Alvarez: Principal Investigator**

**Essilor International, S. A.**
Clinical Correlate to Predict Progressive Lens Acceptability
The objective of this study is to evaluate phoria adaptation and vergence facility in incipient presbyopes before and after one month of wearing progressive additive lenses in 80 subjects. Data collection is complete. Currently, working on data analysis and two manuscripts are in preparation.

**COMPLETED**

**CAREER BES-0447713 T.L. Alvarez:** Principal Investigator 2005-2011

**National Science Foundation**
Mapping the Mind in Search of Oculomotor Learning Strategies
The objective of this study was to understand oculomotor learning and adaptation in healthy controls using eye movements and functional MRI.
The Vergence Component: An Indicator for Adaptation in Progressive Lens Wear?
This proposal successfully enrolled 65 subjects in a longitudinal study to understanding why some individuals can easily adapt to wearing progressive lenses where other cannot.

CBET 0941229 T.L. Alvarez: Principal Investigator
National Science Foundation
Graduate Research Supplement for Women or Minority Students
Goal: Increase participation of underrepresented groups in engineering

T.L. Alvarez: Principal Investigator
National Science Foundation Advance
Development of a flexible visual stimulator for fMRI and home training
Goal: Develop an instrument for visual stimulation during fMRI experiments that is more flexible than the current instrument which was successful developed and tested

CBET 0537072 T.L. Alvarez: Principal Investigator
National Science Foundation
Graduate Research Supplement for Women or Minority Students
Goal: Increase participation of underrepresented groups in engineering

T. L. Alvarez: Principal Investigator
Essilor International S.A.
The Impact of Vergence Adaptive Process of Progressive Lens
This proposal successfully enrolled 30 presbyope and 31 nonpresbyopes to study vergence adaptation to progressive additive lenses, proposal was to study 60 subjects total.

T. L. Alvarez: Principal Investigator
Department of Defense and VA Medical Center
Effects of Light Stimulation
This study successfully completed the study of 30 binocularly normal controls to understand how attention influences saccades.