Visual Neuroscience: Modern Challenges and Australian Pioneers

27-28 June 2013

New Law School Lecture Theatre 101
University of Sydney

Supported by the ARC Centre of Excellence in Vision Science
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DIRECTOR’S WELCOME

Dear Colleagues,

This year, our ASM has a personal aspect, as well as a theme. The theme is visual neuroscience, with an emphasis on the areas of visual neuroscience pioneered by Professor Peter Bishop, during his years (1952-1967) in the Department of Physiology, at this University, and later (1967-83) at the Australian National University. There will be tributes to Professor Bishop, and to the many colleagues of his time, at the beginning and end of the Program.

The greater part of the program, however, is modern visual neuroscience, the latest findings on retinal organisation and stability, on thalamic and cortical processing, on optics, and parallel processing, from scientists active in these fields. Young scientists will present volunteer talks and posters, on their work in related areas. Acknowledgement of the past, but an emphasis on the present and future. I think ‘Prof’ would have approved.

A special feature of the meeting will be the attendance of Guests of Honour, men and women who worked with Bishop, going back to the middle of the last century. Theirs are the minds of the generation which rebuilt this field of science, after the exhaustion of world war. Also, members of Professor Bishop’s family will attend, for parts of the Meeting. It will be a privilege to have them with us.

And we will find a moment to acknowledge those of Professor Bishop’s generation who could not join us.

The site of the Meeting, in the Law School Annexe, is across the road from the Anderson Stuart Building. It is an appropriate environs, for that Building was (and remains) the home of the Department of Physiology, where Bishop built the unique laboratories, in which the foundations of visual neuroscience, in Australia and beyond, were laid.

For this Meeting, warmest thanks go to Professors Bogdan Dreher and Paul Martin, for their help in the organisation of the Program, and to the Institute's COO, Charean Adams who, with the Bosch Facility Officers and supporting staff Wannit Tongkao-on and Cindy Guy, has dealt with all the aspects of conference organization and planning with a professionalism that makes itself invisible. Important thanks also to the ACEVS, the ARC Centre of Excellence in Vision Science, for financial support.

Science is an intensely human endeavour. It involves ideas, and data, evidence and disproof. But it also involves people – their enthusiasm, judgment, commitment, generosity and collegiality. This Meeting celebrates both science and the people who laid the foundations of the field in which so many of us work.

Jonathan Stone
Executive Director
Peter Orlebar Bishop

Noel Thurgate, 1988

This portrait hangs in the Anderson Stuart Building, University of Sydney
FOREWORD

We take this opportunity to commemorate and celebrate the life and scientific contributions of Professor Peter Orlebar Bishop, a distinguished visual physiologist, researcher and teacher.

Nearly three-quarters of a century ago Peter graduated in Medicine at Sydney University. During World War II he served as a Surgeon Lieutenant in the Royal Australian Navy. After the War, Peter returned briefly to his alma mater and in 1946 obtained a Fellowship of the Sydney University Postgraduate Committee. Together with his young family (wife Hilare and two young daughters) he travelled to Oxford. Later on, he moved to the University College, London where he learned electronics from scratch and built a superb quality high-gain DC amplifier.

In 1950, Peter joined the Department of Surgery and the Department of Physiology of the Sydney University. Soon after, he took on the supervision of several BSc (Med) students, with whom he started his truly novel and insightful research on the mammalian visual pathway. In 1954, Peter was appointed a Professor and a Head of the Department of Physiology. His substantial teaching workload included designing, developing and delivering a daunting number of lectures and practical classes. Peter set about building a strong and effective research and teaching Department. From the early days he was supported by a number of skilled and talented technical staff. Their contributions were substantial; they often designed, developed, built, supported and maintained high quality mechanical and electronic equipment in the days before commercial “off the shelf” resources became a reality. Peter’s research, conducted with several members of staff and a number of students, concentrated on the mechanisms of transmission of information from retina through the dorsal lateral geniculate nucleus to the primary visual cortex, the optics of mammalian eye and mechanisms underlying binocular stereoscopic vision. Most importantly, Peter encouraged, stimulated and supported students in medical and science programs to undertake serious research. Indeed, many of the students inspired by Peter’s example went on to develop their own internationally recognised programs.

In 1967 Peter was elected a Fellow of the Australian Academy of Science. The same year, he was appointed Professor of Physiology at the John Curtin School of Medical Research at the Australian National University. In Canberra, together with a number of Australian and young researchers from overseas, Peter continued his active world-class research on the mammalian visual system, especially of the cortical mechanisms underlying binocular stereoscopic vision. Again, many of Peter’s Canberran collaborators developed their own eminent research programs. In 1993, Peter Bishop (together with two other prominent sensory neuroscientists - Horace Barlow and Vernon Mountcastle) was awarded the prestigious Australia Prize, now known as the Prime Minister’s Prize for Science.

Peter passed away on June 3rd 2012. To celebrate his lifetime work, his former students and colleagues as well as a number of young researchers (many of them scientific grandchildren of Peter) have developed and contributed to a set of presentations.

The presentations will describe novel and stimulating research on diverse aspects of the visual sciences. They include discussion of parallel pathways in primate retina, colour vision in dichromatic mammals, the mechanisms underlying inhibition in the dorsal visual thalamus, roles of feedforward and intracortical mechanisms in establishment of orientation selectivity in mammalian visual cortex; corticothalamic feedback influencing the parallel information stream, transmission of sensory information from the dorsal thalamus to cortex; analyses of responses of single neurones in primary
visual cortex (area V1) and the middle temporal area (area MT).

Other aspects of modern visual sciences to be discussed during the meeting include new technologies such as adaptive optics; the roles of optics and physiological stress in the development of myopia; molecular factors that define the avascular area in primate retina; the significance of purines in degenerative conditions of mammalian retina; mechanisms underlying perceptual suppression in strabismus; characterization of neural networks underlying the extraction of stereoscopic depth in human and non-human primates; darkness as a potential therapy for amblyopia and for retinopathy of prematurity. Interestingly, non-vertebrates such as fiddler crabs make very effective and fast decision based on the information provided by their supposedly relatively ‘low power’ visual system.

Although eyes are constantly moving, the human eye is sensitive to actual motion of visual objects, detecting motion smaller than a single cone and optimising spatial vision. It appears that the subcortical/cortical interactions play an important role in the establishment of optokinetic reflex and eye-hand coordination during the target reaching in primates.

A new study of influences of the phases of the moon on visual acuity in humans concludes that acuity is higher at full moon. Interestingly, the arrival of boab trees in the Kimberley region of Western Australia have been dated at 70,000 years, that is, the time when the modern humans started to migrate from Africa. It is argued that the arrival of boabs coincided with arrival of humans who developed a distinct Bradshaw Rock Art culture characterizing the Kimberley region.

In summary, Peter Bishop’s own work has been characterised not only by the great methodological precision but also by the great intellectual rigor and imagination. Indeed Peter provided an intellectual environment which supported, encouraged and stimulated his students and colleagues. Thus, even after his death Peter Bishop remains a real guru of the Australian visual neuroscience.

Ann Jervie Sefton
Guests of Honour

Associate Professor Vladimir Balcar
Dr Brian Cleland
Dr Lynne Cottee
Professor David Crewther
Dr Alan Freeman
Professor Yutaka Fukuda
Ms Eva Henry
Professor Graham Johnston
Professor Douglas Joshua
Professor James Lance
Professor William Levick
Dr Sally McFadden
Dr Jerry Nelson
Professor Sandra Rees
Dr Ken Sanderson
Professor Ann Sefton
Mr Robert Tupper
Professor Mathew Vadas
PROGRAM 27th June

REGISTRATION  8.00am – 8.45am

WELCOME

8.50  Professor Jonathan Stone
      Director, Bosch Institute
      Professor Paul R. Martin
      ARC Centre of Excellence in Vision Science

SESSION 1  9.00am – 11.00am

TRIBUTE SESSION
Chair: Professor William Levick

9.00  Emeritus Professor David I. Vaney
      Queensland Brain Institute, University of Queensland, Australia
      Peter Bishop: His Research and His Scientific Legacy

RETINA, THALAMUS, PARALLEL PROCESSING
Chair: Professor James Lance

9.30  Associate Professor Ulrike Grünert
      Save Sight Institute, University of Sydney, Australia
      Parallel Pathways in Primate Retina

10.00  Associate Professor Péter Buzás
       Institute of Physiology, Medical School, University of Pécs, Hungary
       Colour Cells of the Cat LGN

10.30  Professor Diego Contreras
       Department of Neuroscience, University of Pennsylvania School of Medicine, Philadelphia, United States of America
       Inhibitory Mechanisms in the Visual Thalamus

11.00 – 11.30 am       Morning Tea and Interactions with the Exhibitors

SESSION 2  11.30 am – 1.30 pm  ...sponsored by PATHTECH

CORTICAL PROCESSING

Co-Chairs: Dr Ken Sanderson/Professor Douglas Joshua

11.30  Professor Martin Usrey
       University of California, Davis, United States of America
       Parallel Processing in the Corticogeniculate Pathway of the Macaque Monkey

12.00.  Professor Trichur Vidyasagar
        Department of Optometry & Vision Sciences, University of Melbourne, Australia
        Integration of Feedforward and Intracortical Mechanisms in Visual Cortical Function
12.30 Professor Michael Ibbotson  
National Vision Research Institute, Australian College of Optometry and Department of Optometry and Vision Sciences, University of Melbourne, Australia  
Finding the Simple Cell Within

1.00 Dr Samuel Solomon  
Cognitive, Perceptual and Brain Sciences, University College London; Discipline of Physiology, University of Sydney, Australia  
Population Signals for Motion Vision

1.30 - 2.30 pm Lunch and Posters

SESSION 3  2.30pm – 4.00 pm

PHYSIOLOGICAL OPTICS AND RETINAL ORGANISATION  
Co Chairs: Dr Alan Freeman, Dr Sally McFadden

2.30 Professor Melanie Campbell  
Department of Physics and Astronomy and School of Optometry and Vision Science, University of Waterloo, Canada  
The Importance of the Eye's Optics in Myopia, Ocular Diagnosis and Therapy and as a Window on the Brain

3.00 Associate Professor Joseph Carroll  
Department of Ophthalmology, Medical College of Wisconsin, United States of America  
Imaging Photoreceptor Disruption in the Human Retina

3.30 Associate Professor Jan Hemmi  
School of Animal Biology & UWA Oceans Institute, University of Western Australia, Australia  
Topography of Vision in Fiddler Crabs – Sampling Array and Photoreceptor Sensitivity

4.00 – 4.30 pm Afternoon Tea

SESSION 4  4.30pm - 6.20pm

Co-Chairs: Emeritus Professor Sandra Rees/ Dr Dario A. Protti

YOUNG SCIENTIST ORAL PRESENTATIONS

4.30 Sook Chung  
Department of Clinical Ophthalmology and Eye Health, University of Sydney, Australia  
Microarray Analysis and Glycolytic and mTOR Pathway Profiling of a Conditional, Selective Müller Cell Ablation in a Transgenic Murine Retina

Alice Brandli  
Discipline of Physiology and Bosch Institute, University of Sydney, Australia  
Remote Ischemia Neuroprotection Potential in a Light Damage Model

Terrence Middleton  
Department of Physiology, University of Sydney & Bosch Institute, Australia  
Seeing Smoke: Cannabinoid Modulation of Inputs to Retinal Ganglion Cells
4.57  
Dr Jin Yu Huang  
Discipline of Biomedical Science & Bosch Institute, University of Sydney, Australia  
The Effects of Excitation and Inhibition on the Sharpness of Spatial-Tuning Curves and Response Output of Retinal Ganglion Cells

Dr Kumiko Percival  
Save Sight Institute, University of Sydney & ARC of Excellence in Vision Science, Australia  
Retinal Ganglion Cells Projecting to the Koniocellular Superficial (K1) Layer of the Lateral Geniculate Nucleus in Marmoset Monkey

Dr Aaron Camp  
Sydney Medical School, School of Medical Sciences and Bosch Institute, University of Sydney, Australia  
Noise Normalizes Firing Output of Mouse Lateral Geniculate Nucleus Neurons

5.30  
Dr Kenny Cheong  
Save Sight Institute, University of Sydney & ARC Centre of Excellence in Vision Science, Australia  
Antidromic and Visual Evoked Response Latency in Marmoset Lateral Geniculate Nucleus

Dr Alexander Pietersen  
ARC Centre of Excellence in Vision Science & Save Sight Institute, University of Sydney, Australia  
Relation of Koniocellular Pathway Activity to Low Frequency (Delta) Electroencephalogram Power in Anaesthetised Marmosets

Dr Ryan Maloney  
School of Psychology and ARC Centre of Excellence in Vision Science, University of Sydney, Australia  
Orientation Anisotropies in Human Primary Visual Cortex Depend on Contrast

5.53  
Saman Haghgooie  
Department of Physiology, Monash Vision Group, Monash University, Australia  
Simultaneous Mapping of Receptive Fields and Response Properties of Large Neuronal Populations in Extrastriate Cortex

Dr Tristan Chaplin  
Department of Physiology, Monash University, Australia  
Visual Areas in the Marmoset Cortical Atlas

Dr Hsin-hao Yu  
Physiology, Monash University, Australia  
The Organization of the Middle Temporal area (MT) and the Lateral Geniculate Nucleus (LGN) in Monkeys with Early-Life Lesions of the Primary Visual Cortex
PROGRAM 28 JUNE

SESSION 1  9.00am – 10.30 am

AMBLYOPIA, STRABISMUS AND CORTICAL PROCESSING OF DISPARITY

Co-Chairs: Dr Jerry Nelson/Professor John Morley

9.00  Lifetime Professor Emeritus Donald Mitchell
Department of Psychology & Neuroscience, Dalhousie Univ., Halifax N.S., Canada
Complete Darkness Promotes Fast Recovery from Amblyopia in Kittens

9.30  Professor Jonathan Horton
Program in Neuroscience, UCSF, San Francisco, CA, United States of America
Visual Suppression in Strabismus

10.00  Professor Guy Orban
Department of Neuroscience, University of Parma, Italy
Cortical Processing of Higher-Order Disparity Signals

10.30 – 11.00 am  Morning Tea and Interactions with the Exhibitors

SESSION 2  11.00 am – 1.00 pm

RETINA AND EYE: DEVELOPMENT, DEGENERATION, METABOLISM

Co-Chairs: Dr Brian Cleland/Professor Graham Johnston

11.00  Associate Professor Erica Fletcher
Department of Anatomy and Neuroscience, University of Melbourne, Australia
The Significance of Purines in Degenerative Conditions of the Retina

11.30  Professor Tailoi Chan-Ling
Discipline of Anatomy and Histology, University of Sydney
Dark Rearing (DR) as a means of mimicking ‘Physiological Hypoxia’: A rationale for non-invasive treatment of Retinopathy of Prematurity (ROP)

12.00  Professor Jan Provis
John Curtin School of Medical Research and ANU Medical School, Australian National University
The macula, vascular patterning and the fovea.

12.30  Professor Sheila Crewther
School of Psychological Science, La Trobe University, Melbourne
Myopia- an ion driven response to physiological and oxidative stress

1.00 – 1.45pm  Lunch and Posters

1.45. – 2.00pm  Presentation of Prizes
SESSION 3  2.00pm – 3.30pm

EYE MOVEMENTS AND FORM AND MOTION VISION

Co-Chairs: Associate Professor Vladimir Balcar/Professor David Crewther

2.00  Senior Professor Klaus-Peter Hoffmann
Department of Neuroscience, Ruhr University Bochum, Bochum, Germany
Old Brain – New Brain In(ter) Action

2.30  Dr Austin Roorda
University of California, Berkeley, United States of America
How the Eye Sees a Stable and Moving World

3.00  Professor Colin Clifford
School of Psychology, University of Sydney, Australia
Functional Imaging of Human Visual Cortex

SESSION 4  3.30pm - 4.30pm

NEW HORIZONS

Chair: Professor Mathew Vadas

3.30  Emeritus Professor Liam Burke
Department of Physiology, University of Sydney, Australia
Does the Moon Affect Visual Acuity?

4.00  Emeritus Professor Jack Pettigrew
Queensland Brain Institute, University of Queensland, Australia
The Mystery of Bradshaw Rock Art

4.30 – 5.00 pm  Closing Remarks

Bishop Family

Professor Chris Murphy
Head, School of Medical Sciences

Professor Jonathan Stone
Bosch Institute Executive Director

Mr Paul Fegan
Bosch Institute Advisory Board Chairman

5.00 – 7.00 pm  Poster Session and Social Drinks
including group photograph
Emeritus Professor David Vaney

Peter Bishop: His Research And His Scientific Legacy

David Vaney is an Emeritus Professor at the University of Queensland and is passionately interested in the neuronal architecture of the retina. Born and educated in New Zealand, David moved to Australia in 1975 to undertake a PhD in Bishop’s department at JCSMR, where he was supervised by Austin Hughes and collaborated with Bill Levick. He held postdoctoral fellowships with Heinz Wässle at the Max Planck Institute in Tübingen (1979-1980) and Horace Barlow at the University of Cambridge (1981-1984). Returning to Australia, David held NHMRC research fellowships at the National Vision Research Institute in Melbourne (Director: Abbie Hughes) and, since 1989, at the University of Queensland, where he was a foundation member of the Vision, Touch & Hearing Research Centre (Director: Jack Pettigrew). David was elected President of the Australian Neuroscience Society from 2008-2009 and was awarded the 2010 Boycott Prize for career achievement in retinal neuroscience. He retired from the Queensland Brain Institute in 2010 and is now an undergraduate student of photography at the Queensland College of Art, Griffith University.
TRIBUTE SESSION

Peter Bishop: His Research And His Scientific Legacy

Abstract

David Vaney
University of Queensland

Peter Bishop’s contributions to visual neuroscience were of two kinds. First, Bishop’s own research on the primary visual pathways and the striate cortex in particular – characterised as it was by intellectual rigor and methodological precision – brought important novel insights into the functional organisation of the visual system. Second, Bishop provided the intellectual milieu, material resources and academic freedom that provided a thriving environment for the faculty members of the Physiology Departments at the University of Sydney and the ANU, whether they had been recruited externally or had come through the ranks as students, postdocs or research fellows. Thus Peter Bishop, or ‘Prof’ as he was universally known, saw that his scientific legacy lay not only in his own research publications but also in the vitality of the ‘Bishop School’ at large. The award of the 1993 Australia Prize to Peter Bishop recognised both his outstanding personal research and his broader contributions to promoting sensory neuroscience. The legacy endures, not only in the many members of the Bishop School who became full professors, but also in their students and postdocs who now occupy senior positions at universities throughout Australia and overseas.
Associate Professor Ulrike Grünert

Parallel Pathways in Primate Retina

Save Sight Institute, University of Sydney, Sydney

Dr Ulrike Grünert is Associate Professor in Ophthalmology and Visual Science at the Save Sight Institute of the University of Sydney, Australia. She studied Biology and received her PhD in Zoology in 1985 from the Goethe University in Frankfurt, Germany. She subsequently spent two years at the University of Florida with a postdoctoral fellowship of the Deutsche Forschungsgemeinschaft (DFG). In 1988 she returned to Germany and took up a position as a group leader in the Neuroanatomy department of Prof Heinz Wässle at the Max-Planck-Institute for Brain Research in Frankfurt. At the Max-Planck-Institute she became interested in the mammalian retina.

In 1994 she was awarded the Habilitation from the Goethe University in Frankfurt and obtained a Feodor-Lynen-fellowship from the Alexander-von-Humboldt foundation to continue her research at the Department of Physiology of the University of Sydney. In 1997 she took up a position as NHMRC senior research associate at Sydney and in 2003 a position as a Lions Vision Research Fellow at the National Vision Research Institute of Australia in Melbourne. She was appointed Honorary Principal Fellow with title Associate Professor at the University of Melbourne. In 2010 she took up her current position at the Save Sight Institute. Her research interest is focused on the functional neuroanatomy of the primate retina.
Parallel Pathways in Primate Retina

Abstract

Ulrike Grünert, Paul R. Martin, Patricia R. Jusuf, Brett A. Szmajda, Kumiko A. Percival, and Peter Buzás

Save Sight Institute, University of Sydney, Sydney,

Peter Bishop was one of the first scientists to identify functional parallel pathways in the visual system (P.O. Bishop, D. Jeremy & J.W. Lance, 1953. The optic nerve. Properties of a central tract. J. Physiol., 121, 415-432). Bishop and his co-workers showed that there are at least two parallel pathways at the level of the optic tract that project to higher brain areas. We now know that these parallel pathways start at the first synapse of the retina, the cone pedicle. In primate retina, cone pedicles are connected to at least 10 types of bipolar cells. These bipolar types transfer the visual information to about 20 ganglion cell types that project to different regions in the brain. The projections of the two major ganglion cell populations in the primate retina are well understood; midget ganglion cells project to the parvocellular layers and parasol ganglion cells project to the magnocellular layers of the dorsal lateral geniculate nucleus (Leventhal et al., 1981; Perry and Cowey, 1981). In addition, it has been shown that specific retinal ganglion cell types project to the superior colliculus and pretectum (Rodieck and Watanabe, 1993). We studied the connectivity and projections of retinal ganglion cells in the marmoset Callithrix jacchus using retrograde tracer injections and photofilling (Dacey et al., 2003). Our studies showed that retinal ganglion cells presumed to carry signals originating in short-wavelength sensitive (S or blue) cones preferentially project to the koniocellular layer K3 (Szmajda et al., 2008). Most recently we identified a population of ganglion cells that appears unique to the koniocellular layer K1. This cell type has a similar dendritic field size and stratification as ON and OFF parasol cells but differs from parasol cells in that it has a more densely branching dendritic tree and numerous spine-like protrusions. This K1 projecting cell type resembles the narrow thorny ganglion cell identified previously in macaque and human retina (Peterson and Dacey, 1999; Dacey et al., 2003). Our results suggest a functional segregation of pathways within the koniocellular layers.
Associate Professor Péter Buzás

Colour Cells of the Cat LGN

Institute of Physiology, Medical School, University of Pécs, Hungary

Dr Péter Buzás is an associate professor of physiology at the University of Pécs, Hungary. After graduating as a biologist at the University of Szeged in 1994, he specialised in visual neuroscience. After doing research on the retinas of frogs and rabbits with Róbert Gábriel and on functional maps in the cat visual cortex with Zoltán Kisvárday and Professor Ulf T. Eysel, he received his PhD in 1999 from the Ruhr-Universität Bochum, Germany. He continued working in this field in Bochum until 2004 when he moved to the National Vision Research Institute of Australia to join Professor Paul R. Martin. Here, he got interested in colour vision and the intricacies of parallel visual pathways. In 2006, he received a faculty position at his current institute. Here, funded by the Hungarian Scientific Research Fund (OTKA), he started exploring the neural pathway for colour vision in non-primate mammals. Between 2008 and 2011 he was a Bolyai Fellow of the Hungarian Academy of Sciences. He received his habilitation in 2011. He teaches medical physiology in German, English and occasionally, Hungarian.
RETINA, THALAMUS, PARALLEL PROCESSING

Colour Cells of the Cat LGN

Abstract

Péter Buzás

Institute of Physiology, Medical School, University of Pécs, Hungary

Cats have been known since the 1970's to possess dichromatic colour vision based on short wavelength sensitive (S) and medium-long wavelength sensitive (ML) cone photoreceptor classes. A few examples of colour coded neurones were also described in the cat retina and lateral geniculate nucleus. However, the neural pathways carrying colour signals in cats or indeed, in any non-primate mammal remained largely unexplored. We have recently characterised a population of colour opponent (blue-ON) cells in recordings from the dorsal lateral geniculate nucleus (LGN) of anaesthetised cats. We found five points of similarity to previous descriptions of primate blue-ON cells. Firstly, cat blue-ON cells receive ON-type excitation from S-cones, and OFF-type excitation from ML-cones. We found no blue-OFF cells. Secondly, the S- and ML-cone driven receptive field regions of cat blue-ON cells are closely matched in size, consistent with specialisation for detecting colour contrast. Thirdly, the receptive field centre diameter of cat blue-ON cells is about 3 times larger than the centre diameter of non-colour opponent receptive fields at any eccentricity. Fourthly, S- and ML-cones contribute weak surround inhibition to cat blue-ON cells. These data show that blue-ON receptive fields in cats are functionally very similar to blue-ON type receptive fields previously described in macaque and marmoset monkeys. Finally, cat blue-ON cells are found in the same layers as W-cells, which are thought to be homologous to the primate koniocellular system. Based on these data, we suggest that cat blue-ON cells are part of a "blue-yellow" colour opponent system that is the evolutionary homologue of the blue-ON division of the koniocellular pathway in primates.
Professor Diego Contreras

Inhibitory mechanisms in the visual thalamus

Dr Diego Contreras is a Professor of Neuroscience at The University of Pennsylvania School of Medicine. He is funded by the Eye Institute of the National Institutes of Health. He received his Medical Degree in 1988 from the Universidad Autonoma of Madrid, in Madrid, Spain. He received his doctorate in 1996 from Laval University in Quebec, Canada, where he learned intracellular recordings in vivo and studied the cellular basis of rhythm generation in the thalamocortical system under the supervision of Dr. Mircea Steriade. Next, he completed a post-doctoral appointment at New York University under the supervision of Dr. Rodolfo Llinas, where he learned voltage sensitive dye imaging in slices in vitro and studied spatiotemporal pattern of activation of thalamocortical slices. His current research focuses on the cellular mechanisms of visual information transfer in the thalamus in vivo and the role of corticothalamic feedback.
RETINA, THALAMUS, PARALLEL PROCESSING

Inhibitory mechanisms in the visual thalamus

Abstract

Leif Vigeland, Larry Palmer and Diego Contreras

Department of Neuroscience, University of Pennsylvania School of Medicine, Philadelphia. USA

The essential substrate for image representation in primary visual cortex is the spatiotemporal pattern of LGN input, which is dependent on time-varying patterns of excitation and inhibition and their interactions with the intrinsic properties of relay cells, especially T-type calcium channels. Furthermore, there is a shocking difference between the rich and diverse behavior of thalamic relay and reticular cells described during sleep and epilepsy and the rather simplistic understanding of the mechanism underlying thalamic responses to visual stimulation. Our data show that the interactions between visual stimulation and synaptic and intrinsic processes in LGN relay cells are far more complex than previously thought. We show that (a) there are at least three demonstrable types of inhibition within the LGN, which shape the receptive fields of relay cells and their spike trains in time. Surprisingly, the main mechanism of spike suppression to center stimuli in X cells is suppression of retinal input, or disfacilitation, rather than postsynaptic inhibition, while postsynaptic inhibition is more prevalent in Y-cells. Surround stimuli instead, engage postsynaptic inhibition in both cells types. However, in almost all cases postsynaptic inhibition is short lasting (30-50 ms), has a very negative reversal potential (~ -90 mV) and is always concurrent with disfacilitation. Finally, powerful Cl-dependent postsynaptic inhibition preceding the excitatory response to center stimuli and associated with each individual retinal input is the mechanism that defines lagged cells. (b) T-currents play a continuously graded role in shaping relay cell output rather than working in an either on or off mode as previously suggested. Pharmacologically blocking T-current in vivo reveals a drop of spike output at all Vms during visual responses and not only at hyperpolarized ones.
Professor Martin Usrey

Parallel Processing in the Corticogeniculate Pathway of the Macaque Monkey

Dr W. Martin Usrey is Professor of Neurobiology, Physiology, and Behaviour at the University of California, Davis. He received his PhD in 1994 from Duke University and conducted postdoctoral training at the Rockefeller University and Harvard Medical School. He has received the Presidential Early Career Award for Scientists and Engineers (PECASE), the Charles Judson Herrick Award from the American Association of Anatomists, and the Scientific Innovations Award from the Brain Research Foundation. He also received fellowship awards from the Alfred P. Sloan Foundation, the Klingenstein Foundation, and the McKnight Foundation.
CORTICAL PROCESSING

Parallel Processing in the Corticogeniculate Pathway of the Macaque Monkey

Abstract

Farran Briggs1,2 and W. Martin Usrey1

1University of California, Davis
2Geisel School of Medicine at Dartmouth University

Few pathways in the nervous system are as prominent, yet as poorly understood, as the corticothalamic feedback pathway. Across sensory systems, corticothalamic feedback completes a reciprocal loop of information exchange between the thalamus and cerebral cortex. Such organization provides the cortex with the opportunity to regulate and shape the nature of its input dynamically. Although corticogeniculate neurons are the single greatest source of synaptic input to the lateral geniculate nucleus (LGN) of the thalamus, we know surprisingly little about their functional properties. This is particularly true in primates where magnocellular (M), parvocellular (P), and koniocellular (K) streams dominate both the anatomical and functional organization of feedforward projections in the early visual system.

Using electrical stimulation to identify corticogeniculate neurons in the behaving macaque monkey, we distinguish three groups of neurons with response properties that closely resemble those of neurons in the M, P, and K layers of LGN. Our results indicate that corticogeniculate feedback in the primate is stream specific, and provide strong evidence in support of the view that corticothalamic feedback can influence the transmission of sensory information from the thalamus to the cortex in a stream-selective manner.
**Professor Trichur Vidyasagar**

*Integration of feedforward and intracortical mechanisms in visual cortical function*

*Trichur Vidyasagar* is a Professor at The University of Melbourne. His relationship with the Peter Bishop legacy is a long and consistent one over a 40-year period. During his medical studies at the University of Madras (1970-75), he got interested in vision, inspired largely by the discoveries made by Hubel & Wiesel in Harvard and those by the energetic group of Peter Bishop at ANU. He pursued this interest at the University of Manchester, where his graduate work in visual physiology was supervised by Janus Kulikowski, who was already collaborating with Peter Bishop. Since then, a significant part of Vidyasagar’s research has been devoted to the challenges that Bishop’s group posed to the Harvard schema of the visual system. From Manchester, he went to Goettingen to work with Otto Creutzfeldt, who was the other major challenger of Hubel & Wiesel. In 1989, he moved to the ANU, where he was fortunate to inherit Geoff Henry’s laboratory, which was moved to Melbourne when he took up a position in the Dept of Optometry & Vision Sciences in 2002. His research is presently supported by grants from the NHMRC and the ARC.
CORTICAL PROCESSING

Integration of feedforward and intracortical mechanisms in visual cortical function

Abstract

Trichur Vidyasagar

Department of Optometry & Vision Sciences, University of Melbourne

In the classical model proposed by Hubel & Wiesel, a striate cortical simple cell derives its orientation selectivity purely from the excitatory convergence of a number of geniculate afferents with circular receptive fields (RFs). Over the years, many studies, notably those from Canberra and Goettingen, raised serious questions about this scheme. They stressed the possible roles of intracortical inhibition and the biases for stimulus orientation already observed in responses of neurones in the retina and lateral geniculate nucleus (LGN). In support of this, we have recently found evidence for a number of mechanisms contributing to the response properties of striate cortical cells: (1) Non-specific inhibition acting on outputs of single LGN cells with an orientation bias can lead to orientation selectivity matching that typically seen in striate cortical cells. (2) LGN and striate cells with overlapping RFs show a higher degree of coherence in their spike trains if their orientation preferences are matched, indicating that cortical orientation selectivity is probably derived from LGN biases. (3) Single geniculate afferents in striate layer 4 show orientation preferences matching that of the orientation domain that they terminate in. (4) A model that assumes non-specific intracortical inhibition acting on a geniculate input biased for a stimulus orientation can explain not only the typical narrow tuning for orientation seen in target striate cells, but also their other response properties, such as the selectivity for spatial frequency and length of stimuli.
Professor Michael Ibbotson has, since 2011, been the Director of the National Vision Research Institute of Australia and a Research Professor in the Department of Optometry and Vision Science, University of Melbourne. He received his PhD from Queen Mary, University of London in 1990. After his PhD he moved to Australia and worked at the Australian National University until 2011. He was Head of the Visual Sciences Group at ANU for four years (2006-2011). He is presently funded by grants from the ARC, the NHMRC and several philanthropic organisations, notably Lions International and the Cooper and Lucas foundations. He has worked in the USA for extended periods with Professor Mike Mustari in Atlanta and Seattle, and also spent time at New York University with Professor Tony Movshon. His research interests are broad, with current projects investigating retinal physiology, visual cortical processing, the development of a prosthetic retinal device for human implantation and bio-mimetics, which involves translating discoveries made in the insect visual system into robotics.

Finding the simple cell within
CORTICAL PROCESSING

Finding The Simple Cell Within

Abstract

Michael R. Ibbotson, Shaun L. Cloherty and Markus A. Hietanen

National Vision Research Institute, Australian College of Optometry and Department of Optometry and Vision Sciences, University of Melbourne

Cells in primary visual cortex are classified into two cell types (simple and complex). Simple cells are phase-sensitive, while complex cells are usually thought of as being phase-insensitive. Simple cells are good at detecting where edges are in their receptive fields, while complex cells are highly sensitive to texture. Using moving gratings we have shown that complex cells become phase-sensitive as contrast is reduced or following adaptation, i.e., they begin to behave like simple cells. However, when using moving gratings we could not learn anything about the spatial structure of their receptive fields. Therefore, in another experiment, we presented stationary contrast reversing cosine gratings of optimal orientation and spatial frequency within the receptive fields. To quantify phase sensitivity of response modulations we presented gratings with a range of spatial phases. At each spatial phase we varied the contrast of the gratings to determine whether the response modulation of complex cells increased as contrast was reduced. We show that the majority of our complex cells show significant increases in their response modulation at low contrast relative to that at high contrast. Moreover, at high contrast, modulation of the responses was largely independent of the spatial phase of the stimulus, while at low contrast we observed significant variation in response modulation for different stimulus phases. The results show that receptive field structure is contrast dependent, also implying that cell classification is not contrast invariant. Models of cortical coding need to accommodate this finding.
Dr Samuel Solomon

Population signals for motion vision

Sam Solomon received his PhD from Sydney in 2002 and undertook postdoctoral work in New York and Oxford before returning in 2006 to join Faculty at the University of Sydney. In 2013 he moved to University College London. Sam's research tries to identify the neural machinery that is important in perceptual tasks. His early research has addressed how contrast and colour are encoded in parallel pathways through the early visual system of primates, and how visual cortex recombines these signals. His recent work has concentrated on the analysis of visual motion by cortical neurons. Results of these scientific experiments have been published in over 40 papers in scientific journals.
CORTICAL PROCESSING

Population signals for motion vision

Abstract

Samuel G Solomon\textsuperscript{1,2}, Selina S. Solomon\textsuperscript{2}, Spencer C. Chen\textsuperscript{2}, John W. Morley\textsuperscript{3}

\textsuperscript{1}Cognitive, Perceptual and Brain Sciences, University College London,
\textsuperscript{2}Discipline of Physiology, University of Sydney,
\textsuperscript{3}School of Medicine, University of Western Sydney

The middle-temporal (MT) area of primate visual cortex is an important stage in the analysis of visual motion, and the response properties of single units in area MT are well established. We know much less about the response of populations of neurons in area MT. Here we characterised functional connectivity of neurons in area MT of marmoset, a New World primate, where the area lies exposed on the cortical surface. Our analyses used standard methods to reveal the spatial- and temporal distribution of ‘noise correlations’. The amplitude of noise correlations in area MT decreased with distance between pairs of neurons, and with difference in their preferred direction. Analysis of correlation time-course showed that synchronous spiking is restricted to nearby neurons with highly overlapping receptive fields; noise correlations over wider areas of cortex, perhaps the whole hemifield representation, reflect mechanisms with longer time courses. Noise correlations between pairs of neurons in V1 were similar in time course but three times the amplitude of those for pairs of neurons in area MT. We conclude that neurons in area MT are more likely to show noise correlations when they are close together, when their receptive fields overlap in space, and when they have similar preferred directions. Decorrelation of activity on transition between area V1 and area MT may be the result of mechanisms known to be important for motion analysis – convergence, opponency, and gain control.
Dr Melanie C.W. Campbell is Professor in Physics and Astronomy and the School of Optometry and Vision Science, University of Waterloo, Canada. She received a BSc from University of Toronto, an MSc in Physics, University of Waterloo and a PhD in Applied Mathematics and Physiology from ANU in 1982. Following a CSIRO Fellowship at the Institute of Mathematics and Statistics, she took up an NSERC University Research Fellowship at the University of Waterloo. She shared the 2004 Rank Prize in Optoelectronics for her work cited as "an initial idea (that) has been carried through to practical applications that have, or will, demonstrably benefit mankind." She is a Fellow of the Optical Society of America, a Fellow of the Institute of Physics (UK), holds an honorary Professional Physicist designation from and is a former President of the Canadian Association of Physicists. Campbell was also a co-founder of Biomedical Photometrics Inc, now Huron Technologies. Her current research focuses on the optical quality of the eye, improved diagnostic imaging of ocular and systemic diseases and on light based ocular therapies.
PHYSIOLOGICAL OPTICS AND RETINAL ORGANISATION

The Importance of the Eye's Optics in Myopia, Ocular Diagnosis and Therapy and as a Window on the Brain

Abstract

Melanie Campbell

Department of Physics and Astronomy and School of Optometry and Vision Science, University of Waterloo, Canada

Measurements of the optical quality of the eye have increased in precision and repeatability as a result of techniques adopted from astronomy. We have used these to measure and identify possible signals to the direction of eye growth which are up regulated in the presence of lens induced myopia. These and other optical changes measured in myopia have led to a greater interest in the role of the optics of the eye in understanding and treating myopia. As well as measuring the optical quality more precisely, we correct optical blur with adaptive optics and produce high resolution in vivo images of individual retinal cells, including cones in retinal dystrophies. We are also using this technology to explore whether the earliest ocular changes in Type I diabetes are neural or vascular. This may lead to earlier and improved interventions to prevent diabetic retinopathy. I will also discuss ways in which precisely focussed light might be used in the treatment of ocular disease. Imaging the retina can provide a “window on the brain”, potentially enabling diagnosis of neural conditions. Currently, definitive diagnosis of Alzheimer’s disease only occurs after death. Recently we have confirmed the presence of amyloid beta, which forms plaques and which is a marker of the disease, in the ex vivo neural retina of those with the disease and not in age matched normal donors without the disease. We are developing an in vivo imaging technique which we hope will become a more accessible, less invasive and less expensive technique than others under development for the early diagnosis of Alzheimer’s disease.


**Associate Professor Joseph Carroll**

*Imaging Photoreceptor Disruption in the Human Retina*

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*Joseph Carroll, PhD,* is an Associate Professor in the Departments of Ophthalmology, Biophysics, and Cell Biology, Neurobiology & Anatomy, as well as the co-Director of the Advanced Ocular Imaging Program at the Medical College of Wisconsin (MCW). He received his PhD in 2002 from the Medical College of Wisconsin under the guidance of Dr. Jay Neitz, and then did a postdoctoral fellowship at the University of Rochester with Dr. David Williams. His highly collaborative research is focused on elucidating structure-function relationships in the human visual system. He has contributed to the development and application of non-invasive methods for assessing retinal structure and function and has spent his career focusing on understanding various retinal diseases. He has over 50 peer-reviewed publications as well as numerous book chapters and reviews. Currently, the Foundation Fighting Blindness and The National Eye Institute fund his work. He has received a number of awards, including the Karl Kirchgessner Foundation Vision Research Award, the E. Matilda Ziegler Foundation for the Blind Vision Research Award, a Career Development Award from RPB, and a Young Investigator Award from the ALCON Research Institute.
PHYSIOLOGICAL OPTICS AND RETINAL ORGANISATION

Imaging Photoreceptor Disruption in the Human Retina

Abstract

Joseph Carroll

Department of Ophthalmology, Medical College of Wisconsin

The human retina is an easily accessible tissue, and can be imaged using a number of different modalities. The ability to directly visualize the living retina provides an implicit advantage in diagnosing and monitoring retinal disease, however the available resolution of these tools is limited. Adaptive optics (AO) enables correction of the eye’s monochromatic aberrations, and as a result provides nearly diffraction-limited imaging. Current systems are capable of imaging the smallest photoreceptor cells in the living retina, rods and foveal cones. With the expanding use of AO imaging has come an appreciation that significant cellular damage can exist in the presence of “normal” anatomy on conventional imaging modalities.

The purpose of this presentation is to describe our efforts in using AO imaging to advance our understanding of various ocular conditions, including inherited retinal degenerations, closed globe ocular trauma, and macular hole. The clinical value of these images can be appreciated through detailed comparison of AO images to those obtained with conventional imaging tools.
**Associate Professor Jan Hemmi**

*Topography Of Vision In Fiddler Crabs – Sampling Array And Photoreceptor Sensitivity*

*Dr Jan Hemmi* is an ARC Future Fellow and Associate Professor at the University of Western Australia. He received his doctorate in neuroscience in 1998 from the Australian National University (ANU). After graduating, he had a short post-doctoral appointment with Professor Rowland Taylor, then at the John Curtin School of Medical Research at the ANU before moving back to the Research School of Biological Sciences to take up a post-doctoral position with Professor Jochen Zeil. He then became a Research Fellow at the ANU, where he stayed until 2012 when he moved to the University of Western Australia to take up his Future Fellowship. His research is focused on the decision-making processes that underlie animal behaviour, with a particular interest in how behaviour is organised around sensory and cognitive constraints and abilities. He addresses these issues in several study systems, including marsupials, crabs, ants and lizards, using behavioural, anatomical and physiological techniques.
PHYSIOLOGICAL OPTICS AND RETINAL ORGANISATION

Topography of vision in fiddler crabs – sampling array and photoreceptor sensitivity

Abstract

Jan M. Hemmi, Marcin Falkowski & Jochen Smolka
School of Animal Biology & UWA Oceans Institute, University of Western Australia

Fiddler crabs are highly social animals that live in dense colonies in the tropical and sub-tropical, open, intertidal mudflats of the world. They carry their eyes on long stalks high above their bodies and observe the world through eyes that sample almost the entire visual sphere with only 8000 pixels (Ommatidia) per eye. This is 40 times fewer pixels than that used in the simplest mobile phone camera. Despite this very low resolution sampling array, the crabs are visually highly competent and rely on visual information to make crucial decisions throughout their lives. They use vision to identify species, to recognise individual conspecifics, measure the distance of intruders to their home burrows and effectively avoid predation by small and fast bird predators. The secret to these skills is a highly evolved and sophisticated sampling array and a range of behavioural strategies that support and complement vision. A complete optical eye reconstruction measuring ommatidial density and size has shown several specialised areas within the crabs’ sampling array that optimise biological information transfer within the constraints of a small eye. These areas trade off the use of eye space with visual acuity and contrast sensitivity. We are currently using intracellular recordings from individual photoreceptors to map out how the crabs allocate photoreceptors with different spectral, polarisation and spatial sensitivities across their visual field in order to make effective and fast decisions.
### ABSTRACTS, YOUNG INVESTIGATORS ORAL PRESENTATIONS

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12 **Hsin-Hao Yu**

The organization of the Middle Temporal area (MT) and the Lateral Geniculate Nucleus (LGN) in monkeys with early-life lesions of the primary visual cortex
1. "REMOTE ISCHEMIA NEUROPROTECTION POTENTIAL IN A LIGHT DAMAGE MODEL"

Brandli, A., Spana, S., and Stone, J.

Discipline of Physiology and Bosch Institute, University of Sydney and ARC Centre of Excellence in Vision Science

**Purpose:** Remote ischemic pre-conditioning (RIP) has found to be protective of heart and brain against ischemic injury. We have tested whether RIP is protective to the retina in the face of light-induced damage.

**Methods:** To generate ischemia remote from the retina, one hind limb was made ischemic with a pressure cuff applied for up to 10 min. To test the neuroprotective potential of RIP, RIP was delivered immediately before exposure of the animal to damaging light (1000 lux, 24 hours, >12 hours dark adaption). 7 days later, the ERG was recorded and structural status of the retina were assessed between RIP and light exposed, and three control groups -light damaged, RIP-exposed and untreated (n =6 per group). ERGs were analysed for the amplitude of the a- and b-waves, and normalised to baseline (mean ± SEM).

**Results:** RIP preserved photoreceptor and bipolar function against light damage (a-wave: 27% ± 3 vs. 7.0% ± 5, P < 0.01, n = 6) and (b-wave: 25% ± 4 vs. 3% ± 5, P < 0.01, n = 6). RIP was associated with a reduction in the upregulation by Muller cells of a stress-inducible protein (0.4 ± 0.09 vs. 0.5 ± 0.04 p< 0.0001, n = 6 ), with a mitigation of the thinning of the outer nuclear layer (0.3 ± 0.01 vs. 0.3 ± 0.0 p< 0.0001, n =6) and a reduction in the number of photoreceptors undergoing apoptosis (250 ± 6 vs. 214 ± 6  p< 0.0001, n =6).

**Conclusions:** Remote ischemic preconditioning has marked neuroprotective effects in the retina, and may offer a non-invasive therapeutic treatment to prevent or mitigate photoreceptor degeneration of the retina.

2. "VISUAL AREAS IN THE MAMMOT CORTICAL ATLAS"

Tristan A. Chaplin¹, Hsin-Hao Yu¹, Piotr Majka², Cecil C. Yen³, Jakub M. Kowalski², Daniel K. Wójcik², Afonso C. Silva³, and Marcello G.P. Rosa¹

¹ Department of Physiology, Monash University
² Nencki Institute of Experimental Biology, Poland
³ National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, MD, USA

Digital brain atlases are fast becoming the key to consolidating the large amount of data being produced by a growing number of complementary methodologies. Traditional mapping techniques such as electrophysiological recordings, cytoarchitectural analysis and tracer injections can be combined with newer imaging methodologies such as fMRI, MRI myelin mapping and diffusion imaging to create multimodal atlases of the brain. We have been developing such an atlas for the marmoset monkey, a promising primate animal model. Here, we describe information collated so far for visual processing regions of the cortex. The cortex has been subdivided into 115 cytoarchitecturally defined areas of which more than 20 are visual processing areas, and we have constructed both surface and volumetric based atlases. These form the standard reference space to which other data modalities are registered. We have registered electrode recording sites of V1 to the atlas in order to create a standard V1 retinotopic map. We have also registered connection data from tracer injections in the FEF as well as other visually connected frontal areas. Finally, we registered MRI myelin maps to the atlas, which allow in vivo parcellation of visual areas such as V1, MT and the FEF. In the future, the same methods will be used to incorporate cortical thickness, fMRI and diffusion imaging data. This marmoset atlas has already been warped to atlases of other species, including macaques and humans, allowing data from one species to be mapped to another for interspecies comparisons.
3. “NOISE NORMALIZES FIRING OUTPUT OF MOUSE LATERAL GENICULATE NUCLEUS NEURONS”

Rajiv Wijesinghe, Samuel G. Solomon, and Aaron J. Camp

Sydney Medical School, School of Medical Sciences and Bosch Institute, The University of Sydney

The output of individual neurons in the visual thalamus is dependent on both synaptic and intrinsic membrane properties. While it is clear that the response of an individual neuron can be facilitated or inhibited based on the summation of its constituent synaptic inputs, it is not clear whether subthreshold activity, (e.g. synaptic “noise”- fluctuations that do not change the mean membrane potential) also serve a function in the control of neuronal output. Here we studied this by making whole-cell patch-clamp recordings from 29 mouse Dorsal Lateral Geniculate Nucleus neurons. For each neuron we measured neuronal gain in response to either injection of current noise, or activation of the metabotropic glutamate receptor-mediated cortical feedback network (synaptic noise). As expected, injection of current noise via the recording pipette induces shifts in neuronal gain that are dependent on the amplitude of current noise, such that larger shifts in gain are observed in response to larger amplitude noise injections. Importantly we show that shifts in neuronal gain are also dependent on the intrinsic sensitivity of the neuron tested, such that the gain of intrinsically sensitive neurons is attenuated divisively in response to current noise, while the gain of insensitive neurons is facilitated multiplicatively by injection of current noise- effectively normalizing the output of the dLGN as a whole. In contrast, when the cortical feedback network was activated, only multiplicative gain changes were observed. These network activation-dependent changes were associated with reductions in the slow afterhyperpolarization (sAHP), and were mediated at least in part, by T-type calcium channels. Together, this suggests that dLGN neurons have the machinery necessary to compute multiple output solutions to a given set of visual stimuli depending on the current level of network stimulation.

4. “ANTIDROMIC AND VISUAL EVOKED RESPONSE LATENCY IN MARMOSET LATERAL GENICULATE NUCLEUS”

Cheong S.K.1,2, Pietersen A.N.J.1,2, Solomon S.G.1,3, Dreher B.4, and Martin P.R.1,2,4

1 Save Sight Institute, The University of Sydney
2 ARC Centre of Excellence in Vision Science
3 Institute of Behavioural Neuroscience, University College, London
4 School of Medical Sciences, The University of Sydney

Purpose: To study connectivity of the “Blue-ON” koniocellular (K) visual pathway from the lateral geniculate nucleus (LGN) to the primary visual cortex (V1). We also measured the contribution of conduction latencies to visually evoked response latencies in the parallel visual pathways.

Methods: Single unit, extracellular recordings were made in the LGN of sufentanil-anaesthetised marmosets (Callithrix jacchus, n = 4). Electrical current (0-5 mA, 50 µs) was injected into V1 using bipolar electrodes. Antidromic activation of LGN cells was assessed using the collision test and conduction latencies were measured. Visual response latencies were measured in LGN using a 70% Michelson contrast, spatially uniform stimulus filling the receptive field. Receptive fields were characterised using drifting achromatic and short wavelength sensitive (S)-cone isolating gratings.

Results: 23 LGN cells were activated antidromically from V1: 4 Blue-ON K cells; 1 “non-Blue” ON K cell; 6 parvocellular (P); and 12 magnocellular (M) cells. The P cells had latencies of 1.89±0.16 ms (mean±SD); M cells 1.17±0.23 ms; and Blue-ON K cells 1.80±0.27 ms. The ON K cell had a latency of 2.39 ms. Thalamocortical latencies were on average 3±1% (mean±SD) of the visual response latency and were positively correlated with visual response latencies (r² = 0.68, p = 0.002). Orthodromic activation was observed in three M cells with latency 2.04±1.53 ms (mean±SD).

Conclusion: Blue-ON K LGN cells make direct connections to V1. The latency of this connection is similar to that of P cells. The conduction latency of thalamocortical fibres contributes very little to the overall latency of visually-evoked signals arriving at V1.
5. “MICROARRAY ANALYSIS AND GLYCOLYTIC AND MTOR PATHWAY PROFILING OF A CONDITIONAL, SELECTIVE MÜLLER CELL ABLATION IN A TRANSGENIC MURINE RETINA”

Sook Chung, Weiyong Shen, Jean Yang, Kaushala Jaywadara, Penghao Wang, Mark Gillies

Department of Clinical Ophthalmology and Eye Health, University of Sydney

Müller cells, the principal glia cells in mammalian retina, play a critical role in retinal homeostasis. We have developed a transgenic Cre-Lox model for selective, conditional Müller cell ablation to examine the relationship between Müller cell dysfunction and retinal diseases. The purpose of this study was to examine differentially expressed genes and their related pathways with microarray analysis, then to profile metabolic pathways in areas of Müller cell ablation.

Affymatrix microarray was performed on whole retina samples 1 week, 1 month and 3 months after induced Müller cell ablation. Data were analysed with limma package (p<0.05) and qRT-PCR was used for array validation. Isolation of patches of Müller cell ablation was achieved by laser capture microdissection (LCM) and qRT-PCR was conducted on pathway related genes. Immunofluorescence microscopy was used to validate results.

Neuroprotection and apoptosis-related genes were upregulated 1 week after Müller cell ablation, angiogenesis, tight junction and metabolic-pathway related genes were downregulated later. Further analysis of glycolytic and mTOR pathways with tissue obtained by LCM revealed significant downregulation of genes related to these pathways in patches of Müller cell loss compared with controls. Immunofluorescent studies revealed that the downregulations mainly occurred in the photoreceptor segments, although Enolase1 colocalised with Müller cells.

We found reduction of transcription and expression of proteins involved in key metabolic pathways in patches of Müller cell ablation. This study provides new insights into the relationship between Müller cell dysfunction and retinal diseases.

6. “SIMULTANEOUS MAPPING OF RECEPTIVE FIELDS AND RESPONSE PROPERTIES OF LARGE NEURONAL POPULATIONS IN EXTRASTRIATE CORTEX”

Saman Haghgooie, Hsin-Hao Yu, Amanda Davies, Nicholas Price, Marcello Rosa

Department of Physiology, Monash Vision Group, Monash University, Clayton, VIC 3800

Purpose: Traditional approaches to characterization of responses in visual cortex have relied on sequential sampling of single cells, or small populations. However, the usefulness of brain-machine interfaces is likely to depend on more sophisticated approaches, including simultaneous monitoring of activity of large populations of neurones. Here, we demonstrate the feasibility of stable recordings from up to 96 multiunits across the second [V2] and dorsomedial [DM] visual areas.

Methods: Marmosets were anaesthetized with sufentanil (8 µg/kg/h) and N2O (70% in oxygen), and the eyes were focused on a computer screen where visual stimuli were projected, over an area encompassing more than 40˚ of the visual field. Recordings were obtained through 96-channel “Utah” arrays, inserted in dorsal extrastriate cortex, including parts of areas V2 and DM.

Results: Following a period of stabilization of several hours, high signal-to-noise ratio responses could be obtained from all recording channels. Confirming earlier results using single electrodes, we found that receptive fields in DM were larger than those in V2, and that DM comprises a representation of the upper visual field that is adjacent to V2. The response onset latencies measured at center of the receptive fields were 48±19 ms in V2, compared to 64±15 ms in DM. Orientation tuning bandwidths, measured with gratings, were similar in DM and V2 (mean, 68.5±35 degrees).

Conclusion: Current technologies already allow high-throughput characterization of neuronal response properties across many sites, including multiple visual areas. When combined with algorithms currently under development for online unit sorting, these automated routines will allow an unprecedented level of insight on sensory processing by neuronal populations.
7. “THE EFFECTS OF EXCITATION AND INHIBITION ON THE SHARPNESS OF SPATIAL-TUNING CURVES AND RESPONSE OUTPUT OF RETINAL GANGLION CELLS”

Jin Y. Huang1,3 and D.A. Protti2,3

1 Discipline of Biomedical Science
2 Discipline of Physiology
3 Bosch Institute, The University of Sydney, NSW 2006

In the mammalian brain, the responses of neurons are determined by the balance between excitatory and inhibitory inputs. To study the effects of this balance between excitation and inhibition on neuronal responses, retinal ganglion cells (the output neurons of the retina) were used as model neurons. Thus, the aim of this study is to investigate whether different levels of inhibition modulate the spatial-tuning properties and neuronal output of ganglion cells.

Methods: Using whole-mount mouse retinae, dynamic clamp recordings were made from 40 ganglion cells. Light-evoked excitatory and inhibitory conductances recorded in response to different stimulus sizes were injected into the cell bodies. The ratios between excitatory inputs and inhibitory inputs varied between 1:0 and 1:2.

Results: Injection of balanced excitation and inhibition (ratio 1:1) generated area response functions typical of physiological responses displaying surround inhibition. Increases in the level of inhibition resulted in more prominent surround inhibition. Increases in the level of inhibition also resulted in slower rising membrane potential over time and lower amplitude of membrane potential. In addition, the number of spikes decreases as the level of inhibition increases.

Conclusion: The balance between excitation and inhibition is important in sharpening the spatial-tuning and response output of retinal ganglion cells.

8. “ORIENTATION ANISOTROPIES IN HUMAN PRIMARY VISUAL CORTEX DEPEND ON CONTRAST”

Ryan T. Maloney, Colin W. G. Clifford

School of Psychology and ARC Centre of Excellence in Vision Science, University of Sydney

The mechanisms of orientation processing in mammalian visual cortex appear matched to the environment, such that larger populations of cells are tuned to the cardinal orientations (horizontal and vertical) than oblique orientations. Perceptually, this property is manifested in poorer sensitivity to the oblique compared to the cardinal orientations in a wide variety of tasks – the so-called oblique effect. Surprisingly, some recent functional magnetic resonance imaging (fMRI) studies have revealed an opposite pattern of anisotropy – namely, an increased response to the oblique orientations over the cardinals: the inverse oblique effect. It has been proposed that this might reflect efficient coding strategies optimised to the particular diet of orientations encountered during natural viewing. As such, it might be expected that the form of anisotropy would change as the quality or strength of the oriented stimulation changes. Here, the fMRI BOLD response was measured in the visual cortex of human subjects (n=5) as a function of the orientation of a sinusoidal grating, across different stimulus contrasts.

The results revealed a shift from the previously observed inverse oblique effect at high contrast to a pattern of anisotropy resembling an oblique effect at low contrast. This is consistent with the idea that primary visual cortex adaptively changes its coding strategy as a function of signal-to-noise ratio.
9. “SEEING SMOKE: CANNABINOID MODULATION OF INPUTS TO RETINAL GANGLION CELLS”

Terence P Middleton\textsuperscript{1,2} and Dario A Protti\textsuperscript{1,2}

\textsuperscript{1} Department of Physiology, University of Sydney, Australia
\textsuperscript{2} Bosch Institute, Sydney, Australia

The endocannabinoid system is found throughout the brain and is implicated in many mechanisms including short-term plasticity. This is achieved by the on demand synthesis and release of cannabinoids from an excited cell which then retrogradely activates presynaptic receptors dampening neurotransmitter release.

Cannabinoids and their receptors have also been localised throughout the retina suggesting a possible involvement of the cannabinoid system in retinal processing and vision. We investigated the effects of a cannabinoid agonist (WIN55212-2, 5\textmu M) on the spontaneous synaptic inputs and light responses in retinal ganglion cells (RGCs). Using patch clamp recordings in whole mount retina we found that cannabinoids reduce the release probability of inhibitory GABAergic transmission and excitatory glutamate transmission in both young and adult mouse retina.

These changes in release probability lead to changes in the light response of RGCs as cannabinoids reduced the centre excitation and surround inhibition and also narrowed the range of contrast sensitivity. These results suggest that the endocannabinoid system in the retina behaves as a modulator of synaptic transmission, similar to its function in other areas of the brain and likely has a role in the visual system.

10. “RELATION OF KONIOCELLULAR PATHWAY ACTIVITY TO LOW FREQUENCY (DELTA) ELECTROENCEPHALOGRAM POWER IN ANAESTHETISED MARMOSETS”

Pietersen A.N.J\textsuperscript{1,2,3}, Munn B\textsuperscript{5}, Cheong S.K\textsuperscript{1,2,3}, Townsend R\textsuperscript{5}, Gong P\textsuperscript{5}, Solomon S.G\textsuperscript{1,4}, and Martin P.R\textsuperscript{1,2,3}

\textsuperscript{1} ARC Centre of Excellence in Vision Science, The University of Sydney
\textsuperscript{2} Save Sight Institute, The University of Sydney
\textsuperscript{3} School of Medical Sciences, The University of Sydney
\textsuperscript{4} Institute of Behavioural Neuroscience, University College, London
\textsuperscript{5} School of physics, The University of Sydney

Purpose: We previously reported that some neurons in intercalated (koniocellular, KC) layers of the lateral geniculate nucleus (LGN) show high variability in maintained discharge rate that is inversely correlated to low frequency power in the electroencephalogram (EEG) in primary visual cortex (V1) \cite{1}. Here we investigate the source of this variability, specifically its time-relation to low frequency EEG.

Methods: LGN neuron extracellular spikes (n=107) and local field potential from V1 were recorded in sufentanil-anaesthetised marmosets (\textit{Callithrix jacchus}, n=12). The visual stimulus was a uniform grey field \textasciitilde 15 degrees square at 50 Cd/m\textsuperscript{2}. Granger causality analysis was performed on LGN neuron maintained discharge rate and V1 delta frequency EEG strength. Phase of KC neuron spikes relative to cortical delta oscillations were calculated by filtered Hilbert transform of V1 data. Data are expressed as mean\pmSD.

Results: KC neurons showed significantly higher maintained discharge rate variance (36.83\pm46.72, n=37) compared to Parvocellular (9.13\pm9.84, n=45) and Magnocellular (12.55\pm15.19, n=25) neurons. Granger causality analysis of 25 epochs from 7 KC neurons showed that power in delta EEG is better in predicting firing rate in LGN (1.28\pm0.13) than LGN firing rate is in predicting delta EEG power (0.91\pm0.1, p=0.027). LGN spikes occur during any phase of V1 delta frequency oscillation with equal probability.

Conclusion: These results indicate that decreases in delta frequency oscillation strength in the primary visual cortex precede increased activity in LGN KC layers. LGN spikes are not phase locked to V1 delta frequency oscillation.

\cite{1} Cheong S.K. et. al., (2011) PNAS 35, 14659-14663.
11. “RETINAL GANGLION CELLS PROJECTING TO THE KONIOCELLULAR SUPERFICIAL (K1) LAYER OF THE LATERAL GENICULATE NUCLEUS IN MARMOSET MONKEY”

Percival KA, Martin PR, Grünert U

1 Save Sight Institute, University of Sydney, Australia
2 Australian Research Council Centre of Excellence in Vision Science, University of Sydney, Australia

Purpose: Retinal projections to the K3 layer of the koniocellular (KC) division of the dorsal lateral geniculate nucleus (LGN) have been shown to represent a distinct pathway dominated by small bistratified and large sparse ganglion cells (Szmajda et al., 2008). Here, we show evidence for further segregation of pathways within the KC layers.

Methods: Ganglion cells were retrogradely labeled from tracer injections into the LGN of anaesthetised marmosets (Callithrix jacchus). Retrogradely labeled cells were photofilled (Dacey et al., 2003) to reveal their dendritic morphology. Morphological characteristics of ganglion cells (dendritic field diameter, branch density and stratification level within the inner plexiform layer) were quantified.

Results: We have identified a group of ganglion cells that is unique to injections that included the K1 layer. These cells were similar in dendritic field diameter to parasol ganglion cells from comparable eccentricities. The K1 layer projecting cells differed from parasol cells in that they exhibited more densely branching dendritic trees and numerous spine-like protrusion. At eccentricities > 2.5mm the dendritic branch density of K1 projecting cells (435.6mm dendritic length per mm^2 SD 66.9mm, n = 9 cells) was on average 1.5 times larger than that of parasol cells (297.8mm SD 52.0mm, n = 5 cells, p < 0.002, Wilcoxon rank sum test).

Conclusions: K1 projecting ganglion cells show morphological characteristics distinct from previously described K3 projecting cells and parasol cells. This subdivision of morphologically distinct ganglion cell types to distinct KC layers may reflect a functional segregation of pathways within the KC layers.


Hsin-Hao Yu, Tristan A. Chaplin, Gregory W. Egan, David H. Reser, Katrina H. Worthy & Marcello G.P. Rosa

Physiology, Monash University

Patients who suffer from striate cortex (V1) damages can retain unconscious visual functions within the affected parts of their visual fields (“blindsight”). This condition is more commonly observed in patients who sustain lesions in their childhood; however, non-human primate studies of residual vision have primarily introduced lesions in adulthood. The physiological consequences of early-life V1 lesions remain largely unknown. To examine if younger brains have greater capacity for reorganization and repair, we characterized the response properties of neurons in the Middle Temporal area (MT, a major recipient of V1 efferents), and the lateral geniculate nucleus (LGN, a major source of V1 afferents) in five marmoset monkeys with partial unilateral V1 lesions placed within 6 postnatal weeks. Unlike in adult-lesioned marmosets, where a portion of MT neurons can be found to respond weakly to stimuli presented in the scotomas, virtually all neurons in the deafferented region of MT showed robust responses to visual stimulation. Response strength and latency for neurons with receptive fields outside the scotomas were similar to those with receptive fields inside. In addition, the normal visuotopic organization of MT was maintained. However, direction selectivity, a key physiological characteristic of MT which is known to be preserved in many cells following adult V1 lesions, was absent. LGN neurons in the degenerated zone responded robustly to visual stimuli, with normal-sized receptive fields following the canonical LGN visuotopy and layer-specific eye-dominance. The results suggest that LGN could be a source of MT activation in the absence of V1.
ABSTRACTS, INVITED SPEAKERS JUNE 28

Professor Emeritus Donald Mitchell

Complete Darkness Promotes Fast Recovery From Amblyopia In Kittens

*Dr Donald Mitchell* is a Lifetime Professor Emeritus at Dalhousie University. He was initially trained as an optometrist in Melbourne but finding himself too young to earn the respect of patients, was urged to begin a research career while he matured in appearance. With a modicum of success he has been trying to grow up ever since. He obtained his PhD at the University of California (Berkeley) followed by a postdoctoral position at Florida State University. He has been at Dalhousie University since 1970 apart from 2 years as Foundation Director of the National Vision Research Institute in Melbourne (1978-80). His colleague, Dr Kevin Duffy is Associate Professor at Dalhousie University. He received his PhD from McMaster University followed by postdoctoral research at Harvard University where he worked with Drs David Hubel and Margaret Livingstone.
AMBLYOPIA, STRABISMUS AND CORTICAL PROCESSING OF DISPARITY

Complete darkness promotes fast recovery from amblyopia in kittens

Abstract

Donald E. Mitchell and Kevin Duffy

Department of Psychology & Neuroscience, Dalhousie Univ., Halifax N.S., Canada

Prompted by observations that short periods of darkness reverse maturation of stable cytoskeletal components in the kitten visual cortex, we examined whether darkness might effectively reset the cortex to a more plastic state. To explore this possibility, we examined whether a 10 day period of complete darkness could alter the speed or extent of recovery from an early period of monocular deprivation (MD). In a recent paper (Curr. Biol. 23: 382-386, 2013) we reported on the effects of a 10 day period of darkness imposed either immediately after a 1 week period of MD imposed on 30 day old kittens, or else 5 to 8 weeks later. Surprisingly, kittens placed in darkness immediately after MD at first appeared blind in both eyes but over the next 50 days vision in both eyes improved gradually but at all times a the same pace to reach normal acuity levels. The vulnerability of the vision of the non-deprived eye to the effects of darkness appears restricted to the first 2 postnatal months. When darkness was imposed 5-8 weeks after the period of MD there was no immediate effect on the vision of either eye but thereafter the vision of the deprived eye improved rapidly to attain normal acuity in only 5-7 days. This rapid elimination of the amblyopia in the deprived eye was unaccompanied by any reduction in the vision of the fellow eye. We now report that darkness eliminates amblyopia in kittens for which MD was imposed from eye-opening and to at least 8 weeks of age and that shorter periods (5d) of darkness are ineffective. About 1/3 of the kittens that acquire normal visual acuity in each eye develop stereoscopic vision. We propose that darkness may alter levels of various key molecules, including neurofilament protein, that serve as part of a “braking” system that progressively limits plasticity in the developing visual cortex. It is possible to contemplate the use of “darkness therapy” as an adjunct to treatment of human amblyopia.
Dr Jonathan C. Horton is the William F. Hoyt Professor of Ophthalmology at the University of California, San Francisco. He received his undergraduate degree at Stanford University, where he majored in medieval history. In 1984 he received an MD and PhD from Harvard University, where he was a graduate student in the laboratory of Dr. David H. Hubel and Dr. Torsten N. Wiesel. The title of his PhD dissertation was “Cytochrome Oxidase Patches: A New Cytoarchitectonic Feature of Primate Visual Cortex”. He completed a medical internship and one year of neurology residency at Massachusetts General Hospital, followed by an ophthalmology residency at Georgetown University and a fellowship in Neuro-Ophthalmology and Pediatric Ophthalmology at UCSF. He has been a faculty member in the Departments of Ophthalmology, Neurology, and Physiology at UCSF since 1990. His current research is focussed on strabismus, using clinical, psychophysical, physiological, and anatomical methods to investigate this disease.
AMBLYOPIA, STRABISMUS AND CORTICAL PROCESSING OF DISPARITY

Visual Suppression in Strabismus

Abstract

Jonathan C. Horton
Program in Neuroscience, UCSF, San Francisco, CA USA

Misalignment of the eyes can lead to double vision and visual confusion. However, these sensations are rare when strabismus is acquired early in life, because the extra image is suppressed. To explore the mechanism of perceptual suppression in strabismus, the visual fields were mapped dichoptically in human subjects with exotropia. The maps showed a vertical border between the center of gaze for each eye, splitting the visual field into two separate regions. In each region, perception was mediated by only one eye, with suppression of the other eye. Unexpectedly, stimuli falling on the fovea of the deviated eye were seen in all subjects. However, they were perceived in a location shifted by the angle of ocular deviation. This plasticity in the coding of visual direction allows accurate localization of objects everywhere in the visual scene, despite the presence of strabismus. To test the impact of visual suppression on neuronal activity in primary (striate) visual cortex, the pattern of cytochrome oxidase staining was examined in macaques raised with exotropia. No ocular dominance columns were visible in opercular cortex, where the central visual field is represented, indicating that signals coming from the central retina in each eye were perceived. However, the border strips at the edges of ocular dominance columns appeared pale, reflecting a loss of activity in binocular cells from disruption of fusion. In calcarine cortex, where the peripheral visual field is represented, there were alternating pale and dark bands resembling ocular dominance columns. To interpret the cytochrome oxidase staining pattern, [3H]proline was injected into the right eye. In the right calcarine cortex, the pale cytochrome oxidase columns matched the labeled proline columns of the right eye. In the left calcarine cortex, the pale cytochrome oxidase columns overlapped the unlabeled columns of the left eye in the autoradiograph. Therefore, metabolic activity was reduced in the ipsilateral eye’s ocular dominance columns which serve peripheral temporal retina, in a fashion consistent with the topographic organization of suppression scotomas in the visual fields of humans with exotropia.
**Professor Guy Orban**

*Cortical processing of higher-order disparity signals*

*Guy A Orban, MD, Ir, PhD* is an invited professor at The University of Parma and a holder of an advanced ERC grant (2013-2018). His current research focuses on the visual processing of observed actions and the role of parietal cortex therein. He was associate professor, professor and full professor at the medical school of the K.U. Leuven from 1976-2011 and part-time professor at the LUC from 1987-1999. During his years in Leuven he developed fMRI in the alert monkey and parallel imaging in human and non-human primates, and discovered the gradient selective neurons in various cortical areas (MT/V5, FST, TEs, AIP). He was invited Professor at l'Ecole Normale Supérieure, Paris, from 2003-2010 and held the European Chair of the Collège de France 2006-2007. He was a Visiting Fellow, John Curtin School Medical Research Canberra, in the fall of 1975, when he did a post-doctoral with PO Bishop and a research assistant and senior research assistant of the National Fund for Scientific Research (Belgium), 1970-79.
AMBLYOPIA, STRABISMUS AND CORTICAL PROCESSING OF DISPARITY

Cortical processing of higher-order disparity signals

Abstract

Guy A. Orban

Department of Neuroscience, University of Parma, Italy

The cortical processing of disparity is often restricted to the extraction of stereoscopic depth. Here we explore two higher-order aspects of disparity processing: the extraction of 3D shape and 3D kinematics. The extraction of 3D shape from disparity is relatively well understood (GA Orban Ann. Rev. Neurosci. 2011). The neuronal mechanism involves disparity-gradients selective neurons coding for first and second order gradients of depth in parietal, temporal and premotor cortex. Parallel imaging in human and non-human primates indicates that such neurons are located in a widespread network of temporal, parietal and premotor regions of human cortex. The extent of this network might be one of the reasons why this function is far less affected by degeneration in posterior cortical atrophy than 3D shape from other cues. More recently we have investigated the processing of 3D kinematics in the human brain, which involves ventral premotor cortex. This premotor activation is consistent with a role of these regions in action understanding and imitation. Indeed stereopsis is needed to recover 3D kinematics and relative 3D position of body parts given that monocular cues do not operate well on non-rigid bodies.
Associate Professor Erica Fletcher

The significance of purines in degenerative conditions of the retina

A/Prof. Fletcher is an Associate Professor and Reader in the Department of Anatomy and Neuroscience, where she heads the Visual Neuroscience Laboratory. She is a clinically trained optometrist who holds both MSc and PhD degrees. A/Prof Fletcher’s interest in the mechanisms of photoreceptor degeneration stem back to her doctoral studies, which were completed under the supervision of Prof Michael Kalloniatis at the University of Melbourne. In 1996, Dr Fletcher was awarded a highly coveted, CJ Martin Award from the NH&MRC to undertake her post-doctoral training with Prof. Dr. Heinz Wässle, at the Max-Planck Institute for Brain Research in Frankfurt, Germany. She joined the Department of Anatomy and Neuroscience as a lecturer in 2003. In 2006 she was awarded the Irvin M and Beatrice Borish Award from the American Academy of Optometry for her contribution to vision research. Dr Fletcher’s research interests remain primarily focused on understanding the causes of retinal diseases.
RETINA AND EYE: DEVELOPMENT, DEGENERATION, METABOLISM

The significance of purines in degenerative conditions of the retina

Abstract

Erica L Fletcher¹, Kirstan A Vessey¹, Andrew Jobling¹, Una Greferath¹, Ben Gu², James S Wiley², Robyn H Guymer³
¹Department of Anatomy and Neuroscience, ²Florey Neurosciences Institute, ³Centre for Eye Research Australia, The University of Melbourne, Victoria Australia

Age-related macular degeneration (AMD) is a leading cause of blindness in people over 50 years of age. Early signs of AMD include thickening of Bruch’s membrane, a basement membrane located beneath the retina, and the presence of deposits, called drusen, that develop between the RPE and Choroid. Advanced disease is characterized by death of photoreceptors and pathological growth of blood vessels into the retina. Our data implicates the purinergic receptor, P2X7 in the regulation of photoreceptor function and integrity as well as the development of early AMD. Our work shows that photoreceptors and immune cells of the retina, called microglia, express P2X7 receptors. Loss of P2X7 function attenuates retinal function. Inheritance of loss of function single nucleotide polymorphisms of P2X receptors was found to increase risk of developing advanced forms of AMD in a cohort of patients. Moreover, our studies show that aged P2X7null mice develop drusen-like deposits across the retina, thickening of Bruch’s membrane and concomitant photoreceptor dysfunction and loss. In view of the importance of P2X7 in regulating the function of immune cells, we next examined whether dysfunction in immune cells was associated with the development of early signs of AMD. Transfection of HEK293 cells with a truncated form of P2X7R (the same truncation as expressed in P2X7null mouse) showed significantly reduced phagocytosis compared with wildtype cells. The ability of macrophages isolated from patients with AMD to phagocytose fluorescently labeled beads was also reduced. These results implicate loss of function in P2X7 receptors in the development of early AMD and suggest that loss of phagocytosis by immune cells could play an important role. In particular, when the normal mechanisms that remove debris from base of the retina are impaired, abnormal deposition of debris may occur, leading to the formation of drusen and other signs of disease.
Professor Tailoi Chan-Ling

Dark Rearing (DR) as a means of mimicking ‘Physiological Hypoxia’: A rationale for non-invasive treatment of Retinopathy of Prematurity (ROP)

Tailoi Chan-Ling, M Optom, PhD NH&MRC Principal Research Fellow & Professor of Neurobiology and Visual Science, The University of Sydney; Secretary - International Society for Eye Research; Executive Leadership Group, Bosch Institute; Member – International Liaison Committee for Microcirculation; Council Member – World ROP Congress. Tailoi is a glial-vascular neurobiologist with special interest in astrocytes, pericytes and human neural stem cells. She has a record of contribution to the understanding of the molecular and cellular mechanisms in the formation of the retinal and choroidal vasculature

RETINA AND EYE: DEVELOPMENT, DEGENERATION, METABOLISM

Dark Rearing (DR) as a means of mimicking ‘Physiological Hypoxia’: A rationale for non-invasive treatment of Retinopathy of Prematurity (ROP)

Abstract

Tailoi Chan-Ling¹, Samuel J. Adamson¹, Rita Maccarone², Mark Koina³, Jennifer Lau⁴, Peter Kozulin⁵, Riccardo Natoli⁵, Jan Provis⁵, Silvia Bisti², Robert A. Linsenmeier⁴

¹.Retinal & Developmental Neurobiology Laboratory; Bosch Institute; The University of Sydney; 2. Biomedical & Science Technology, University of L’Aquila, Italy; 3. ACT Pathology, Canberra Hospital, Garran ACT; 4. Department of Biomedical Engineering, Northwestern University, Evanston IL, USA; 5. ARC Centre of Excellence In Vision Science, Australian National University, Canberra, Australia

At birth, the lungs of premature infants lack surfactants, and as a result are less effective at supplying the oxygen needs of the infant. As a consequence, premature infants are treated with oxygen to protect the
developing brain from damage. The initiating event in the pathogenesis of ROP is when the infant is placed in the high oxygen tension required to protect the brain from damage. However, because the choroid has a limited autoregulatory ability, the inner retina becomes flooded with oxygen. These higher-than-normal levels of oxygen result in a down-regulation of hypoxia-induced vascular endothelial growth factor (VEGF), the stimulus for normal retinal vascular formation. Reduction in VEGF expression reduces the density and rate of formation of the retinal vasculature, such that when infants are no longer requiring oxygen supplementation for their vital function, the formation of retinal vasculature is mismatched to that required by the metabolic demand of the neurons, resulting in tissue hypoxia and pathological vaso-proliferation. Our rationale behind dark rearing (DR) is that total darkness results in continuous depolarization of the photoreceptors, which requires an energy (oxygen) intensive repolarisation. As the energy consumption in the tissue would thus be doubled, so would the oxygen consumption and this induced “physiological hypoxia” would restore VEGF levels and normal blood vessel development.

To test this hypothesis, Sprague-Dawley rat pups were DR from birth to postnatal day 30, (P30) and under hyperoxic conditions (55-60 or 70-75% O2) with and without DR, and sacrificed at regular intervals. Retinas were examined for vascular density index; pericyte and astrocyte ensheathment, transmission electron microscopy (TEM); and VEGF & hypoxia inducible factor-1α (HIF1α) expression. Retinal function was assessed using functional electroretinogram (fERG) in P18 & P30 DR rats versus rats in 12hr light/dark cycle. P30 was selected to represent the likely upper limit of DR required for a premature infant. Recovery group rats were returned to cyclic light at P30 and recorded at P60 & P90.

Our results showed (see poster by Adamson S. et al.,) that DR rats raised in room air had significantly higher blood vessel density compared to age-matched controls. For all groups, average b-wave amplitudes from DR rats vs, dark/light cycle rats were not significantly different. DR protects vessels from oxygen-induced vasoobliteration without harmful effects on normal microvascular cell interactions (as evidenced by normal astrocytic and pericytic ensheathement), retinal morphology (as studied using TEM) and visual function (as assessed by fERG). DR also attenuates increased VEGF that normally leads to pathological vasoproliferation after hyperoxia exposure in ROP.

We suggest that DR precludes the initiation of ROP, offering a viable, noninvasive treatment for prevention of ROP and that DR could serve to supplement other strategies to minimise the damaging effect of retinopathy of prematurity. This is timely, given the push for clinical adoption of anti-VEGF therapy for ROP, where possible systemic effects are not fully investigated.
Professor Jan Provis

The Macula, Vascular Patterning And The Fovea

Jan Provis is Professor of Anatomy and Associate Dean in the Medical School at The Australian National University (ANU), and Associate Director of the ARC Centre of Excellence in Vision Science. She is Chair of Retina Australia’s Grants Assessment Committee, and member of the Scientific Advisory of the Ophthalmic Research Institute of Australia. Jan commenced her research career as Post-Doctoral Fellow at the University of Sydney Department of Clinical Ophthalmology in 1980, studying development of the human retina. Between 1988 and 2003 she was a lecturer, senior lecturer and Associate Professor in Anatomy at the University of Sydney, while maintaining an honorary position in the Department of Clinical Ophthalmology studying development and aging of the primate retina. Jan moved to the ANU in 2004, where she has focused on identification of the genes that regulate development of human central retina, and the factors that destabilize central retina and promote AMD. Jan’s work provides a broad perspective on how the macular / foveal part of the primate retina has evolved, how it develops, the molecular factors involved, the functional constraints, and why the macula is vulnerable to degeneration. She has co-edited a major text on Macular Degeneration and participates in a number of national and international collaborations.
RETINA AND EYE: DEVELOPMENT, DEGENERATION, METABOLISM

The macula, vascular patterning and the fovea

Abstract

Jan M Provis

ARC Excellence in Vision Science, John Curtin School of Medical Research and ANU Medical School, The Australian National University, Canberra, ACT.

The fovea centralis is specialization of the central retina that is associated with high acuity vision. The word ‘fovea’ is Latin for ‘pit’ - a depression in the surface of the retina. But what advantages does the pit per se confer on central vision, and how does it come about? Furthermore, are the adaptations associated with the fovea in any way linked to our vulnerability to macular degeneration? The use of new generation optical coherence tomography (OCT) has facilitated gathering of information on the morphometry of the macula and fovea in a very large sample of the population, revealing greater diversity in foveal morphology than was understood from a relatively small sample of histological specimens. In combination with molecular analyses, and data from preterm infants scanned using hand-held OCT devices, we are now beginning to understand the diversity of appearances of the fovea, and the impact of both genes and the neonatal environment on its development. We now know that during development, definition of an avascular area is a prerequisite for formation of a fovea. Furthermore, it appears that the molecular factors that define the avascular area leave the adult macula dependent on a microvasculature that is vulnerable to inflammatory events.
Professor Sheila Crewther

Myopia- An Ion Driven Response To Physiological And Oxidative Stress

Dr Sheila Crewther began her studies in Science at Melbourne University then moved to the US to complete her PhD in Neuroscience at Caltech under Nobel Prize Winner Professor Roger Sperry in 1978. Sheila has professional qualifications in Psychology, Education and Optometry and these underlie her continuing research into the cognitive and behavioural neuroscience of neuroplasticity in neurodevelopmental and neurodegenerative anomalies. The aim is to use this knowledge to design better therapeutic and behavioural management regimes. Currently Dr Crewther is the Professor of Neuroscience at La Trobe University, Melbourne.
RETINA AND EYE: DEVELOPMENT, DEGENERATION, METABOLISM

Myopia- an ion driven response to physiological and oxidative stress

Abstract

Sheila Gillard Crewther

School of Psychological Science, La Trobe University, Melbourne

Myopia is the most common visual disorder worldwide, is increasing dramatically in prevalence and is a significant risk factor for many sight threatening diseases, yet its aetiology is unclear. Epidemiological studies in low vision and unselected school populations have highlighted the influence of environmental and lifestyle factors in the development of refractive errors while application of multiple clinical and biological techniques [biometrics, electrophysiology, ultrastructure, elemental microanalysis, immunology, molecular and most recently transcriptome gene expression] in chicks have led to development of the Retinal Ion Driven Efflux Model (RIDEM) of Myopia. Ultrastructure and elemental microanalysis have provided evidence of severe but reversible physiological and oxidative stress that is demonstrable as systematic osmoregulatory changes in the pattern of ion and protein distribution across the 3 layers of the eye with refractive status and during recovery. Comparison of our recent chick transcriptome results with those of a very recent series of meta-analyses of a number of Genome Wide Association Studies in human myopia are in close agreement and further implicate oxidative stress in the visual cycle, ion driven solutes, metabolic and cytoskeleton changes, and DNA damage in the development of the abnormally large eyes with thinned choroid and retina that characterize clinical myopia. Such gene expression results validate the chick model and further suggest a basis for therapeutic management.
After his retirement from the Dept. of General Zoology and Neurobiology Klaus-Peter Hoffmann is Senior Professor at the Dept. of Neuroscience at the Ruhr-University in Bochum, Germany and Guest-Professor at the Neurophysics Group at the Phillips University in Marburg, Germany. He received his PhD degree in Natural Science from the Ludwig-Maximilians-University in Munich 1970 and his Habilitation from the same University in 1974. From 1970 to 1972 he was a post-doc in Peter O. Bishop’s laboratory in Canberra, Australia. His main research interest is the comparative neurobiology of cortical and subcortical interactions in the organisation of visuo-motor behaviour like eye-movements and reaching. This includes the analysis of brain functions in trained monkeys and human subjects but also work on organotypic cell cultures and brain slices. He was chairman of the review Committee and of the Council of Scientists of the Human Frontier Science Programme. From 1990 to 1992 he was President of European Brain and Behaviour Society. His work has contributed to the understanding of the parallel pathways in the visual and visuo-motor system.
EYE MOVEMENTS AND FORM AND MOTION VISION

Old Brain – New Brain In(ter) Action

Abstract

Klaus-Peter Hoffmann

Department of Neuroscience, Ruhr University Bochum, Bochum, Germany

Two examples will be discussed to illustrate the importance of interactions of cortical and subcortical areas in the sensori-motor system of mammals, in particular primates. A key visual structure for gaze stabilizing reflexes like the optokinetic reflex is the nucleus of the optic tract (NOT) in the pretectum. In the adult it receives direct input from direction selective ganglion cells and from movement sensitive cortical areas like area MT/MST. During the ontogenetic sequence retinal terminals arrive first and drive the neurons in NOT in its specific direction selective manner. During a sensitive period inputs matching this direction selective subcortical template are selected from cortical visual areas. It will be shown that any disturbance during this sensitive period will severely disrupt the establishment of proper binocular integration for a symmetric optokinetic reflex.

In a second example the cortical subcortical interaction for eye-hand coordination during target reaching will be elucidated. A possible neuronal substrate for gaze anchoring at the target reached for lies in the rostral superior colliculus (SC) whereas the caudal part of the SC is involved in target representation for saccades and reaching. The SC neurons involved in saccades receive input mainly from the cortical frontal eye field whereas the neurons involved in reaching receive input from the dorsal premotor area.
Dr Austin Roorda

How The Eye Sees A Stable And Moving World

Austin Roorda received his Ph.D. in Vision Science & Physics from the University of Waterloo, Canada in 1996. In his postdoctoral appointment at the University of Rochester, he used the world's first adaptive optics ophthalmoscope to measure the properties of human photoreceptors, which included generating the first-ever maps of the trichromatic cone mosaic. From 1998 to 2004, he was at the University of Houston College of Optometry, where he designed and built the first Adaptive Optics Scanning Laser Ophthalmoscope (AOSLO). Since January 2005, he’s been at the UC Berkeley School of Optometry where he is the current chair of the Vision Science Graduate Program. He is a Fellow of the Optical Society of America and of the Association for Research in Vision and Ophthalmology and is a recipient of the Glenn A. Fry award, the highest research honor from the American Academy of Optometry. His current research involves the development and use of adaptive optics and other advanced technology for clinical and basic applications.
EYE MOVEMENTS AND FORM AND MOTION VISION

How the eye sees a stable and moving world

Abstract

Austin Roorda

University of California, Berkeley, United States of America

Human eyes, even while fixating, are in constant motion. Even though the range of this motion can be much larger than the smallest features that we can resolve, we are unaware of it. At the same time, we remain exquisitely sensitive to actual motion of objects in the world with an ability to detect motion that is smaller than a single foveal cone. Results from experiments and simulations suggest that this adaptation is not a way to cope with uncontrolled eye motion, but is actually a mechanism intended to optimize spatial vision.
**Professor Colin Clifford**

*Functional Imaging Of Human Visual Cortex*

*Prof Colin Clifford* is Professor of Experimental Psychology at The University of Sydney and a Chief Investigator of the ARC Centre of Excellence in Vision Science. He received his doctorate in Psychology in 1997 from University College London followed by a post-doctoral position in Biomedical Engineering at Boston University and a Macquarie University Research Fellowship. He has held ARC fellowships continuously since 2002 and is currently an ARC Future Fellow. His research is presently funded by grants from the ARC and NHMRC and focuses on vision, how context affects our perception, and how our visual awareness might be related to the underlying neural processing.
EYE MOVEMENTS AND FORM AND MOTION VISION

Functional imaging of human visual cortex

Abstract

Colin Clifford

School of Psychology, University of Sydney, Australia

Functional magnetic resonance imaging offers a window into the activity of specified areas in the human brain in its normal state. But what has it told us that we could not have predicted from earlier electrophysiological studies on other mammals? I will review three sets of findings. First, the response of areas as early as V1 is modulated by global patterns of complex form. In contrast, single neurons in V1 of anaesthetized macaque have been reported to show no such modulation (Smith, Bair & Movshon, 2002). Second, information about conjunctions of different visual attributes such as colour and direction-of-motion is available as early as V1. In contrast, recordings from V1 of the awake macaque reveal a paucity of cells showing joint selectivity for colour and motion (Horwitz & Albright, 2005). Third, human area V4 is located entirely in ventral visual cortex, rather than being split between ventral and dorsal as in the macaque (e.g. Gattass, Sousa & Gross, 1988). Taken together, these findings indicate certain aspects of vision where we should be cautious in extrapolating the results of animal studies to human. Work currently underway is investigating whether the activity of human V1 is modulated by complex patterns of motion as well as form, and to what extent the coding of feature conjunctions in early visual areas is correlated with the perceptual binding of those features.
Emeritus Professor Liam Burke

Does The Moon Affect Visual Acuity?

Liam Burke is an Emeritus Professor of Physiology in the University of Sydney. He was recruited to the Department of Physiology by Peter Bishop in 1956 and is still in the same department as an Honorary member. He was introduced to the study of visual physiology by Peter Bishop and has not been able to escape that topic.
NEW HORIZONS

Does the Moon affect visual acuity?

Abstract

Liam Burke, Dave F. Davey and Johahn Leung

Department of Physiology, University of Sydney, Australia

Of course, the Moon contributes to ambient luminance and therefore influences vision. However, it also has two indirect effects on vision. The visual acuity of an eye affected by macular oedema is highest at the time of the full moon and lowest at the time of the new moon. A second indirect effect occurs in both oedematous and normal eyes when there is a coincidence of a lunar quarter and a zero lunar declination. At this time the effect may be an increase in visual acuity or a decrease. Such a coincidence occurs rarely, only once a year for each quarter. How does the Moon produce these effects? For the first (luminance) effect it is not necessary to be viewing the Moon at the time at which the acuity is measured, i.e. the Moon is not acting directly on the retina. In many animals reproduction is dependent on the full moon and is mediated via the endocrine system. Oestrogen is released at the full moon and is associated with ovulation and with increased permeability of the endothelial epithelium. We suggest that a similar mechanism occurs in the oedematous eye. Macular oedema is due to increased permeability in the blood-retinal barrier and, if it is similar to the blood-brain barrier, it will be affected by oestrogen. However, whereas oestrogen increases the permeability of the endothelium, it decreases the permeability of the blood-brain barrier. A decrease in the permeability of the blood-retinal barrier would reduce the oedema and would improve acuity. Reproduction in at least one primate (Lemurs) is dependent on the full moon and it is thought that this may also have been the case in humans in the more distant past. The second indirect effect of the Moon, at the lunar quarters, is such a rare event (once or twice a year) that it can have no physiological importance, so it is likely to be something inherited evolutionarily. Many invertebrates spawn only once a year and obviously this is important for the survival of their species. In some cases, e.g. some corals, there is a coincidence of quarter and zero declination. In other cases, e.g. some crinoids, there is a coincidence of quarter and maximum declination. In human vision it is possible that the influence is gravitational, because at the quarters the gravitational effect in the oceans is minimal (neap tides) and in the atmosphere gravity is maximal at the zero declination. However, whether gravity can affect vision, and if so what the mechanism is, remains unclear.
Emeritus Professor Jack Pettigrew

The Mystery of Bradshaw Rock Art

Jack Pettigrew is Emeritus Professor of Physiology at the University of Queensland. Trained in Medicine, he practiced briefly but returned to the laboratory as a result of an inspiring and productive stint with PO Bishop, who supplied a brilliant world-leading lab. environment and a key instrument, a Risley bi-prism, with which to scoop two Nobel Laureates in the field. Jack spent 10 years in the US, at Caltech, where he worked on the visual and auditory systems of owls and on developmental plasticity of kitten visual cortex, which he showed with colleagues was dependent on the diffuse, executive, monoaminergic system. For the last thirty years he has been Professor of Physiology at the University of Queensland, where he established the Vision Touch and Hearing Research Centre, an ARC Special Research Centre that became renowned for its diverse range of studies in comparative neuroscience. Mysterious Bradshaw rock art is a multi-disciplinary retirement project.
NEW HORIZONS

The Mystery of Bradshaw Rock Art

Abstract

Jack Pettigrew

Queensland Brain Institute, University of Queensland, Australia

Bradshaw rock art is a distinctive, finely-delineated style that is narrowly localized to the Kimberley region of NW Australia, with the oldest examples even more localized to the NW coast. The distribution of art corresponds to the distribution of boabs (Adansonia gregorii), the only species of baobab tree found outside of Africa and Madagascar, and which is depicted in the art. Molecular genetics of boabs show that they are recent arrivals in Australia, at 70,000 years ago, when the migrations of modern humans out of Africa began, making it likely that the Bradshaw culture brought baobabs from Africa and so must also be 70,000 years old. The art itself is difficult to age, because it is uniquely composed of a biofilm of black fungi and crimson cyanobacteria whose replenishment vitiates radiocarbon measurements. Molecular genetics of the microorganisms supports an ancient age, but precision dates are elusive because there is no accurate knowledge of the mutation rates of these new species of microbes. Calibration of the time scale of the molecular trees of fungi and cyanobacteria may be made possible using Uranium series dating from the rare cases where art has a mineral skin. No human artefacts have ever been unearthed beneath the art. Moreover, the distribution of boab haplotypes around the coast suggests that they must have dispersed on the floodplain before this was inundated at the end of the last Ice Age. Other evidence supports a picture of a Pleistocene culture living on a fertile, well-watered floodplain, with wandering, trained-artist shamans visiting the elevated escarpment for spiritual painting.
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1. “DARK REARING (DR) AS A MEANS OF MIMICKING ‘PHYSIOLOGICAL HYPOXIA’: RATIONALE FOR NON-INVASIVE TREATMENT OF RETINOPATHY OF PREMATURITY (ROP)”

Samuel Adamson1, Rita Maccarone2, Mark Koina3, Jennifer Lau4, Peter Kozulin5, Riccardo Natoli6, Jan Provis6, Silvia Bisti2, Robert Linsenmeier4, and Tailoi Chan-Ling1

1 Bosch Institute
2 University of L’Aquila, Italy
3 ACT Pathology, ACT
4 Northwestern University, USA
5 ARC CoE In Vision Science, ANU

ROP is a leading cause of infant blindness, with current treatments invasive and only used in late stage disease. We examined DR as an intervention to attack the cause of the disease, rather than the symptoms. ROP is initiated by hyperoxia-induced regression of retinal vasculature via VEGF down-regulation. We hypothesized that neonates in high-O2 environments should be subject to total darkness, causing a “metabolic sump”, driven by continuous ion currents in the photoreceptor outer segments. To test this hypothesis, SD rat pups were raised in room air ± DR from birth to postnatal day 30, (P30) and under hyperoxic conditions (55-60% or 70-75% O2 from P0 to P4, then returned to room air/normal light) with and without DR and sacrificed at regular intervals from P4 to P30. Additional litters were raised in DR or normal light under the Penn model of ROP (50% to 10% O2, switching every 24 hours from P0-P14), with 4 days recovery in room air/normal light then sacrificed at P18. Retinas were examined for vascular density index (VDI); pericyte/astrocyte ensheathment, transmission electron microscopy (TEM) & VEGF expression. Retinal function was assessed using electoretinogram in P18 & P30 DR rats versus rats in cyclic light, and a recovery group returned to cyclic light from DR at P30 with electoretinograms recorded at P60 & P90. P30 was selected to represent the likely upper limit of DR required for premature infants. We showed that DR-room air rats had significantly higher blood vessel density compared to controls (VDI = 43±1.0 vs. 38±1.1 p<0.05), and that DR protects vessels from oxygen-induced vaso-obliteration at P7 under 55-60% O2 (VDI = 29 ±1.1 v 28 ± 1.3 p=0.05) and protects from harmful effects on normal microvascular cell interactions as shown by near normal mural cell ensheathment via NG2 and SMA immunohistochemistry. DR also attenuates increased VEGF that normally leads to pathological vasoproliferation post hyperoxia in ROP. We have shown that DR is neuroprotective, as evidenced by evaluation of retinal cell ultrastructure via TEM in a 50/10% O2 model of ROP, and that long term DR has no detectable effects on retinal function, as evidenced by no statistical difference (p=0.005, n=6 for all groups) in b-wave amplitude in DR and normal light rats at P30 and P90, and no detectable effects on retinal cell morphology through ultrastructural evaluation of long-term (P90) DR rats and controls via TEM.

2. “TRANSMEMBRANE DOMAIN NRG1 MUTANT MICE SHOW ALTERED NEUROBEHAVIOURAL RESPONSES TO THC EXPOSURE IN A CONDITIONED PLACE PREFERENCE PARADIGM”

Clarke, David4,5; Low, Jac Kee.1,2,3; Karl, Tim1,2,3 and Arnold, Jonathon C. 4,5

1 Schizophrenia Research Institute, Darlinghurst, NSW, Australia
2 Neuroscience Research Australia, Randwick, NSW, Australia
3 School of Medical Sciences, University of New South Wales, Sydney, NSW, Australia
4 Brain and Mind Research Institute, Sydney, NSW, Australia
5 Department of Pharmacology, University of Sydney, NSW, Australia

Background and Aims: Our work in mice has shown that the schizophrenia candidate gene neuregulin 1 (Nrg1) modulates schizophrenia-relevant neurobehaviours actions of cannabinoids. A recent human study showed single nucleotide polymorphisms in NRG1 significantly increased the risk of developing cannabis dependence.

Method: To test whether the Nrg1 modulates the rewarding effects of cannabinoids, we tested male heterozygous Nrg1 mutant (Nrg1 HET) mice and wild type-like littermates (WT) in the conditioned place preference (CPP) paradigm for their neurobehavioural response to repeated Δ9-tetrahydrocannabinol (THC, 5 mg/kg i.p. on alternate days, 10 days). Changes in chamber preference were assessed to elucidate the rewarding effect of THC. After which the brains were stained for ΔFosB, a marker of long-term neuroadaptive changes.

Results: A significant aversion to THC was found in the Nrg1 HET mice that was not observed in THC-treated WT mice. Several reward and motivation related brain regions such as the dorsal lateral septum, the medial preoptic area and the medial amygdala postdorsal, showed significant differences in the number of ΔFos B positive cells.

Conclusion: Nrg1 mutation appears to increase the aversive nature of repeated THC exposure.
3. “NEURAL POPULATION DYNAMICS CHANGE PERCEIVED ORIENTATION”

Maria del Mar Quiroga¹, Adam P. Morris¹,², and Bart Krekelberg¹

¹ Center for Molecular and Behavioral Neuroscience, Rutgers University, Newark, NJ, USA
² National Vision Research Institute, Australian College of Optometry, Carlton, Victoria

Recurrent connections are known to play a role in the coding of orientation in primary visual cortex (e.g. for contrast invariance) but many questions remain regarding their precise functional role and possible byproducts. Previously, we implemented a recurrent model of orientation selectivity and tested responses to pairs of gratings presented briefly in succession (adapter and test). The model generated repulsive shifts in tuning curves that matched those found experimentally in V1. Unlike the shifts produced with long adaptation periods (thought to underlie the tilt after-effect [TAE]), which are well accounted for by plasticity, the repulsive shifts we observed were the result of slow population dynamics only. These effects on tuning curves gave rise to attractive shifts in the population response towards the adapter, suggesting that perception of the test orientation should be biased towards the adapted orientation. To test this prediction, we asked human subjects to determine which of two Gabors (test and reference) presented simultaneously for a short period of time (≤100 ms) at either side of the fixation dot was tilted more clockwise. Crucially, the test was preceded by another oriented Gabor (adapter) in the same location (≤100 ms), while the reference was preceded by a non-oriented pattern matched for contrast and spatial frequency. Both test and reference were succeeded by non-oriented patterns to reduce afterimages. The psychometric curves exhibited significant shifts consistent with an attraction of perceived orientation of the test towards the adapter. The observed effect matches the predicted effect of population dynamics, and is opposite in direction to the more commonly studied TAE. Population dynamics therefore affect the coding of information and behavioral responses at fast timescales and can produce adaptation-like effects even without any form of neural plasticity.

4. “SUPERPARAMAGNETIC IRON OXIDE NANOPARTICLES EXPOSURE TO HUMAN NEURAL STEM CELLS PRE-DISPOSE THEM TOWARD THE ASTROCYTIC LINEAGE AND HAS THE POTENTIAL TO INFLUENCE CELL MIGRATORY CAPABILITY”

Steven Eamegdool¹, Binh Pham², Michael Weible II³, Saeed Shahhossein Dastjerdi¹, Brian Hawkett², and Tailoi Chan-ling²

¹ Department of Anatomy, Bosch Institute, University of Sydney
² Key Centre for Polymers and Colloids, School of Chemistry, University of Sydney
³ Biomolecular and Physical Sciences, Griffith University

Current therapies involving stem cell transplantation have remained ineffective due to lack of spatial integration of stem cells into the sites of injury. Monitoring their survival, migration, localization and differentiation after infusion by Magnetic Resonance Imaging (MRI) can greatly enhance their clinical application. This study investigated the biological impact of introducing our customized superparamagnetic iron oxide nanoparticles (SPIONs) into human fetal neural stem cells (hNSCs), in terms of viability, iron loading capacity, cellular differentiation and migratory capability. This will permit future studies involving MRI tracking of labeled hNSCs in vivo and their utilization in cell-based therapies.

The SPIONs were synthesized and stabilized with short chain steric block copolymers. Rhodamine B was used to label 5% of the stabilizer molecules. Super-resolution microscopy was used to determine SPION intracellular location. Cell viability was assessed using MTT assay, Click-iT EdU kit, and Muse cell analyser. Iron uptake was determined using Graphite Furnace Atomic Absorption Spectrometry. Cells were subjected to immunocytochemical staining, and visualised with confocal microscopy to determine hNSC lineages. Light microscopy was used to determine cell migration.

Our results showed that SPIONs were observed throughout the cytoplasm, but concentrate within the nucleus after 24 hrs, 5 – 20 µg/mL. Extended exposure to NPs (beyond 3 days, at 10 µg/mL) caused a reduction in hNSCs migratory capacity by 62.5%, however, exposure to NPs for 24 hr, below 20 µg/mL, did not detrimentally affect hNSCs viability and migration. Finally, exposure to SPIONs resulted in an increased number of astrocytes, from 20% to 32%.

The biological effects of nanoparticles on the stem cell population of interest need to be determined prior to their application in cell transplantation therapies. We found that hNSC labeled with NPs exhibited an increased differentiation towards the astrocytic lineage and decreased migratory capacity with prolonged exposure.
5. P2X7R-MEDIATED PHAGOCYTOSIS IN DEVELOPING CENTRAL NERVOUS SYSTEM.

Michael D. Lovelace\textsuperscript{1,2}, Ben Gu\textsuperscript{3}, Steven Eameddool\textsuperscript{1,2}, James S. Wiley\textsuperscript{3}, David G. Allen\textsuperscript{2,4}, Michael W. Weible II\textsuperscript{1,2,5}, and Tailoi Chan-Ling\textsuperscript{1,2}

\textsuperscript{1}Discipline of Anatomy and Histology, Sydney Medical School, The University of Sydney, Sydney, New South Wales, Australia
\textsuperscript{2}Bosch Institute, The University of Sydney, Sydney, New South Wales, Australia
\textsuperscript{3}Florey Institute of Neuroscience and Mental Health, University of Melbourne, Melbourne, Australia
\textsuperscript{4}Discipline of Physiology, Sydney Medical School, The University of Sydney, Sydney, New South Wales, Australia
\textsuperscript{5}Biomolecular and Physical Sciences, Griffith University, Queensland, Australia

Department of Anatomy and Histology, University of Sydney, NSW, 2006

Clearance of apoptotic cells is essential in the early development of the central nervous system (CNS) but the receptors mediating this process have not been identified. Recently we have shown a role for P2X7 as a scavenger receptor for apoptotic cells in a serum-free, non-inflammatory environment. Using immunocytochemical staining and functional assays, we demonstrated the presence of functional P2X7 on the surface of cultured human neural precursor cells (hNPCs). The commitment to the neuronal lineage was associated with a reduction to P2X7 responsiveness. We identified a population of neuronal precursors that highly expressed P2X7 receptors and doublecortin (DCX) and were found to have phagocytic capability. Phagocytosis experiments utilizing both fluorescent yellow-green bead and apoptotic human neuronal cells as targets showed preincubation with ATP, which inhibits the phagocytic function of P2X7, reduced uptake of both targets by the DCX\textsuperscript{high}/P2X7\textsuperscript{high} neuronal progenitors. These experiments suggest that neuronal progenitors utilize P2X7 receptors as scavenger receptors for the clearance of apoptotic cells from the developing CNS.

6. “INFLUENCE OF IMAGE TEXTURE ORIENTATION RELATIVE TO MOTION DIRECTION ON RESPONSE OF PRIMATE AREA MT NEURONS AND HUMAN PERCEPTION”

Saba Gharaei\textsuperscript{1}, Chris Tailby\textsuperscript{2}, and Samuel G. Solomon\textsuperscript{1,3}

\textsuperscript{1} Discipline of Physiology, Bosch Institute and ARC Centre of Excellence in Vision Research, University of Sydney
\textsuperscript{2} Florey Institute of Neuroscience and Mental Health, Melbourne Brain Centre
\textsuperscript{3} Cognitive, Perceptual and Brain Sciences Research Department, University College London

We investigate how responses of neurons in marmoset MT and human perception depend on the orientation (and bandwidth) of image textures relative to their direction of motion. Extracellular single-unit recordings were made from area MT of anaesthetised (sufentanyl-forte, 9 µg/kg/hr) marmosets (n = 2). The stimulus was a texture with varying orientation bandwidth. Textures moved orthogonal, parallel or 45 degrees relative to the dominant orientation. Neurons were classified as ‘pattern cells’ or ‘component cells’ using standard techniques. Human observers (n = 7) reported the perceived motion direction of the same stimuli. Human participants accurately reported the correct motion direction when textures moved orthogonal or parallel to their dominant orientation. For oblique motion, participants reported directions intermediate to the true direction and that orthogonal to the dominant orientation. Neuronal responses depended on cell class. In 5 pattern cells direction-tuning curves were unimodal for all textures. Preferred direction was the same for parallel and orthogonal motion direction, but for oblique was intermediate to the true motion direction and that orthogonal to the dominant orientation. In 8 component cells, responses were strong and unimodal for orthogonal motion, but weak and bimodal for parallel motion. For oblique motion, direction tuning curves were aligned to the dominant orientation of the textures. Response of pattern and component cells was similar for oblique and orthogonal motion but different for parallel motion. In neurons, and in human observers, oblique motion leads to characteristic inaccuracies in motion computations. Response of pattern cells to parallel motion was consistent with the reports of human observers.
7. “CNS INFLAMMATION AND BONE MARROW NEUROPATHY IN TYPE 1 DIABETES”

Ping Hu¹, Jeffrey S. Thinschmidt¹, Yuanqing Yan², Sugata Hazra³, Ashay Bhatwadekar³, Sergio Caballero³, Tatiana Salazar⁴, Jaleel A. Miyan³, Yumei Feng⁴, Wencheng Li⁴, Andrei Derbenev⁴, Andrea Zsombok⁴, Maria Tikhonenko⁵, Susan P. McGorray⁶, Daniel R Saban⁷, Michael E. Boulton⁸, Julia V Busik⁵, Mohan K. Raizada⁹, Tailoi Chan-Ling⁴* and Maria B. Grant²*

*The senior authors contributed equally to this manuscript

¹ Department of Anatomy, Bosch Institute, University of Sydney, Australia
² Department of Pharmacology and Therapeutics, University of Florida, Gainesville, FL
³ Faculty of Life Sciences, The University of Manchester, Manchester, United Kingdom
⁴ Department of Physiology, Tulane University, New Orleans, LA
⁵ Department of Physiology, Michigan State University, East Lansing, MI
⁶ Department of Biostatistics, University of Florida, Gainesville, FL
⁷ Department of Ophthalmology, Duke University, Durham, NC
⁸ Department of Anatomy and Cell Biology, University of Florida, Gainesville, FL
⁹ Department of Physiology and Functional Genomics, University of Florida, Gainesville, FL

Using pseudo rabies virus expressing green fluorescence protein, we found that efferent bone marrow-neural connections trace to sympathetic centers of the central nervous system (CNS) in normal mice but that this was markedly reduced in type 1 diabetes (T1D) suggesting a significant loss of bone marrow innervation. This loss of innervation was associated with a change in hematopoeisis towards generation of increased numbers of monocytes as well as an altered diurnal release of monocytes in T1D rodents and patients. In the hypothalamus and granular insular cortex of T1D mice, bone marrow derived microglia/macrophages were activated and found at greater density than in controls. Infiltration of CD45⁻/CCR2⁻/GR-1⁻/Iba-1⁻ bone marrow derived monocytes into the hypothalamus could be mitigated by treatment with minocycline, an anti-inflammatory agent capable of crossing the blood brain barrier. Our studies support the need to target central inflammation in the management of T1D.

8. “ENCODING OF DEPTH FROM OCULAR SIGNALS IN THE MEDIAL PARIETAL CORTEX OF MACAQUES”

Kostas Hadjidimitrakis¹,², Giacomo Placenti³, Federica Bertozzi², Rossella Breveglieri², Annalisa Bosco³, Marcello Rosa¹ and Patrizia Fattori²

¹ Department of Physiology and Monash Vision Group, Monash University
² Department of Pharmacy and Biotechnology, University of Bologna

Interacting in the peripersonal space requires coordinated arm and eye movements to visual targets in depth. In primates, the medial posterior parietal cortex (PPC) represents a crucial node in the process of visual-to-motor signal transformations. The medial PPC area V6A is a key region engaged in the control of these processes because it jointly processes visual information, eye position and arm movement related signals. However, to date, there is no evidence in the medial PPC of spatial encoding in three dimensions. Here, using single neuron recordings in behaving macaques, we studied the neural signals related to binocular eye position in a task that required the monkeys to perform saccades and fixate targets at different locations in peripersonal and extrapersonal space. A significant proportion of neurons were modulated by both gaze direction and depth, i.e., by the location of the foveated target in 3D space. The population activity of these neurons displayed a strong preference for peripersonal space in a time interval around the saccade that preceded fixation and during fixation as well. This preference for targets within reaching distance during both target capturing and fixation suggests that binocular eye position signals are implemented functionally in V6A to support its role in reaching and grasping.
9. “DECODING EYE-POSITION SIGNALS IN PRIMARY VISUAL CORTEX”

Adam P. Morris¹,² and Bart Krekelberg¹

¹ Center for Molecular and Behavioral Neuroscience, Rutgers University, Newark, NJ, USA
² National Vision Research Institute, Australian College of Optometry, Carlton, Victoria

Visual input would be of little use if not accompanied by knowledge of eye position; indeed, it is the combination of these signals that allows the brain to localise and interact with objects meaningfully. Eye-position signals have been observed throughout visual cortex – including the primary visual area (V1) – but little is known about how well such signals represent the eye during different types of oculomotor behavior. To examine the representation of eye-position in macaque V1, we recorded the extracellular activity of multiple neurons simultaneously as the animal performed sequences of fixations, saccades, and smooth-pursuit eye movements. Throughout the task, the neurons were stimulated visually by a flickering noise stimulus. Consistent with previous reports, we found that many neurons showed systematic modulations of visually-evoked activity by the position of the eyes in the orbit (i.e. 'gain fields'). These modulations occurred similarly during fixation and smooth pursuit. To assess the dynamics, accuracy, and reliability of these eye position signals, the neural data from each trial were decoded (using maximum-likelihood estimation) to provide moment-to-moment estimates of eye position. The results show that the representation of eye position is accurate during fixation and updated rapidly in response to eye movements (within 50-100ms). These findings suggest that V1 carries a robust representation of eye position and is therefore likely to provide a useable head-centric representation of visual space.

10. “CELL CYCLE CHANGES IN WEST NILE VIRUS-INFECTED HUMAN RETINAL PIGMENT EPITHELIUM”

L. Munoz-Erazo¹, M.C. Madigan², and N.J.C. King¹

¹ Pathology, Bosch Institute, University of Sydney, Sydney, NSW, Australia
² Optometry & Vision Science, University of NSW, Kensington, NSW, Australia

Ocular complications in West Nile Virus (WNV)-infected humans can lead to degradation of the outer blood-retinal barrier, comprising the retinal pigmented epithelium (RPE) and junctional complexes. Functional impairment of this barrier can impair vision.

In a previous microarray study of WNV-infected primary human RPE (hRPE), we found a number of cell-cycle-related genes were upregulated. To further investigate these changes, in the current study we investigated the effects of WNV infection on RPE cell cycle gene expression, and DNA content of RPE cell line ARPE-19 (using flow cytometry). Additionally, we investigated the effects of WNV infection on RPE migration and proliferation using scratch wound assays. Cell cycle related genes found to be upregulated >2-fold included ID1, DDIT3 and PML. For RPE monolayers a statistically significant decrease (p<0.05) in wound closure time was found 24-hours post WNV infection when compared with uninfected monolayers (n=4). Flow cytometry showed statistically significant decreases (p<0.05) in G1/G0 and increases in S-phase in WNV-infected cells at 48 and 72 hours post infection (n=4). Furthermore, at 48 hours post-infection, G2/M was decreased. Interestingly, increased numbers of WNV⁺, NS1⁺ cells were observed in the G2/M phase, compared NS1⁻ cells.

These observations suggest that WNV infection modifies the migration, proliferation and cell cycle characteristics of hRPE cells. Whether this is the result of soluble factors produced by WNV-infected hRPE (such as IFN-β1), or a replication/survival strategy by WNV, is unknown and is currently under investigation.
11. “MECHANISMS OF GLUCOSE DEPRIVATION-INDUCED SENSITIVITY TO NOVEL ANTI-METABOLITES IN MULTI-DRUG RESISTANT CANCER CELLS”

Nicole Seebacher, Patric J. Jansson, and Des R. Richardson

Iron Metabolism and Chelation Program, Department of Pathology, University of Sydney, Sydney, New South Wales, 2006, Australia

The efficacy of chemotherapeutics on cancer cells has been severely limited by P-glycoprotein (P-gp)-induced drug resistance. During glucose starvation, an increase in cancer cell sensitivity to our novel di-2-pyridylketone thiosemicarbazone (DpT) iron chelators (PNAS 2006;40:14901-6) was observed. As cancer cells exhibit an altered metabolism characterised by elevated glycolysis they exist in a limited glucose state (Cell 2008;134:703-707). These studies aimed to elucidate the mechanisms involved in DpT iron chelator-mediated cellular toxicity during glucose-deprivation.

One week of glucose starvation significantly (p<0.001) increased sensitivity of P-gp expressing cells to DpT chelators (>3 fold decrease in IC50), while remaining resistant to other chemotherapeutics. In contrast, glucose-deprivation did not affect the sensitivity of non-P-gp expressing cells. This effect was reversible by P-gp inhibition using the selective P-gp inhibitors, Valspodar and Elacridar. Within two hours of glucose starvation, translocation of NFκB to the nucleus occurred and this observation coincided with an increase in oxidative stress. This was followed by an increase in HIF-1α expression. After one week of glucose starvation, there was an increase in P-gp expression and activity and this occurred only in cells expressing HIF-1α.

Glucose-deprivation caused P-gp expressing cells to have increased sensitivity to DpT iron chelators. This effect was not observed in cells not expressing P-gp. The increased sensitivity was caused by a HIF-1α-dependent increase in the expression of P-gp. Initial studies examining NFκB translocation to the nucleus suggested its involvement in the activation of HIF-1α following activation by oxidative stress. This investigation provides insight into the improved efficacy of DpT chelators under conditions of glucose-deprivation that are commonly found in tumors.

12. “CORRELATES OF MOTION DEFINED SURFACE SEGREGATION IN EARLY HUMAN VISUAL CORTEX”

Gabriel J. Vigano, Ryan T. Maloney, and Colin W. G. Clifford

School of Psychology and ARC Centre of Excellence in Vision Science, University of Sydney

Surface perception is a fundamental component of vision, providing an efficient way to identify and distinguish between objects in the world. Surface segregation is a relatively fast process which can aid in binding features, which has traditionally been identified as a slow process. For example, a stimulus alternating in two visual features simultaneously (eg. colour and motion) at a high alternation rate appears transparent. Both sets of features persist simultaneously and the pairing can be easily identified. However, at a slower alternation rate, the representation of multiple surfaces breaks down and consequently, the feature binding task becomes difficult. In this experiment, we investigated feature-based surface transparency through fMRI and found that perceptual transparency was correlated with neural activity in early visual areas. Arrays of grey dots moving clockwise and counter-clockwise were displayed in strips which reversed direction at two alternation rates (15Hz and 5Hz). In the transparent condition, strips contained dots rotating in opposite directions. In the alternating condition, all strips contained dots rotating in the same direction. At the fast alternation rate, the transparent and alternating displays were indistinguishable, and this was reflected in the univariate and multivariate pattern analysis of the BOLD responses. However, there was a large difference between the displays at the slower alternation rate. This resulted in a significant interaction effect in the univariate analysis of the % change in BOLD response in several low level visual areas.
13. “IMMUNOHISTOCHEMICAL IDENTIFICATION AND CHARACTERIZATION OF A MID-FIELD AMACRINE CELL TYPE IN MARMOSET RETINA”

Felix Weltzien$^{1,2}$, Stefano Di Marco$^3$, Dario A. Protti$^3$, Teresa Daraio$^1$, Paul R. Martin$^{1,2,3}$, and Ulrike Grünert$^{1,2}$

$^1$ Department of Ophthalmology and Save Sight Institute
$^2$ Australian Research Council Centre of Excellence in Vision Science
$^3$ School of Medical Sciences, The University of Sydney, Australia

Amacrine cells are the most diverse class of retinal neurons. In primates more than 25 different types of amacrine cell have been described. Here, we analysed the morphology, density and distribution pattern of a subset of amacrine cells that express the Ca$^{2+}$ binding protein secretagogin in the marmoset (Callithrix jacchus) retina. Retinas were either subjected to standard immunohistochemistry or pre-labelled with an antibody specific for secretagogin and subsequently immunopositive cells were injected with Dil. Secretagogin immunoreactivity was present in mid-field amacrine cells with somata in the inner nuclear layer (79%), as well as displaced amacrine cells with somata in the ganglion cell layer (21%). The somas of regular and displaced amacrine cells together form a regular mosaic suggesting that they form a single population. Secretagogin positive cells have a peak density of 585 cells/mm$^2$ in central retina, which decreases to 55 cells/mm$^2$ in peripheral retina. In the inner nuclear layer secretagogin positive cells make up 0.3% of the total amacrine cell population. Co-immunostaining indicates that secretagogin immunopositive cells use GABA as their neurotransmitter. The processes of secretagogin positive amacrine cells were broadly stratified in the middle two thirds of the inner plexiform. DiI injection of individual cells revealed that these cells have dendritic trees, which are decorated with small spines and large varicosities. Our results suggest that secretagogin positive cells form a subpopulation of GABAergic amacrine cells, which reveal a close resemblance to the “spiny” amacrine cell described in macaque by Mariani (1990).

14. “CONTRAST-DEPENDENT PHASE SENSITIVITY OF COMPLEX CELLS IN MOUSE PRIMARY VISUAL CORTEX”

Molis Yunzah$^{1,2}$, Nathan A Crowder$^3$, Michael R Ibbotson$^{1,2}$, and Shaun L Cloherty$^{1,2}$

$^1$ National Vision Research Institute, Australian College of Optometry
$^2$ ARC Centre of Excellence in Vision Science, Department of Optometry and Visual Sciences, University of Melbourne
$^3$ Psychology Department, Dalhousie University Life Sciences Centre, Canada

The mammalian primary visual cortex (V1) consists of two classes of neurons: simple and complex cells. When presented with a moving sine-wave grating, phase-sensitive simple cells produce responses that oscillate in phase with the grating, whereas complex cells exhibit largely unmodulated responses. However, the phase-sensitivity of V1 neurons is not a fixed property. We have demonstrated in cats that the responses of a subset of complex cells become more phase-sensitive when the stimulus contrast is reduced. This phenomenon is consistent with a hierarchical model in which complex cells receive multiple simple cell inputs. We hypothesise that these simple cells exhibit different contrast response functions and that as contrast is reduced, inputs from simple cells with high contrast threshold ‘drop off’, resulting in more phase-sensitive responses produced by the remaining simple cell inputs. To test this hypothesis we examined the phase-sensitivity of the complex cells in mouse V1. We recorded extracellular spiking responses from 56 cells in mouse V1 while presenting drifting luminance modulated sine-wave gratings at 12 different contrasts. The phase-sensitivity of complex cell responses was then compared between different stimulus contrasts. We found that 18% of recorded complex cells showed significant negative correlations between contrast and phase-sensitivity (t-test, P < 0.001). Similar to our observations in cats, reducing stimulus contrast increases phase-sensitivity of a subset of complex cells in mouse V1. This adds to evidence suggesting that the mouse is a suitable model for investigating cortical visual processing.
15. “HIGHER-ORDER TEXTURE STATISTICS INFLUENCE AND ENABLE SEGMENTATION IN SYNTHETIC AND NATURAL TEXTURES”

Elizabeth Zavitz1,2 and Curtis Baker2

1 Physiology, Monash University
2 Ophthalmology, McGill University

Localization and characterization of boundaries based on discontinuities in the retinal image is an important function of early vision. In addition to boundaries defined by luminance, the visual system can segment more complex boundaries defined by texture properties such as contrast and orientation. However there is evidence that early visual processes are influenced by more complex texture properties as well. Here, we manipulated the higher-order texture properties of sparseness, global phase structure and local phase structure using synthetic micropattern textures designed to mimic properties of natural textures. We measured separately the extent to which these higher-order statistics influenced and enabled boundary segmentation by testing human psychophysical observers on a two-alternative forced-choice orientation judgment. We found that a texture’s global phase structure and sparseness, impaired segmentation of boundaries defined by contrast or orientation. The presence or absence of local edge alignments, on the other hand, did not measurably affect segmentation performance. An energy model with two free parameters (decision noise and nonlinearity shape) explained performance for contrast and orientation boundaries when a compressive nonlinearity was employed. We found that human observers were able to segment boundaries defined by sparseness, but not those defined by local phase structure. Nevertheless, local phase structure did influence segmentation thresholds. The same model with parameters as fit previously predicted the statistics that enabled segmentation, but did not capture the influence of local phase structure. These results suggest that sparseness in particular is an important texture attribute, and that boundary segmentation includes some intermediate compressive process (such as normalization).

16. “SPATIAL DISTRIBUTION OF CORRELATED NEURONAL ACTIVITY IN MARMOSET LATERAL GENICULATE NUCLEUS”

Zeater N.1,2, Solomon S.G.1,3, Dreher B.3, Morley J.W.4,5, and Martin P.R.1,2,3

1 ARC Centre of Excellence in Vision Science, The University of Sydney
2 Save Sight Institute, The University of Sydney
3 School of Medical Sciences, The University of Sydney
4 School of Medicine, The University of Western Sydney
5 School of Medical Sciences, The University of New South Wales

Purpose: The fidelity of visual signals relaying through the dorsal lateral geniculate nucleus (LGN) are modified by stimulus independent correlated activity (‘noise correlations’) between neurons of the LGN. Here we asked whether noise correlations are spatially restricted or widespread in the LGN of marmoset monkeys (Callithrix jacchus).

Methods: Extracellular recordings of neuronal activity were made in the LGN of Sufentanil-anaesthetised adult marmosets (n = 2). We used a NeuroNexus 32 channel probe comprising two shanks separated by 0.4 mm; each shank has 16 recording points separated by 0.05 mm. Isolated single-cell activity from pairs of cells at three sites was recorded and noise correlation calculated. Recording sites in LGN were verified anatomically.

Results: Strength of noise correlation fell with distance between recording points in the range 0.1 - 1 mm. Noise correlations between sites driven by the same eye were stronger than noise correlations between sites driven by different eyes.

Conclusions: Noise correlations are propagated by at least 1 mm within marmoset LGN. Persistence (although weaker) of correlations at sites driven by different eyes suggests an extra-retinal source.
BOSCH INSTITUTE – KEY CONTACTS

EXECUTIVE DIRECTOR

Professor Jonathan Stone
E: jonstone@anatomy.usyd.edu.au
T: +61 2 9351 4740   F: +61 2 9351 6470

RESEARCH THEME LEADERS

CANCER, CELL BIOLOGY & DEVELOPMENT
Professor Des Richardson
E: des.richardson@bosch.org.au
T: +61 2 9036 6548   F: +61 2 9351 3429

CARDIOVASCULAR RESEARCH
Associate Professor Stuart Cordwell
E: stuart.cordwell@sydney.edu.au
T: +61 2 9351 6050  F: +61 2 9351 4726

INFECTION, IMMUNITY & INFLAMMATION
Professor Nicholas King
E: nicholas.king@bosch.org.au
T: +61 2 9351 4553  F: +61 2 9351 3429

NERVOUS SYSTEMS, SENSES & MOVEMENT
Associate Professor William Phillips
E: william.phillips@bosch.org.au
T: +61 2 9351 4598  F: +61 2 9351 2058

ORGAN & TISSUE REPLACEMENT
Dr Alexandra Sharland
E: Alexandra.sharland@bosch.org.au
T: +61 2 9351 2897 or +61 2 9515 5416  F: +61 2 9351 2058

ADMINISTRATION

CHIEF OPERATING OFFICER
Charean Adams
E: charean@medsci.usyd.edu.au
T: +61 2 9114 0567  F: +61 2 9351 8400

ADMINISTRATION ASSISTANT
Wannit Tongkao-on
E: wtong9162@uni.sydney.edu.au
T: +61 2 9351 5169  F: +61 2 9351 2510

Cindy Guy
E: cindy.guy@sydney.edu.au
T: +61 2 9351 2694  F: +61 2 9351 4229

Bosch Institute Administration Address
Room E214, Ground Floor, Anderson Stuart Building (F13)
The University of Sydney, NSW 2006
E: charean@medsci.usyd.edu.au
T: +61 2 9114 0567  F: +61 2 9351 8400

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