OPHTHALMOLOGY & VISUAL SCIENCES

29TH ANNUAL RESEARCH DAY

Keynote Speaker

Dr. Wallace Alward

A Thirty Year Journey with a Glaucoma Family
Changing the Way That We Teach

Monday, April 9
2018

The Westin Nova Scotian
8am-4pm

DALHOUSIE UNIVERSITY

nova scotia health authority

IWK Health Centre

29th Annual Research Day

Dalhousie University Department of Ophthalmology and Visual Sciences

0800	**Coffee, Tea and Registration**	
0830	**Opening Remarks and Introduction of the Keynote Speaker**	
0835	**Faculty of Medicine 150th Anniversary Address by the Dean of Medicine: Dr. David Anderson**	
0845	Dr. Lee Alward Keynote Speaker	A thirty year journey with a glaucoma family
0935	Dr. William Best	Dalhousie medicine – Undergraduate ophthalmology education – Targeted needs assessment
0950	Tareq Yousef	Melanopsin-immunoreactive neurons in the teleost retina
1005	Dr. Lucas Torres	Influence of Bruch's membrane opening area on OCT diagnostic accuracy
1020	Dr. Harald Gjerde	The utility of a *fzd4-/-* zebrafish model in the screening of novel treatments for familial exudative vitreoretinopathy (FEVR)
1035	***Break***	
1055	Dr. Wesley Chan	Transverse venous sinus stenosis on magnetic resonance imaging in patients with idiopathic intracranial hypertension – A pilot study
1110	Dr. Amit Mishra	Effects of cannabinoid CB1 receptor activation on retinal ganglion cell calcium and chloride dynamics
1125	Dr. Danielle Cadieux	A grounded theory study of self-directed learning approaches to operative education in senior surgical residents
1140	Dr. Corey Smith	Identifying repeatability measures of optical coherence tomography angiography
1155	***Lunch – Harbour Room***	
1300	Dr. Lee Alward Keynote Speaker	Changing the way we teach
1320	Dr. Tom Zhao	Azobenzene photoswitch BENAQ fails to restore vision in an acquired model of photoreceptor degeneration
1335	Dr. Brennan Eadie	Optical coherence tomography parameters distinguishing post-acute phase ischemic and glaucomatous optic neuropathies
1350	Justine Sy	Functional changes in retinal ganglion cell activity following light-induced retinal damage
1405	***Break***	
1425	Dr. Aishwarya Sundaram	Settle plate testing to measure air quality in a tertiary care ophthalmology department
1440	Delaney Henderson	Characterizing longitudinal ***in vivo*** changes of RGC in a model of experimental glaucoma
1455	Dr. Amr Zaki	Incidence and predictors of anxiety and pain associated with intravitreal injections
1510	**Closing Remarks**	
1515	**Wine and Cheese Reception and Award Presentations to Follow**	

Welcoming Remarks

Today's event marks the 29th Annual Research Day for the Department of Ophthalmology & Visual Sciences at Dalhousie University. The program reflects how research has grown and been fostered within the Department.

We are honored to welcome our Keynote Speaker and External Guest Judge, Dr. Wallace Alward, Professor and Vice-Chairman at the University of Iowa. Dr. Alward's talks are entitled: A Thirty Year Journey with a Glaucoma Family and Changing the Way We Teach.

Please enjoy today's presentations.

Research Committee
Department of Ophthalmology and Visual Sciences

Acknowledgements

The Department of Ophthalmology and Visual Sciences would like to thank the following individuals for serving as judges for the 29th Annual Research Day:

Dr. Wallace Alward
Department of Ophthalmology and Visual Sciences
University of Iowa
Iowa City, IA

Dr. Jayme Vianna
Department of Ophthalmology and Visual Sciences
Dalhousie University
Halifax, NS

Dr. Jeremy Murphy
Department of Ophthalmology and Visual Sciences
Dalhousie University
Halifax, NS

DALHOUSIE UNIVERSITY | MEDICINE 150 YEARS

Part of Dalhousie's Bicentennial Celebrations

For the past 150 years, Dalhousie Medical School has been a leading force in improving the quality and outcomes of patient care—through educating doctors and researchers, conducting ground-breaking research, taking innovations out of the lab and into our hospitals and communities, informing public policy, and advocating for forward-looking change. While we do have a tendency to look forward, the Dal Med 150 celebrations provide us with an opportunity to look back, to appreciate the vision and dedication of those who went before us to establish Dalhousie Medical School and help it grow into the renowned institution it is today.

We are delighted to welcome Dr. Wallace Alward as the Department of Ophthalmology and Visual Sciences Faculty of Medicine 150th Anniversary Keynote Speaker.

Dr. Wallace Alward, M.D.

Wallace L.M. Alward, M.D. completed his glaucoma fellowship at the Bascom Palmer Eye Institute. After fellowship he became Director of the Glaucoma Service at the University of Iowa where he is Professor and Vice-Chairman. He holds the Frederick C. Blodi Endowed Chair in Ophthalmology. Dr. Alward has coauthored more than 150 peer-reviewed papers. The main focus of his research over the past two decades has been the molecular genetics of glaucoma. He and his colleagues first described several glaucoma genes: myocilin, PITX2, FOXC1, and TBK1. He has authored two textbooks: Color Atlas of Gonioscopy and The Requisites: Glaucoma. He maintains two websites: one to teach gonioscopy (www.gonioscopy.org) and an introduction to glaucoma for residents (http://curriculum.iowaglaucoma.org). Dr. Alward served as a Director of the American Board of Ophthalmology from 2006 to 2013 and was Chair in 2012. In 2016 he received the inaugural Educator Award from the American Glaucoma Society.

DALHOUSIE MEDICINE – UNDERGRADUATE OPHTHALMOLOGY EDUCATION – TARGETED NEEDS ASSESSMENT

Best, W.[1,2], Belliveau, D.[1,2]

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Background: Ophthalmic complaints are common and cause thousands of visits to physicians yearly. Acquisition of core ophthalmic knowledge and skills is achieved primarily in medical school and a strong curriculum is necessary to prepare students for residency and beyond. However, there is evidence of decline in ophthalmic curriculum content across North America. At Dalhousie, the curriculum consists of a few classroom and skills sessions and no mandatory exposure in clinical years. This has lead to concern that students are underprepared for primary eye care headed into residency. Despite this perceived deficiency, there are no specific tools to assess the strengths and weaknesses of ophthalmology education at Dalhousie and how best to address them.

Purpose: The purpose of this project is to create and implement a comprehensive survey tool that can be used to: (1) identify core areas of deficiency in ophthalmic knowledge and clinical examination and (2) identify student preferences for method of educational delivery of ophthalmic knowledge.

Methods: A literature review and three focus groups with medical students at different stages of training were performed to inform the content of the targeted needs assessment. The survey was then distributed to all Dalhousie medical students currently enrolled (years 1-4) through the Dalhousie Opinio survey software. Data was categorized by year and basic statistics performed.

Results: The surveys collected from Dalhousie University medical students demonstrated the level of confidence of these students when it comes to performing core ophthalmologic skills and assessing various ocular conditions associated with mortality, acute morbidity, and chronic morbidity in relation to their current year of study.

MELANOPSIN-IMMUNOREACTIVE NEURONS IN THE TELEOST RETINA

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Purpose: The expression of the photopigment melanopsin has been well described as a feature of intrinsically photosensitive retinal ganglion cells (ipRGCs). ipRGC activity drives various functions, like circadian rhythms, and provides rudimentary visual information. In mammals melanopsin expression is restricted to ipRGCs while in the zebrafish (*D. rerio*) five teleost melanopsin genes were shown to be expressed in subpopulations of all retinal neuron types, suggesting multiple roles for melanopsin in the teleost retina. We are characterizing further the expression of melanopsin in goldfish (*C. auratus*) and zebrafish retinas. A focus of our current work is to determine if melanopsin is expressed by dopaminergic interplexiform cells (DA-IPCs). Given the role of dopamine as a signal of retinal light-adaptation, melanopsin expression could provide dopaminergic neurons with direct sensitivity to ambient light level.

Methods: Eyes were fixed in 2% paraformaldehyde and immunohistochemistry conducted on whole retinas or frozen sections. Tissue was labelled with one of two melanopsin antibodies: 1) pas350, raised against a 13-amino acid synthetic peptide sequence (CVPFPTVDVPDHA) corresponding to a highly-conserved region of 3 melanopsin proteins (opn4m-1, 2, and 3) or, 2) opn4a, a combination of multiple monoclonal antibodies raised against synthetic peptides corresponding to 3 regions (MMSGAAHSVRKG-TRIVESLSAWND-NDSVMSAYRLVD; TVTSQSSDMSGR-RTSTGKSRLSSA-SKDTAEMPDFKP; VGTNPARRDSRG-LSNAAETPESGH-ESGHIDNHRPQY) of the opn4m-1 protein. To determine if melanopsin is expressed by DA-IPCs, retinas were co-labelled with an antibody against tyrosine hydroxylase (TOH). Imaging was conducted using confocal microscopy.

Results: Both pas350 and opn4a labelled cell bodies and processes in all layers of the goldfish and zebrafish retina. Labelling included presumptive horizontal cells, bipolar cells, amacrine cells, and ganglion cells. We examined 131 TOH-immunoreactive (IR) interplexiform cells and in no case found co-labelling with melanopsin. However, TOH puncta were found opposed to melanopsin-positive somata, and *vice versa*, suggesting possible reciprocal connections between dopaminergic and melanopsin-IR neurons. Another key finding was distinct labelling of horizontal cell axon terminals (HATs) by pas350 in goldfish retina.

Conclusion: Melanopsin is wide-spread in the teleost retina but is not expressed by DA-IPCs. However, an alternative possibility is that melanopsin-IR neurons contact dopaminergic neurons, and *vice versa*. The significance of melanopsin-IR HATs is unclear but could provide clues about their functions, that at present are not known. It also remains to be determined if the somata to which HATs connect might themselves be melanopsin-IR.

This work is funded by an NSERC grant to WHB and a Mathers and NSHRF Scotia Scholar Award to TY.

INFLUENCE OF BRUCH'S MEMBRANE OPENING AREA ON OCT DIAGNOSTIC ACCURACY

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Department of Ophthalmology and Visual Sciences, Dalhousie University, Halifax, Canada; 2. Department of Ophthalmology, University of Campinas, Brazil. 3. Department of Ophthalmology, HCFMUSP, Sao Paulo, Brazil.

Purpose: OCT measurements of minimum rim width (MRW) and retinal nerve fibre layer thickness (RNFLT) depend on Bruch's membrane opening (BMO) area. Therefore, classifications ("within normal limits [WNL]", "borderline [BL], " and "outside normal limits [ONL]") are adjusted to account for BMO area. Our purpose was to determine if diagnostic performance of MRW and RNFLT normative classifications are still influenced by BMO area.

Methods: One eye of 182 open-angle glaucoma patients and 146 healthy control subjects were imaged with OCT (Spectralis, Heidelberg Engineering) to obtain global MRW and RNFLT measurements. Patients and controls were divided into tertile groups of BMO area (small, medium and large) and the proportion of subjects classified by the device as ONL, BL and WNL were analyzed with sensitivity and specificity analysis. BMO area correlations with MRW and RNFLT measurements were also determined.

Results: The median (interquartile range) age of the patients and controls was 71.2 (64.8 to 77.7) and 61.8 (47.0 to 68.0) years, while BMO areas were 1.8 (1.5 to 2.1) and 1.7 (1.5 to 2.0) mm^2, respectively. Visual field mean deviations for patients were -4.7 (-9.2 to -1.9), -3.6 (-7.3 to -1.7) and -3.7 (-8.6 to -1.5) dB for small, medium and large BMO areas, respectively (p=0.12). MRW ONL sensitivity did not change with increasing BMO area (59.0% to 52.5%, p=0.76, Fig. 1), but RNFLT ONL sensitivity increased significantly (59.0% to 80.3%, p=0.04). RNFLT ONL sensitivity was higher than MRW for the medium (p=0.04) and large BMO area groups (p<0.01). MRW and RNFLT WNL specificities were not significantly different for either BMO area subgroups (p>0.12) and did not vary with BMO area (p>0.28). The effect of BMO area on MRW measurements was 1.8 times higher in controls (-59.7 $\mu m/mm^2$) than in patients (-31.8 $\mu m/mm^2$), while this effect on RNFLT measurements was 11.4 times higher in controls (9.7 $\mu m/mm^2$) than in patients (0.8 $\mu m/mm^2$).

Conclusion: Unlike MRW, RNFLT ONL classification had a higher sensitivity to detect glaucoma in larger BMO areas. This higher sensitivity could be explained by the smaller effect of BMO area on the RNFLT in glaucoma patients, compared to controls.

THE UTILITY OF A *FZD4-/-* ZEBRAFISH MODEL IN THE SCREENING OF NOVEL TREATMENTS FOR FAMILIAL EXUDATIVE VITREORETINOPATHY (FEVR)

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Purpose: Familial exudative vitreoretinopathy (FEVR) is a rare, incurable genetic disorder characterized by reduced peripheral retinal vascularization during development. Visual impairment occurs in approximately 40% of eyes, typically during early childhood. About 50% of FEVR cases are due to a gene mutation disrupting the Norrin-FZD4 signaling pathway. We developed a *fzd4-/-* zebrafish model at Dalhousie University in the Berman Zebrafish Laboratory using TALEN technology, with the goal of efficiently screening compounds that ameliorate this vascular defect. Preliminary analyses show a disorganized retinal vascular phenotype present in *fzd4-/-* adult zebrafish, but not in larvae. We aim to develop an efficient approach to image the developing retinas and characterize the developmental profile of zebrafish that will enable medium-throughput drug screening.

Methods: Fluorescence-based microscopy requires the removal of pigment to image the retinal vasculature. In one group of fish, tyrosinase (tyr) mutations were introduced using CRISPR/Cas9 and single-guided RNA technology to remove the pigment. Retinal vasculature of the resultant mosaic tyr mutant- wildtype (WT) and *fzd4-/-* zebrafish were imaged using a Zeiss Lightsheet Z.1 microscope, and analyzed at 7 and 14 days post-fertilization (dpf) using Arivis and Imaris imaging software.

In a second group, the eyes of WT and *fzd4-/-* zebrafish at each week (post-fertilization weeks 1-8) were enucleated and placed in fixative. The retinas were removed, and the retinal vascular network fluorescing with GFP was imaged using a Zeiss Stereo Discovery V20 fluorescent stereomicroscope. ImageJ is used to analyze the images.

Vascular progression, vessel caliber and length, and location of disorganization will be compared between WT and *fzd4-/-* fish at progressive time points, and analyzed using standard error of the mean and P values calculated with one-way ANOVA unpaired t-test. Descriptive statistics will be used to assess vessel patterns in each quadrant.

Results: Preliminary images from the lightsheet microscope show normal development and no difference between WT and *fzd4-/-* zebrafish within 14 dpf. Injected zebrafish did not survive past 14 dpf to be imaged within the lightsheet microscope. In the developmental profile, images were obtained from weeks 1 to 8. Disorganization was seen by week 6 in the *fzd4-/-* fish compared to WT.

Conclusion: Vascular disorganization in the *fzd4-/-* zebrafish looked to appear around week 6. With further analysis, we hope to provide a valuable pre-clinical animal model that will facilitate comparing and evaluating therapeutic responses and vascular phenotypes between WT and *fzd4-/-* mutants, identifying new, prospective therapies for FEVR.

TRANSVERSE VENOUS SINUS STENOSIS ON MAGNETIC RESONANCE IMAGING IN PATIENTS WITH IDIOPATHIC INTRACRANIAL HYPERTENSION – A PILOT STUDY

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Purpose: Idiopathic intracranial hypertension (IIH) is a condition in which increased pressure within the head compresses the brain. This can result in irreversible vision loss and chronic severe headaches. IIH mainly affects overweight women of child-bearing age, many of whom are asymptomatic until they present with vision loss. Ocular examination often reveals optic disc swelling. Years after initial presentation, visual acuity continues to be affected in 20% of IIH patients, even following treatment, while 50% of patients have a visual field abnormality at an average of 18 weeks after instituting treatment.

There is currently no known cause for IIH; however, it has been noted that 90% of patients with IIH have transverse venous sinus stenosis (TVSS) seen on magnetic resonance venography (MRV) of the brain. Whether the venous stenosis has a causal relationship to IIH or is an effect of the increased intracranial pressures is controversial. This study aims to examine the feasibility of prospectively observing transverse venous sinus stenosis in patients with IIH from diagnosis, through treatment, and after treatment.

Methods: Patients diagnosed with IIH according to the Modified Dandy Criteria with evidence of TVSS on their MRI/MRV are recruited to the study. As part of standard of care, all IIH patients receive a MRI/MRV as well as a lumbar puncture as part of their diagnosis for IIH. To follow TVSS over time, participants undergo additional MRV immediately following lumbar puncture, 3-6 months after diagnosis when there has been resolution of IIH symptoms, and one year after diagnosis. Ophthalmological data, such as visual acuity, colour vision testing, documentation of papilledema with disc photographs, optic coherence tomography OCT of the optic discs and maculae, and Goldmann visual fields, are also collected at these follow-up time points. Feasibility data including patient recruitment barriers and logistical issues will also be recorded for protocol optimization.

Results: Since the beginning of patient recruitment in September 2016, 20 suspected IIH patients were screened by either ophthalmology or neurology. Of these 20 patients, 5 were successfully enrolled, 13 did not meet study eligibility criteria for various reasons, one declined participation, and one withdrew from the study. Of the 5 recruited patients, 3 have completed all their MRI/MRV imaging.

Conclusions: With optimized recruitment and study pathway, we successfully enrolled 5 IIH patients and await completion of their imaging studies.

EFFECTS OF CANNABINOID CB1 RECEPTOR ACTIVATION ON RETINAL GANGLION CELL CALCIUM AND CHLORIDE DYNAMICS

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Purpose: The endocannabinoid system has emerged as a potentially important mediator of physiologic and pathologic processes in the eye. Endocannabinoid signaling has been shown to enhance the intrinsic excitability of *Xenopus* retinal ganglion cells (RGCs) via reduction of intracellular chloride (Cl^-) concentration (Miraucourt et al., 2016). In the present work, we are investigating the effect of the CB1 cannabinoid receptor agonist WIN 55,212-2 on mammalian (rodent) RGCs intracellular calcium (Ca^{2+}) and Cl^- concentration using fluorescence microscopy ion imaging techniques. We hypothesized that CB1 agonist will 1) increase the excitability of RGCs, increasing intracellular Ca^{2+} concentration via voltage-gated calcium-channel activation, and 2) decrease intracellular Cl^- concentration, as observed in *Xenopus* RGCs.

Methods: Fluorescent microscope ion imaging was performed on isolated living mouse retinas. For Ca^{2+} imaging, mice that express a genetically-encoded calcium indicator in RGCs, the Thy1-GCaMP3 mouse line, were utilized. For Cl^- imaging we attempted to load RGCs with the membrane-permeable Cl^--indicator, MQAE. The retina was exposed via superfusion to both 50 µM WIN 55,212-2 and 50 µM kainate (an AMPA type glutamate receptor agonist, to mimic glutamatergic input to RGCs).

Results: Kainate produced a marked increase in GCaMP3 fluorescence in mouse retinal ganglion cells, indicating increased intracellular Ca^{2+}. Application WIN 55,212-2 did not alter baseline GCaMP3 fluorescence and attenuated subsequent responses to kainate, an affect that was in most cases not reversible. Attempts to load RGCs by incubation in MQAE have thus far proved unsuccessful.

Conclusion: The absence of an effect of WIN 55,212-2 on baseline Ca^{2+} level, and the reduction by WIN 55,212-2 of kainate-induced Ca^{2+} increases, is not consistent with an increase of RGC excitability by CB1 agonist. However, it has been demonstrated that CB1 agonist may, independent of any effect on RGC excitability, inhibit RGC voltage-gated calcium channels (Lalonde et al., 2006). Therefore, any enhancement of RGC excitability by WIN 55,212-2 may have been masked by inhibition of voltage-gated calcium channels. Intracellular Cl^- imaging studies will be pursued further by facilitating loading of MQAE using electroporation.

A GROUNDED THEORY STUDY OF SELF-DIRECTED LEARNING APPROACHES TO OPERATIVE EDUCATION IN SENIOR SURGICAL RESIDENTS

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Purpose: This study aims to explore the self-directed learning (SDL) practices of senior surgical residents with a focus on operative education. The complexity of the operating room (OR) creates a unique learning environment with multiple challenges for trainees. Surgical residents must be able to balance service requirements, interpersonal factors and time constraints with their educational needs. With the move towards competency based medical education, it is important to consider how surgical trainees acquire the knowledge and skills required to be successful in their residency programs. A model of SDL has been proposed in the context of internal medicine, however, a theoretical framework for surgical residents has yet to be described. The purpose of this study is to explore the social and psychosocial aspects of SDL behaviours of senior surgical residents as they prepare for learning in the operative environment.

Methods: Qualitative research methods will be used. Data will be collected using in-depth interviews with senior residents in surgical disciplines at Dalhousie, University. Interviews will be recorded, transcribed and analyzed using constructivist grounded theory (CGT) with sensitizing concepts from a "Person, Process, Context" model of SDL. All residents in surgical disciplines in post-graduate years 3-5 will be invited to participate. Participants will be asked questions about their thoughts, ideas and practices in relation to SDL when preparing for a day in the OR. Data analysis will involve an iterative process whereby data collection and analysis occur concurrently, with each informing the other. Through this process, the goal is to develop a theoretical model unique to SDL in surgical trainees.

Results/Expected Outcomes: We aim to describe the SDL practices of senior surgical residents surrounding operative education and develop and understanding of factors that may influence this variation. Data collection is expected to begin in Spring 2018 pending ethics approval. Results will be shared through presentations and peer reviewed literature over the next 2-4 years.

Conclusion: In order to support residents in their surgical education, it is valuable to first understand current practice. The value of the proposed study is that it will assess resident's personal and contextual factors that may impact the process of SDL in a surgical context. This understanding will allow residency programs to guide, support and provide feedback to surgical residents throughout their training regarding their SDL practices.

IDENTIFYING REPEATABILITY MEASURES OF OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY

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Purpose: Optical coherence tomography angiography (OCT-A) provides a functional measure of retinal perfusion. However, the repeatability, specifically physiological variability, statistical tools for analysis, and efficacy in patient populations have not been adequately investigated. The purpose of this work is to determine the short-term variability of OCT-A imaging in healthy subjects.

Methods: The Spectralis OCT2 (Heidelberg Engineering) was used to image blood flow patterns with OCT-A of 10 eyes from 5 healthy subjects (n=10). Each subject had a 15˚ x 15˚ scan pattern (384 x 768 lines) centered on the fovea repeated twice on the same day, the following day and approximately one month later for a total of 4 volume scans of the same region. Retinal layer segmentation was completed within the acquisition software and 2D projection images from slabs corresponding to the different vascular plexuses (superficial, intermediate, and deep) were exported. Analyses were performed in MATLAB to calculate perfusion density, vessel length, and number of branch points.

Results: The intraclass correlation coefficient between eyes was ≤ 0.6, indicating a poor relationship between paired measurements from the same subject. Therefore, all eyes were analyzed independently. The repeatability coefficients (limit within which 95% of measurements should be) for repeated imaging on the same day were: 0.04%, 0.02%, and 0.04% for perfusion density; 8798 pixels, 4591 pixels, and 6656 pixels for vessel length; and 525, 326, and 547 for branch points (superficial, intermediate and deep; respectively). The coefficients of variation (standard deviation / mean) in images had the following range across layers: perfusion density (4.28% - 4.77%); vessel length (4.44% - 8.64%); and branch points (9.98% - 16.30%).

Conclusion: We have found that there is greater variability in branch points, across all layers, than perfusion density and vessel length. The repeatability of these metrics is the highest in the intermediate capillary plexus. This work develops quantifiable measures and studies the repeatability in OCT-A images to better determine when retinal perfusion changes have occurred. This is an important step prior to implementing OCT-A imaging as a method for assessing disease progression.

AZOBENZENE PHOTOSWITCH BENAQ FAILS TO RESTORE VISION IN AN ACQUIRED MODEL OF PHOTORECEPTOR DEGENERATION

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Background: It has been demonstrated that the second generation azobensene photoswitch BENAQ has the potential to restore vision in the RD1 photoreceptor degeneration murine model by modulation of the retinal ganglion cells (RGCs) activity, but fail to do so in the wild type mice when RGCs are pharmacologically-isolated from photoreceptor activity. The high polarity of the molecule prevents its easy membrane permeation and thus requires the presence of large pores to penetrate the cells. P2X7 purinergic receptors, responsible for the formation of large membrane pores when excited, are present in the RGCs of the RD1 mouse model but not in the wild type mice. Since P2X7 receptor expression is associated with inflammatory processes, we explored whether BENAQ presents some potential to restore vision in a short-term acquired photoreceptor degeneration model.

Methods: Adult Brown Norway rats, 250-300 g, were injected with an intraperitoneal dose of sodium Iodate (SI), a neurotoxin inducing acute loss of retinal pigmentary epithelial cells and secondary photoreceptor degeneration 1-2 weeks post injection. Electroretinograms were acquired under anesthesia to quantify the photoreceptor loss. Craniotomies were performed over both occipital cortices and Visual Evoked Potentials (VEPs) were obtained for various stimulus conditions. This was followed by an intraocular injection of 2µl of BENAQ 100µM alone or in combination with BzATP (50µM), and VEPs were acquired up to 2 hrs post injection. At the end of the experiments, both retinae (injected and non-injected) were isolated and flat-mounted on a glass slide. They were exposed to YO-PRO, a large size nuclear dye that permeates the cellular membrane only when large pores are present, and counterstained with membrane-permeable dye Hoechst 33342.

Results: Intraperitoneal injections of Sodium Iodate were effective in inducing the required severe photoreceptor degeneration in 3/7 rats. In those rats, despite the reduced retinal activity, flash-VEP responses showed well-defined waveforms of large amplitude. Following MONOCULAR intraocular BANAQ injection (left eye), the computed interhemispheric VEP differences remained constant for more than two hours post injections. In one rat, BzATP was injected simultaneously with BENAQ and here again, the interhemispheric difference remained constant. Exposure of ex-vivo flat-mounted retina to YO-PRO fail to demonstrate any nuclear staining.

Conclusion: We demonstrate that BENAQ has very limited role in restoring vision in acquired photoreceptor dystrophies. This is likely due to differences in the expression and activation of P2X7 receptors in different disease models. We plan to use third-generation, non-polarized membrane-permeable photoswitches in the same conditions.

OPTICAL COHERENCE TOMOGRAPHY PARAMETERS DISTINGUISHING POST-ACUTE PHASE ISCHEMIC AND GLAUCOMATOUS OPTIC NEUROPATHIES

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Purpose: Post-acute phase ischemic and glaucomatous optic neuropathies are often difficult to distinguish. Our objective was to identify optical coherence tomography (OCT) parameters that may help distinguish these two entities.

Design: Cross-sectional study.

Participants: Twelve eyes from 8 patients with post-acute phase non-arteritic ischemic optic neuropathy (NAION) and 12 eyes from 12 patients with glaucomatous optic neuropathy (GON) matched for age (NAION: 66, GON: 67 years) and mean deviation (NAION: -19, GON: -21dB) with automated perimetry (Program 24-2, Humphrey Field Analyzer).

Methods: Patients with NAION underwent clinical assessment, perimetry, OCT imaging, and colour stereo disc photography. OCT imaging (Spectralis, Heidelberg Engineering, Anatomic Positioning System, Glaucoma Module) included a 3.5mm diameter peripapillary circular scan, 24 B-scan radial pattern centred on the optic nerve head, and 61 B-scan raster pattern centred on the macula. Sector analyses were conducted for all patients' nasal and temporal sectors and for superior and inferior sectors with an associated visual hemifield defect in both the NAION and matched GON patient. Paired Student's *t*-tests with Bonferroni correction were used for statistical analyses.

Main Outcome Measures: Data collected from each patient included peripapillary retinal nerve fibre layer (ppRNFL) thickness (global and 6 sectors), minimum rim width (MRW) thickness (global and 6 sectors), and segmented macular layers (total retina, retinal nerve fibre layer, ganglion cell layer, inner plexiform layer, inner nuclear layer, outer plexiform layer, outer nuclear layer, retinal pigment epithelium, inner layers, outer layers).

Results: The ppRNFL was thinner for patients with NAION than GON in the temporal sector (NAION: 39, GON: 50um; P=0.02). The MRW was thicker for patients with NAION in all sectors and globally (NAION: 297, GON 150um; P<0.001). Macular analyses revealed greater thinning centrally in the inner plexiform layer (IPL; NAION: 14, GON 17um; P=0.02), inner nuclear layer (INL; NAION: 19, GON 23um; P=0.02), and outer plexiform layer (OPL; NAION: 21, GON 30um; P=0.03).

Conclusion: Post-acute phase NAION and GON can be distinguished with OCT parameters. For an equivalent amount of visual field loss, NAION patients had thinner ppRNFL temporally, thicker MRW globally, and thinner central IPL, INL, and OPL layers of the macula.

FUNCTIONAL CHANGES IN RETINAL GANGLION CELL ACTIVITY FOLLOWING LIGHT-INDUCED RETINAL DAMAGE

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Purpose: The scotopic threshold response (STR) of the electroretinogram (ERG) corresponds to functional activity of the inner retina, with particular contributions from the retinal ganglion cells (RGCs). However, the large amplitudes of the a-wave and b-wave in the ERG often mask portions of the STR. Previous studies have used light-induced retinal degeneration (LIRD) to selectively cause photoreceptor death, revealing alterations in all ERG wave components. While reductions in the a-wave correlate to the expected loss of photoreceptors in LIRD, it is unclear whether STR reduction after LIRD is due to a loss of RGCs or if there are other underlying mechanisms. The aim of the present study was to examine functional (ERG) and structural (OCT) changes in the retina caused by LIRD to determine whether the effects of phototoxicity extend beyond photoreceptors in the retina.

Methods: C57/BL6 mice (n=4) were exposed to high-intensity light (22,000 lux) for 12 hours. Mydriasis was induced with 1% atropine. Retinal thickness (OCT, Spectralis, Heidelberg Engineering) and ERGs were recorded prior to LIRD (Baseline) and then followed weekly. Changes in a-wave, b-wave and STR amplitudes were reported relative to corresponding baseline measurements.

Results: LIRD caused progressive decreases in retinal function that partially recovered over time. Photoreceptor function (ERG a-wave) was reduced by 10% at Day 7 and by 50% at Day 14. Partial recovery of the a-wave was observed (65% of Baseline) at Day 29. Similar effects were found for bipolar cell function (ERG b-wave). The reduction of the positive STR (pSTR) was delayed until Day 14, when it was reduced by 50%. The pSTR recovered to 65% of Baseline pSTR amplitudes at Day 29. The negative STR (nSTR) was reduced by 55% and showed partial recovery to 75% of Baseline nSTR amplitudes at Day 29. Despite these functional changes observed in the ERG waves, no change in inner or outer retinal thickness was detected with OCT throughout the course of the study.

Conclusion: Preliminary results indicate that our model of LIRD in C57BL/6 mice caused no detectable structural changes of the retina, but induced recoverable decreases in ERG function over a 30 day period. Ongoing work aims to further characterize changes in retinal structure and function caused by LIRD by increasing the level of phototoxicity and extending the experimental timeline. Results of these studies will improve our understanding of the contributions of the STR to the retinal ERG.

SETTLE PLATE TESTING TO MEASURE AIR QUALITY IN A TERTIARY CARE OPHTHALMOLOGY DEPARTMENT

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Purpose: Numerous patient based and extrinsic factors have been implicated in contributing to surgical site infections. Even though air quality has been shown to have an impact in other surgical areas, airborne bacteria have not been explicitly studied as a contributing risk factor for endophthalmitis. The objective of this study is to assess the air quality and evaluate potential factors that contribute to the number and types of airborne micro-organisms found in operating rooms and clinics.

Methods: Settle plate testing will be performed using chocolate agar plates to determine the number of colony forming units per hour in the main operating rooms, minor operating rooms and clinics. Data will be collected on the temperature, humidity, number of door openings, physical movement, time of year, weekday vs. weekend, and type of procedure. Multivariate analyses will be used to determine factors associated with increased microbial numbers. In addition, we will be collecting bacterial swabs of various equipment near the patient's eye in the operating room. Specifically, we will be swabbing the center of the headrest, oxygen pipe used by anesthesia, drops used during the procedure, underside of the microscope, and the tape used at the end of the procedure to determine if these are potential contaminants.

Results: Preliminary pilot study results will determine the location of the plates for the rest of the study. We expect that the study will elucidate whether temperature, humidity, number of door openings, physical movement, weekday vs. weekend, type of procedure and specific operating rooms have any correlation with the number and types of bacteria that contribute to endophthalmitis.

Conclusions: Identifying the factors that potentially contribute to endophthalmitis rates will allow us to develop targeted interventions to minimize infection rates due to airborne bacteria and fungi.

CHARACTERIZING LONGITUDINAL *IN VIVO* CHANGES OF RGC IN A MODEL OF EXPERIMENTAL GLAUCOMA

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Purpose: Retinal ganglion cell (RGC) death is preceded by retraction of dendrites and an overall loss of dendritic branch complexity. Preliminary studies in our laboratory found a 29% decrease in dendritic arbor complexity from baseline over 8 weeks of chronic intraocular pressure (IOP) elevation (mean (SD): 9.8 (0.3) vs 15.2 (1.1) mmHg; control vs. experimental eyes, respectively), however no global RGC loss was observed when quantified with immunohistochemistry. The aim of the present study was to extend the time course to six months to determine whether prolonged IOP elevations would cause greater cell loss and dendritic retraction.

Methods: Five mice (Thy-1 YFP, line H; Jackson Laboratories, ME) received magnetic microbead injection (MMI). IOPs were measured over 6 months with a rebound tonometer (Tonolab, Tiolat, Inc., Helsinki, Finland) and compared to the control untreated fellow eye. Longitudinal *in vivo* imaging (CSLO; Spectralis Multiline, 488 nm laser, Heidelberg Engineering) visualized RGCs expressing yellow fluorescent protein (YFP^+, n=8 cells followed) throughout their axons and dendrites over the 6-month time course. Sholl analysis was used to quantify changes in the dendritic complexity and arbour size of YFP^+ RGCs in each *in vivo* image over time.

Results: MMI caused modest IOP elevation (12.6 (0.5) vs 8.9 (0.1) mmHg, experimental vs. fellow eye, respectively) that was sustained over the 6-month time course. The IOP integral, a measure of cumulative IOP elevation over time, was significantly greater ($p< 0.0001$) in mice followed for 6 months compared to those in the previous 8-week time course group (584.5 (90) vs. 220.6 (116.1) mmHg-days, 6 month vs. 8 week groups, respectively). The dendritic arbour radii decreased by 8.4% (188 (24) to 172 (23) μm; baseline vs. month 6) showing an overall reduction in cell size with prolonged IOP elevation. Also, the peak number of dendrite intersections decreased by 8.7% (29 (1.9) to 26.5 (2.6)); baseline vs. month 6, n= 8 cells) and overall dendritic complexity of RGCs was lost over time (3116 (423) vs. 2684 (301); baseline vs. 6 months, respectively).

Conclusion: Results of the present study show that prolonged IOP elevation caused retraction of dendritic arbours and loss of dendritic complexity of RGCs over time. While the present MMI model did not cause catastrophic cell loss, these findings suggest that even moderate IOP elevation causes changes in dendritic structure, which may have important functional consequences leading up to cell death in glaucoma.

INCIDENCE AND PREDICTORS OF ANXIETY AND PAIN ASSOCIATED WITH INTRAVITREAL INJECTIONS

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Purpose: The use of intravitreal anti-vascular endothelial growth factor (VEGF) has increased significantly over the last decade. Anti-VEGF injection therapy is used in conditions such as neovascular age-related macular degeneration (AMD), diabetic macular edema (DME) and macular edema (ME) secondary to conditions such as central retinal vein occlusion (CRVO).

Anxiety prior to interventional medical procedures have been shown to range from 11% to 80%. The incidence associated with intravitreal anti-VEGF injections has not been fully elucidated in the literature. A study by Segal et. Al showed a positive correlation between elevated anxiety levels and perceived pain endured the procedure indicating the importance of reducing anxiety.

The purpose of this study is to identify the incidence and factors influencing anxiety and pain in our patient population undergoing injections to aid in the development of strategies which will improve patient experience.

Methods: This observational, prospective, non-interventional study will look at patients undergoing treatment with intravitreal anti-VEGF injections (bevacizumab, ranibizumab or aflibercept) for neovascular AMD, DME, and ME and will be recruited at the Eye Care Centre at the Victoria General Hospital in Halifax, NS over a 2-year period.

Prior to intravitreal injection therapy, patients will be asked to take the the state portion of the Spielberger State Trait Anxiety Inventory (STAI-S) to assess pre-injection anxiety levels in addition to a questionnaire assessing possible anxiety triggers. Immediately after receiving the injection, patients will be asked to complete a post-injection Visual Analogue Scale (VAS) pain questionnaire. Data analysis will be performed to identify factors affecting patient anxiety and pain.

Results: The mean STAI-S anxiety score was 46.76 (SD=4.70), n=29. There was no significant difference (p=0.453) in mean STAI-S scores between males (46.2) and females (47.6). Using Pearson's Correlation analysis, the variables of age (r=-0.155, p = 0.423) and number of previous injections (r=-0.225, p=0.240) were weakly associated with STAI-S scores.

The mean VAS pain score was 0.93 (SD=1.62). There was no significant difference (p=0.679) in mean VAS scores between males (0.82) and females (1.08). Using Pearson's Correlation analysis, pre-injection STAI scores (r=-0.026, p = 0.894) were not associated with post-op VAS scores. The number of previous injections (r=-0.349, p=0.063) was weakly associated with VAS scores.

Conclusion: Although in its early stages, this study so far has not shown any significant associations between the level of pre-injection anxiety or post-injections pain scores to the variables being studied.

DR. R. EVATT AND RITA MATHERS TRAINEE SCHOLARSHIPS

The Department of Ophthalmology and Visual Sciences is pleased to announce the Dr. R. Evatt and Rita Mathers Trainee Scholarships in Ophthalmology and Visual Sciences.

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NOTES

EVALUATION

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MONDAY, APRIL 9, 2018

What have you learned through attending Research Day?

Has Research Day stimulated any new ideas for you?

Will you make any changes to your clinical approach based on new information presented today?

Are there any changes you would suggest to improve the organization of future Research Days?

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In keeping with CMA Guidelines, program content and selection of speakers are the responsibility of the planning committee. Support is directed toward the costs of the course and not to individual speakers. This program has received an educational grant or in-kind support from: Allergan, Bayer, Bausch & Lomb and Alcon.

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