gprwmf

CONTENTS

WELCOME MESSAGE

'CULTIVATING INSIGHT, EMBRACING VISION'

The Specialty of Otorhinolaryngology is like a garden. We are here not to passively observe and simply take from it, but to cultivate and develop it.

Over the course of the next two days, you will be exposed to the politics of scientific achievement and be confronted by a number of controversial issues. You will be challenged by epigenetics, mitochondria, foetal surgery, cancer immunotherapy, genetics and microbiometrics, neuronal function, neuroplasticity and epidemiology. You will learn about the clinical and translational work proceeding in relation to the middle ear, the sinuses and the head, neck and thyroid.

You will also experience the fascination of comparative vocalisation and audition, and delve into questions concerning the interaction between the surgeon and the scientist, and consider the future of the academic surgeon-scientist.

For Otorhinolaryngology to develop beyond what it is today, incredible in scope as it is, it must do so through a collaborative team approach. Scientists fully committed to the Specialty working in consultation with and alongside clinicians, who recognise that they depend on science and new technologies to progress what they do. Crossing disciplines and crossing institutions.

Frontiers 2014 presents another unique opportunity to build upon these collaborations, extend knowledge and influence the future. It provides a vehicle by which threads may be drawn together and a new vision embraced for the benefit of mankind.

I hope you enjoy the conference.

Dean Beaumont
Convenor

INTERNATIONAL KEYNOTE SPEAKERS

Professor Robert Ferris

Professor Robert Ferris completed his MD, PhD (Immunology) and residency training in Otolaryngology Head and Neck Surgery at The Johns Hopkins University School of Medicine. He then moved to the University of Pittsburgh as Assistant Professor of both Otolaryngology and Immunology.

In 2005, Professor Ferris was appointed Chief of the Division of Head and Neck Surgery and Director of the Fellowship in Advanced Head and Neck Oncologic Surgery. He was subsequently promoted to Associate Professor and appointed Co-Leader of the Cancer Immunology Program at the University of Pittsburgh Cancer Institute. He is currently the Endowed Professor of Otolaryngology Head and Neck Surgery, Radiation Oncology and Immunology at the University of Pittsburgh Medical Center.

He holds positions with the American Head and Neck Society and Eastern Cooperative Oncology Group, and is on the editorial boards of the *Journal of Clinical Oncology, Clinical Cancer Research, Head and Neck and Oral Oncology*. He has published over 170 peer-reviewed scientific manuscripts, co-authored numerous book chapters and co-edited two books.

Professor Ferris coordinates a number of clinical trials translating novel immunologic agents into the clinic, as well as correlative studies of immune markers in the serum and tumour microenvironment. He is currently investigating immunosuppressive effects that inhibit clinical activity of therapeutic mAb, including cetuximab, checkpoint receptor expression on tumour infiltrating lymphocytes and immune escape mechanisms.

His research interests include cancer immunology and immunotherapy, mucosal tumour immunology, antigen processing and presentation to T cells, role of human papillomavirus in head and neck cancer, and strategies of immune evasion by cancer cells.

Professor Robert Kern

Professor Robert Kern obtained a BS (Biology) from Georgetown University and a MD from Jefferson Medical College. He completed his residency training, a two-year research training fellowship and a MSc (Anatomy) at Wayne State University. He was mentored by the late Professor Thomas Getchell, who was a nationally recognised leader in the field of olfactory physiology.

In 1991, Professor Kern joined Northwestern University as an Assistant Professor and continued his research in the area of olfaction. He was subsequently appointed Chairman of Otolaryngology Head and Neck Surgery at Stroger Hospital (formerly Cook County Hospital) and, in 2006, he accepted the position of Chairman of the Department of Otolaryngology Head and Neck Surgery at the Northwestern University Feinberg School of Medicine.

He holds a number of positions with the American Academy of Otolaryngology and Triological Society, and is on the editorial boards of *Laryngoscope, International Forum of Rhinology and Allergy and American Journal of Rhinology and Allergy*. He has published over 120 peer-reviewed scientific manuscripts, co-authored numerous book chapters and written several books.

Professor Kern's primary clinical interests are the medical and surgical treatment of diseases of the nose and paranasal sinuses, including the minimally invasive endonasal approach to skull base tumours.

His research focuses on the pathophysiology of chronic rhinosinusitis in partnership with Professor Robert Schleimer, the Northwestern University Feinberg School of Medicine Chief of the Division of Allergy and Immunology. Most recently, they were awarded a multi-million dollar grant to examine the epidemiology, pathophysiology, genetics and epigenetics of chronic rhinosinusitis.

Professor Magnus von Unge graduated as a medical doctor from the Karolinska Institute, Stockholm, Sweden. He then became a specialist in Otorhinolaryngology, holding positions as a general otorhinolaryngological surgeon at Västerås Central Hospital and senior ear surgeon at Karolinska University Hospital.

In 2006, Professor von Unge was appointed Associate Professor at the Karolinska Institute. He was subsequently promoted to Professor and Senior Ear Surgeon at Akershus University Hospital, University of Oslo, Norway.

He is a member of the Swedish Surgical Society, Association for Research in Otolaryngology and Politzer Society, and has served on the editorial board of *ACTA Otolaryngologica*.

Professor von Unge presented his scientific thesis on the mechanical properties of the tympanic membrane at the Karolinska Institute. He has also supervised three academical theses investigating changes in the tympanic membrane structure and function in inflammatory middle ear disease. Some of these studies were done in collaboration with the biomedical physics group at the University of Antwerp, Belgium, that resulted *inter alia* in the first paper in English on stem cell application for the treatment of middle ear defects. This collaboration is presently engaged in efforts to develop a mode of measuring ossicular mobility during surgery.

His research focuses on the regenerative properties of the human tympanic membrane for the purpose of tissue engineering and activation of repair processes, as well as other otological issues, such as changes to the chorda tympani in middle ear disease and after middle ear surgery, and the long-term effects of different types of grommets.

Professor Magnus von Unge

INVITED SPEAKERS

Dr Farzaneh Ahmadi
School of Electrical and Information Engineering, The University of Sydney

Dr Daniel Brown
Brain & Mind Research Institute, The University of Sydney

Dr Hannah Burns
Holy Spirit Northside Hospital, Brisbane

Professor Anders Cervin
Department of Otolaryngology, The University of Queensland

Professor Ian Chubb
Chief Scientist of Australia

Professor Susan Clark
Garvan Institute of Medical Research

Dr Susan Coulson
Discipline of Physiotherapy, The University of Sydney

Dr David Hogan
Royal Brisbane and Women's Hospital

Professor Dexter Irvine
Bionics Institute of Australia

Associate Professor Neil McLachlan
School of Psychological Sciences, The University of Melbourne

Dr Hamish MacDougall
School of Psychology, The University of Sydney

Dr Timothy Marr
School of Surgery, The University of Western Australia

Associate Professor David Merritt
School of Biological Sciences, The University of Queensland

Dr Americo Migliaccio
Neuroscience Research Australia

Professor David Thorburn
Murdoch Childrens Research Institute

Professor John Windsor
Department of Surgery, The University of Auckland

Professor Peter-John Wormald
Department of Otolaryngology, The University of Adelaide

SCIENTIFIC PROGRAM

THURSDAY 31 JULY 2014

8.30 – 8.35 am	OFFICIAL WELCOME	Dr Dean Beaumont
Session 1	**Chair: Dr Dean Beaumont**	
8.35 – 9.10 am	*The politics and problems of scientific achievement*	Professor Ian Chubb
9.10 – 9.50 am	*The tympanic membrane: Structure, damage and regenerative processes*	Professor Magnus von Unge
9.50 – 10.30 am	*The epidemiology of chronic rhinosinusitis*	Professor Robert Kern
10.30 – 11.00 am	MORNING TEA	
Session 2	**Chair: Professor John Funder**	
11.00 – 11.40 am	*Developments in immunotherapy for head and neck cancer*	Professor Robert Ferris
11.40 – 11.55 am	*Intramucosal and intracellular staphylococci in sinus disease*	Professor Peter-John Wormald
11.55 – 12.10 pm	*The problems and future of human fetal Otolaryngological surgery*	Dr Hannah Burns
12.10 – 12.40 pm	*The role of mitochondrial structure, function and dysfunction in Otorhinolaryngology*	Professor David Thorburn
12.40 – 1.00 pm	*Auditory system plasticity in adults*	Professor Dexter Irvine
1.00 – 2.00 pm	LUNCH	
Session 3	**Chair: Professor John Harris**	
2.00 – 2.15 pm	*The avian syrinx*	Dr David Hogan
2.15 – 2.30 pm	*Radical versus functional techniques in sinus surgery*	Professor Anders Cervin
2.30 – 2.45 pm	*Tracking the course of acute human vestibular compensation*	Dr Hamish MacDougall
2.45 – 3.00 pm	*Cortical changes following acute lower motor neurone facial nerve paralysis*	Dr Susan Coulson
Session 4	**Chair: Professor William Coman**	
3.00 – 4.00 pm	*Unsolved problems in Otorhinolaryngology*	Panel Discussion
Session 5		
4.00 – 6.00 pm	POSTER PRESENTATIONS	

FRIDAY
1 AUGUST 2014

Session 6	**Chair: Dr Dean Beaumont**	
8.30 – 9.00 am	*Age related effects on the labyrinth and its central connections*	Dr Americo Migliaccio
9.00 – 9.30 am	*The neuroscience and neuropsychology of music*	Associate Professor Neil McLachlan
9.30 – 10.00 am	*Weird Ears: The structure and function of insect auditory systems*	Associate Professor David Merritt
10.00 – 10.30 am	*Fluid dynamics of the inner ear*	Dr Daniel Brown
10.30 – 11.00 am	MORNING TEA	
Session 7	**Chair: Dr Michael Jay**	
11.00 – 11.40 am	*Evaluating thyroid nodules using molecular genetic techniques*	Professor Robert Ferris
11.40 – 12.20 pm	*The etiology and pathogenesis of chronic rhinosinusitis: Implications for therapy*	Professor Robert Kern
12.20 – 1.00 pm	*The intra-operative assessment of ossicular function: Research and clinical implications*	Professor Magnus von Unge
1.00 – 2.00 pm	LUNCH	
Session 8	**Chair: Professor John Furness**	
2.00 – 2.30 pm	*Evolution and Development: Epigenetics and Otorhinolaryngology*	Professor Susan Clark
2.30 – 2.45 pm	*Developing a bionic voice prosthesis*	Dr Farzaneh Ahmadi
2.45 – 3.00 pm	*Nuclear theranostics and radioimmunotherapy*	Dr Timothy Marr
Session 9	**Chair: Professor William Coman**	
3.00 – 4.00 pm	*The Surgeon, the Scientist and the Academic Surgeon/Scientist*	Professor John Windsor
4.00 – 5.00 pm	NETWORKING DRINKS	

SOCIAL PROGRAM

WELCOME DRINKS
WEDNESDAY, 30 JULY 2014

TIME: 5.30 – 7.30 pm
PLACE: The Gallery
Sheraton on the Park
DRESS: Relaxed business attire

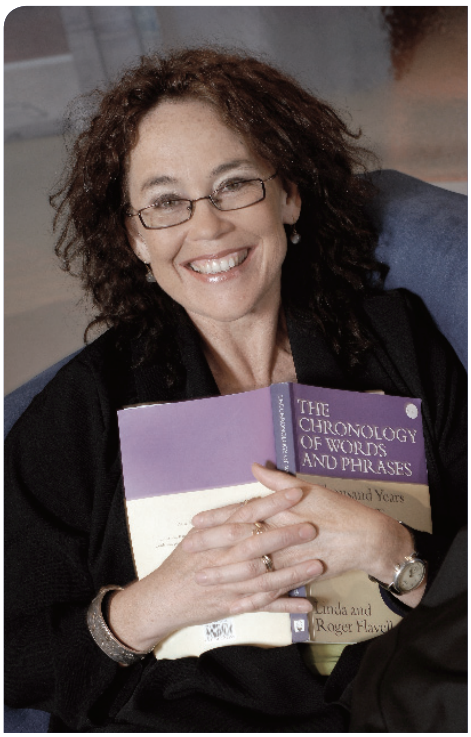
POSTER PRESENTATIONS
THURSDAY, 31 JULY 2014

TIME: 4.00 – 6.00 pm
PLACE: Grand Ballroom II
Sheraton on the Park
DRESS: Relaxed business attire

CONFERENCE DINNER
FRIDAY, 1 AUGUST 2014

PRE-DINNER DRINKS
TIME: 6.30 – 7.00 pm
PLACE: Pre-function area
Sheraton on the Park
DRESS: Lounge Suit

DINNER
TIME: 7.00 – 11.00 pm
PLACE: Grand Ballroom I
Sheraton on the Park
DRESS: Lounge Suit



CONFERENCE DINNER SPEAKER

Professor Kate Burridge is the Professor of Linguistics in the School of Languages, Literature, Cultures and Linguistics at Monash University and a Fellow of the Australian Academy of the Humanities.

Her main areas of research are grammatical change in Germanic languages, the Pennsylvania German spoken by Amish/Mennonite communities in North America, the notion of linguistic taboo, and the structure and history of English. She is a regular presenter of language segments on radio and has been a panelist on ABC TV's *Can We Help?*

Her books include *Euphemism and Dysphemism: Language used as shield and weapon* (with Keith Allan, 1991), *Syntactic Change in Germanic* (1993), *English in Australia and New Zealand* (with Jean Mulder, 1998), *Blooming English: Observations on the roots, cultivation and hybrids of the English Language* (2004), *Weeds in the Garden of Words: Further observations on the tangled history of the English language* (2005), *Forbidden Words: Taboo and the censoring of language* (with Keith Allan, 2006), *Introducing English Grammar* (with Kersti Börjars, 2010), *Gift of the Gob: Morsels of English language history* (2010) and (with Debbie de Lapps) two high school textbooks *Love the Lingo* and *Living Lingo*.

SYDNEY

Sydney is a very exciting place to be in winter, with fun-filled events, celebrations and festivals to ignite the season. There's an overall buzz of happiness in the air, as people explore this city bursting with things to see and do.

Diners in Sydney are spoilt for choice with some of the best restaurants in the country, many with stunning water views, an abundance of fresh produce and dynamic chefs keen to impress. Enjoy checking out the latest trends? Check out vegan-friendly dining, small bars on rooftops and stylish high teas.

From beachside and suburban markets to historic city-centre arcades, boutiques in laneways and hideaway warehouses, Sydney offers a treasure trove of eclectic, stylish and unique designs. Shopping hotspots include the city centre, Bondi, Paddington, Surry Hills, Darlinghurst, Manly, Mosman and Newtown.

Sydney's arts and cultural scene is diverse, engaging and great value. The city is a stage for local and international, established and emerging talent with art and performances around every corner. Go behind the scenes at some of Sydney's major art and cultural institutions, such as the Sydney Theatre Company, Australian Museum and Sydney Opera House.

For a truly unique experience, catch a ferry across Sydney Harbour to visit Australia's native animals at Taronga Zoo or take a ride to Manly Beach and enjoy a relaxing afternoon in the sun.

For more information, please go to *www.sydney.com*.

SYDNEY'S WEATHER

The average maximum in July is 16° C (61° F), whilst the average minimum is 9° C (48° F).

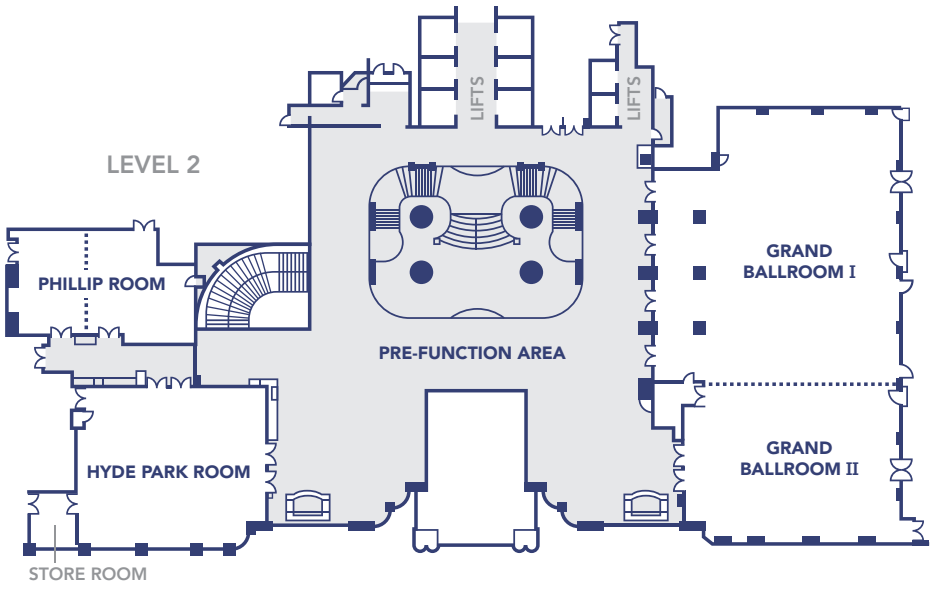
SOURCE:
BUREAU OF METEOROLOGY

GENERAL INFORMATION

VENUE

Sheraton on the Park
161 Elizabeth Street
SYDNEY NSW 2000
Australia

P +61 2 9286 6000
F +61 2 9286 6686



VENUE FLOOR PLAN

BREAKFASTS

Breakfasts are *not* included in the registration fee.

CAR PARKING

Car parking is *not* included in the registration fee.

CHECK OUT

For those delegates staying at the venue, check out time is 11.00 am on the day of departure.

CONFERENCE SECRETARIAT

Please see either Ms Debbie Henningsen or Ms Cheryl Thorogood from The Garnett Passe and Rodney Williams Memorial Foundation at the registration desk if you have a query or require assistance of any kind.

DISCLAIMER

The information contained in this booklet was correct at the time of printing. However, the Foundation reserves the right to change any of the information where necessary without notice.

INSURANCE

Delegates should make their own arrangements with respect to personal insurance.

INTERNET ACCESS

For those delegates staying at the venue, high-speed internet access is available in each room at $20.00 (GST-inclusive) per day, if you wish to use your own device. Alternatively, wireless internet access in *link@sheraton* and all public areas is complimentary.

LIABILITY WAIVER

In the event of industrial disruption or other unforeseen circumstances, the Foundation accepts no responsibility for loss of monies incurred by delegates.

The Foundation accepts no liability for injuries/losses of whatever nature incurred by delegates and/or accompanying persons nor for loss or damage to their luggage and/or personal belongings.

MOBILE PHONES

Mobile phones are not to be used while sessions are in progress. Please ensure that your phones are switched to silent during these times.

NAME BADGES

Name badges must be worn at all times during the conference. If you have lost or misplaced your name badge, please go to the registration desk for a replacement.

NO SMOKING POLICY

The Sheraton on the Park is 100% smoke-free.

REGISTRATION DESK

The registration desk will be open at the following times and locations:-

WEDNESDAY,
30 JULY 2014

Time: 5.30 pm to 7.30 pm
Place: The Gallery
Sheraton on the Park

THURSDAY,
31 JULY 2014

Time: 7.30 am to 6.30 pm
Place: Pre-function area
Sheraton on the Park

FRIDAY,
1 AUGUST 2014

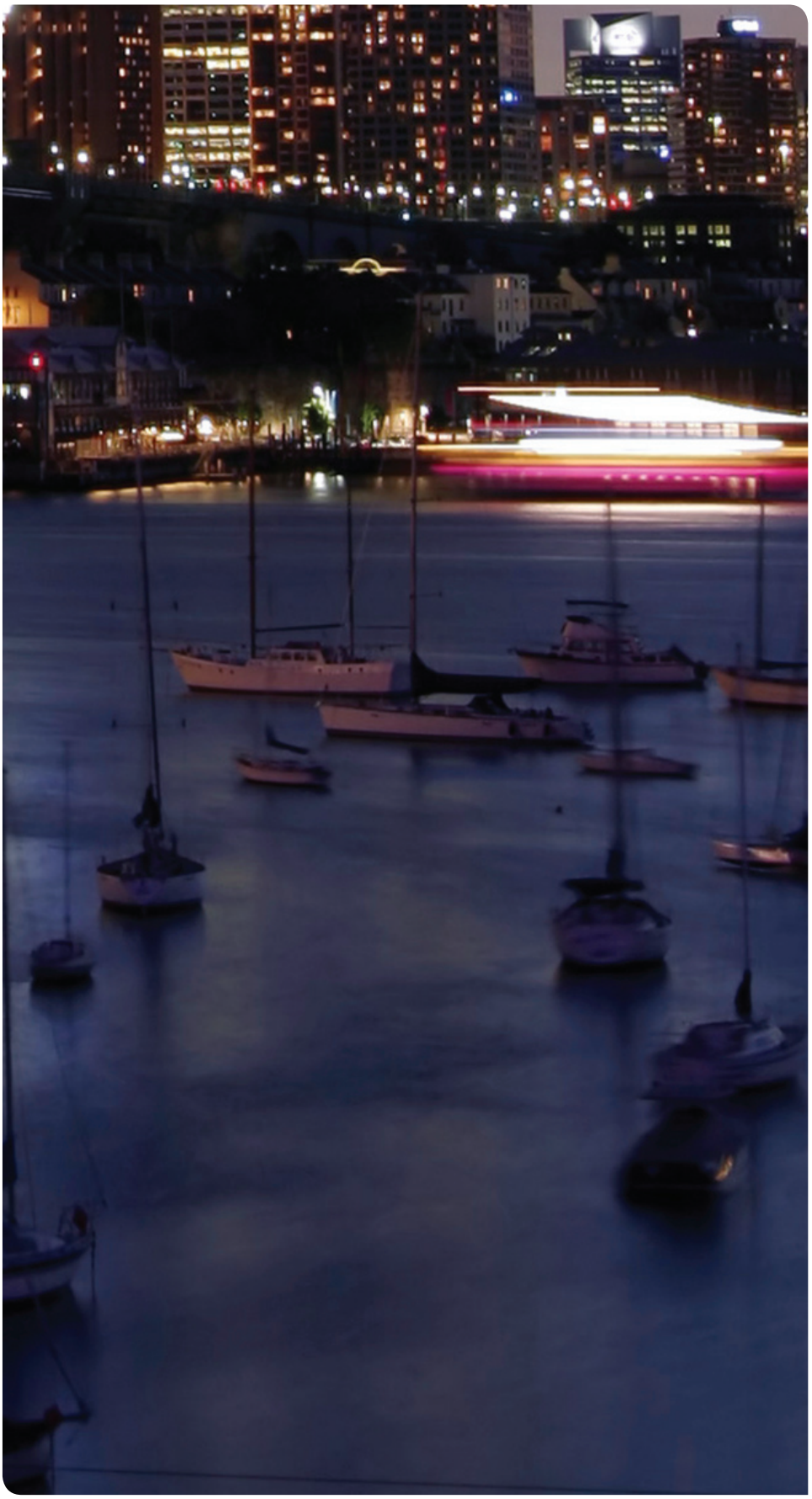
Time: 7.30 am to 5.30 pm
Place: Pre-function area
Sheraton on the Park

TRANSFERS TO SYDNEY AIRPORT

Sydney Airport is located approximately 7.5 kms south of Sydney's CBD - less than 30 minutes by car.

There are many bus, limousine, shuttle and train services operating between the city and Sydney Airport. For more information, please go to www.sydneyairport.com.au or www.airportlink.com.au.

Alternatively, if you wish to catch a taxi, please see the venue's concierge, who will be able to assist you in this regard.



THURSDAY
31 JULY 2014

SESSION 1: 8.35 – 9.10 am

THE POLITICS AND PROBLEMS OF SCIENTIFIC ACHIEVEMENT

Professor Ian Chubb
CHIEF SCIENTIST OF AUSTRALIA

Professor Chubb commenced in the role of Chief Scientist on 23 May 2011.

Prior to that, Professor Chubb was Vice-Chancellor of the Australian National University from January 2001 to March 2011, Vice-Chancellor of Flinders University for six years, and the Senior Deputy Vice-Chancellor of Monash University for two years, while simultaneously the Foundation Dean of the Faculty of Business and Economics for 16 months.

He was Chair of the Higher Education Council (the Commonwealth Government's peak advisory body on higher education) from September 1990 to December 1994 and was, until mid-1994, the Deputy Chair of the National Board of Employment, Education and Training (the Commonwealth's peak advisory body on all matters related to the Employment, Education and Training portfolio).

From January 1986 to September 1990, Professor Chubb was the Deputy Vice-Chancellor of the University of Wollongong and an Honorary Professor of Biology. During the period 1978-1985, he was an academic member of the School of Medicine at Flinders University. Before that, he was at Oxford University where, during the period 1971-1977, he was a Welcome Foundation Scholar, a Junior Research Fellow of St John's College and a Royal Society Research Fellow. He spent 1969-1971 as a J F & C Heymans Research Fellow at Ghent University, Belgium.

His research focused on the neurosciences and was supported by the National Health and Medical Research Council, the Australian Research Grants Scheme and by various Foundations.

Professor Chubb was President of the Australian Vice-Chancellors' Committee (AVCC) for 2000 and 2001, Vice-President for 1998 and 1999 and an elected member, or member, of the Board of the AVCC between 1996 and 2006. From January 2000 to December 2001, he was a member of the Prime Minister's Science, Engineering and Innovation Council (PMSEIC). He serves, or has served, on numerous other boards and committees related to his university or Commonwealth responsibilities.

In 1999, he was made an Officer of the Order of Australia (AO) for "service to the development of higher education policy and its implementation at state, national and international levels, as an administrator in the tertiary education sector and to research particularly in the field of neuroscience". In 2006, he was made a Companion (AC) in the order for "service to higher education, including research and development policy in the pursuit of advancing the national interest socially, economically, culturally and environmentally and to the facilitation of a knowledge-based global economy".

THE TYMPANIC MEMBRANE: STRUCTURE, DAMAGE AND REGENERATIVE PROCESSES

Professor Magnus von Unge
INTERNATIONAL KEYNOTE SPEAKER

TM retraction or cholesteatoma are often observed in adults that were otitis prone as children. Our hypothesis is that otitis media impairs its resistance to pressure gradients that may later cause retractions.

Rodents were used in structural and functional assessments. Acute otitis media and otitis media with either serous or mucoid effusion were produced by minor surgical interventions. After different time intervals, the TMs were analysed with light and electron microscopy. A tympanometry model was developed for assessment of the acoustic admittance and an optical moiré interferometry model was developed by which displacement changes under the application of pressure in the ear canal was recorded, as a measure of the quasi-static TM stiffness.

Tympanometry showed reduced admittance in all forms of otitis media. The findings of edema in the TM are the probable structural correlate. This implies that in otitis media not only middle ear fluid but also TM edema may cause hearing impairment.

Displacement in moiré interferometry increased over the entire TMs in otitis media, in a degree that corresponds to the degree of structural changes and the duration of the disease. In addition, local "weak spots" were identified in some TMs. These changes may predispose for later development of retraction pockets.

TM perforations are common in acute otitis media and after trauma. Most perforations heal spontaneously within days and the strength of the TM may appear restored. The lamina propria, with its densely packed collagen fibre bundles, provides its strength. The human lamina propria comprises mostly type II collagen but we also found an abundance of type III, particularly in the inner circular fibre layer, and type II in rodents, the major collagen constituent. The strength tested with moiré interferometry of the spontaneously closed acute perforation in rats was restored after two weeks. There was a lack of fibre orientation in the scar, which seemed to be compensated by an increased amount of tissue. Still after six months, the strength was fairly normal but the lamina propria was not yet normalised.

However, keratinocytes are essential in the repair of TM perforations. In our study on experimental acute perforations, we found a large wave of keratinocytes migrating from the centre of the TM towards the perforation site where they disintegrate to form a keratin mass that eventually spans the perforation. A similar but less intense activity is present near the annulus. The origin of this migration is supposedly regenerative centres. With immunohistochemistry, we identified regions at the umbo, along the manubrium and the annulus that probably are regeneration centres. They stained for Integrin alpha-6 and beta-1 and CK19, indicative for the presence of progenitor cells. These regions also exhibited structural characteristics with densely packed keratinocytes and deep rete into the sub-epithelial layer. Furthermore, a sphere formation, indicative for stem cells, was recently obtained in a cell culture from the TM.

The enhanced closure of fresh and chronic perforations after application of stem cells has encouraged us to proceed with this research.

THURSDAY
31 JULY 2014

SESSION 1: 9.50 – 10.30 am

THE EPIDEMIOLOGY OF CHRONIC RHINOSINUSITIS

Professor Robert Kern
INTERNATIONAL KEYNOTE SPEAKER

Chronic rhinosinusitis (CRS) is a common clinical syndrome defined by expert panels as symptomatic inflammation of the mucosa of the nose and paranasal sinuses of 12 weeks or longer.

This definition does not address etiology, which is poorly understood but believed to be multi-factorial. The cardinal symptoms that define CRS in adults are nasal obstruction, nasal drainage, smell loss and facial pressure. To fulfil the diagnosis of CRS, a patient must suffer from 12 continuous weeks of at least two of these symptoms, one of which must be nasal obstruction or drainage. However, to validate the presumed diagnosis, objective confirmation of sinus mucosal inflammation by nasal endoscopy or sinus CT scan is required.

In western cultures, CRS is associated with massive direct and indirect costs, with apparent recent increases in both prevalence and severity. Treatment recommendations are expert-based, supported by relatively low level evidence. While the majority of individual patients do well, the result in the United States has been an over reliance on antibiotics and surgery, the former contributing to antibiotic resistance and the latter associated with high clinical recurrence rate.

Progress in the management of CRS at the population level is hampered by knowledge deficits in both epidemiology and etio-pathogenesis. Epidemiologic studies are limited by the use of self-reported symptoms and lack of objective confirmation. The problem is exacerbated by the lack of strong CRS-specific patient reported outcome (PRO) instruments, which fail to diagnose the problem or assess disease control.

To address these problems, we have developed a chronic episodic disease model, which more accurately captures the chronic relapsing nature of CRS. The first presentation at this conference will provide best currently available data of the incidence, prevalence and natural history of CRS using a stable, large patient cohort in the United States. This begins the process of, firstly, assessing the true scope of the problem and, secondly, developing clinical relevant phenotypes. Included in this assessment will be the identification of key pre-morbid and post-morbid conditions that are associated with the development of CRS. This will be used to inform the delineation of CRS endotypes based on etiopathogenesis, presented in detail in the second presentation at this conference. Lastly, the implications for the future of CRS therapy will be assessed in light of the emerging epidemiologic and etiologic data presented.

SESSION 2: 11.00 – 11.40 am

THURSDAY
31 JULY 2014

DEVELOPMENTS IN IMMUNOTHERAPY FOR HEAD AND NECK CANCER

Professor Robert Ferris
INTERNATIONAL KEYNOTE SPEAKER

Professor Ferris' laboratory investigates the mechanisms of tumour antigen processing and immunologic evasion used by head and neck cancer cells. His group also studies the induction and phenotype of cytotoxic T lymphocytes (CTL) after treatment with therapeutic mAb, such as the EGFR-specific mAb cetuximab.

He is co-principal investigator for the National Cancer Institute's Head and Neck SPORE (Specialized Program of Research Excellence) and leader of a project comparing suppressive regulatory T cells (Treg) after cetuximab or panitumumab therapy.

Professor Ferris is national co-chair of several phase II and phase III immunotherapy trials investigating anti-PD1 mAb (nivolumab) or TLR8 agonist plus cetuximab-based chemotherapy.

Utilising his clinical practice in head and neck surgical oncology and basic/translational immunology laboratory, he is uniquely positioned to investigate mechanisms of anti-tumour immunity in the microenvironment.

He also studies immune and inflammatory chemokine receptor signals and cellular mechanisms of anti-tumour responses to malignancy, particular immunity and immune escape by head and neck cancer.

In this presentation, Professor Ferris will provide an overview of the agents and therapeutic approaches currently being used or evaluated in the treatment of head and neck cancer. He will describe the promise and future implementation of novel immunotherapeutic strategies, which constitute a new, fourth modality for this challenging disease.

THURSDAY
31 JULY 2014

SESSION 2: 11.40 – 11.55 am

INTRAMUCOSAL AND INTRACELLULAR STAPHYLOCOCCI IN SINUS DISEASE

Professor Peter-John Wormald
DEPARTMENT OF OTOLARYNGOLOGY, THE UNIVERSITY OF ADELAIDE

Professor Wormald is chairman of the Department of Otolaryngology Head and Neck Surgery at The University of Adelaide. He is currently recognised as a world leader in the field.

His medical practice and research interests are devoted to rhinology and endoscopic skull base surgery.

His research interests include the role of the immune system, biofilms in the pathogenesis of chronic rhinosinusitis and new techniques in skull base surgery.

As endoscopic sinus surgery has progressed over the last decade, new pathogenic mechanisms have been put forward for the recalcitrance of Chronic Rhinosinusitis (CRS) for those patients difficult to treat.

In our department, we have performed extensive research into the role of *S. aureus* with particular reference to its biofilm form, the relationship between biofilm formation and clinical recalcitrance, and the relationship between biofilm form and intracellular and intramucosal bacteria.

We have shown how *S. aureus* biofilms are necessary for bacterial adherence and internalisation. We have looked at the interaction between *S. aureus* strains and cell junctional complexes, as well as the interaction between *S. aureus* and intracellular inflammatory mechanisms with particular focus on the role of the inflammasome, AIM 2 complex and the NOD 2 intracellular pathway. In addition, we have identified phenotype switching that occurs during internalisation both *in vitro* and *in vivo* as a further mechanism of how *S. aureus* manipulates the immune system.

This research will be presented as a comprehensive overview of the role of intracellular and intramucosal *S. aureus* in CRS.

SESSION 2: 11.55 – 12.10 pm

THURSDAY
31 JULY 2014

THE PROBLEMS AND FUTURE OF HUMAN FETAL OTOLARYNGOLOGICAL SURGERY

Dr Hannah Burns
HOLY SPIRIT NORTHSIDE HOSPITAL, BRISBANE

Fetal medicine is a relatively young discipline born out of improved antenatal radiological care. Ultrasound, and then magnetic resonance, has allowed the obstetrician to diagnose conditions that would have proved fatal in the past. In doing so, antenatal management and delivery options may provide techniques to safely deliver such infants. An increasing range of fetal abnormalities can now not only be diagnosed *in utero* but may even be treated with fetal surgery in an to attempt to reduce morbidity and mortality.

Otolaryngology can play a crucial role in fetal medicine. Firstly, these diagnostic tools allow identification of conditions that may require post-natal care. In doing so, families can liaise with their treating teams and understand the long-term treatment of their child. Clefting conditions are perfect examples. Secondly, conditions that will require coordinated care to provide a safe delivery can be discussed and deliveries planned in a coordinated manner. Severe Pierre Robin syndrome or lymphangiomas are two such examples. Thirdly, specific delivery methods have been developed, initially to manage congenital diaphragmatic hernia treatment but this has translated into a successful method of treating a range of extreme airway conditions. Thus, the *ex utero* intra partum treatment (EXIT) technique was developed. This technique allows for a number of options, EXIT to airway, EXIT to resection or a EXIT to ECMO. Finally, *in utero* treatment of head and neck conditions are in their infancy with the possibility of *in utero* aspiration and sclerosis of lymphangiomas.

Dr Burns completed a BSc at Victoria University in Wellington, New Zealand before moving to Brisbane to study medicine. She graduated from The University of Queensland, and completed her internship and residency at the Royal Brisbane Hospital.

She undertook advanced training in the specialty and gained her fellowship from the Royal Australasian College of Surgeons in 2008. After a short locum in Toowoomba, she took up a fellowship in paediatric otolaryngology in the United Kingdom.

Her subspecialty interest is in paediatric airway disorders.

THURSDAY
31 JULY 2014

SESSION 2: 12.10 – 12.40 pm

THE ROLE OF MITOCHONDRIAL STRUCTURE, FUNCTION AND DYSFUNCTION IN OTORHINOLARYNGOLOGY

Professor David Thorburn
MURDOCH CHILDRENS RESEARCH INSTITUTE

Professor Thorburn leads the Genetic Disorders Research Theme and Mitochondrial Research Group at the Murdoch Childrens Research Institute. He is a NH&MRC Principal Research Fellow and Honorary Professorial Fellow in the Department of Paediatrics at The University of Melbourne.

He received his PhD from The University of Sydney in 1987 before completing Fulbright and C J Martin Fellowships with Professor Ernie Beutler at Scripps Clinic, La Jolla, California. He is a Fellow, and former President, of the Human Genetics Society of Australasia and a Fellow, and Principal Examiner in Genetics, of the Royal College of Pathologists of Australasia.

His research focuses on inherited disorders of mitochondrial energy generation, which comprise more than 160 monogenic disorders, affecting all organ systems.

At rest, a sedentary human has a power requirement of ~420 kJ/hr (~116 W) and must phosphorylate ~65 kg of adenosine diphosphate (ADP) each day to generate sufficient adenosine triphosphate (ATP) to meet this energy demand. Sugars, fats and proteins are our metabolic fuels and about 95% of ATP generation occurs in the mitochondria via the oxidative phosphorylation (OXPHOS) system. Mitochondrial dysfunction results in pathophysiological consequences, such as inadequate energy generation, redox or metabolite imbalance, oxidative stress, abnormal signalling and cell death.

The five enzyme complexes of OXPHOS comprise over 80 protein subunits encoded by nuclear genes and mitochondrial DNA (mtDNA). Normal OXPHOS function relies on hundreds of additional proteins and RNAs required for mitochondrial biogenesis. At a genetic level, OXPHOS disorders can be caused by mutations in the maternally inherited mtDNA or in nuclear genes, resulting in autosomal recessive, autosomal dominant or X-linked inheritance. Over 160 OXPHOS "disease" genes are known and about another 100 await identification.

Disorders of mitochondrial OXPHOS are the most common group of inherited metabolic disorders, affecting at least 1 in 5,000 births. They pose great challenges in diagnosis and treatment due to their enormous clinical and genetic heterogeneity, encompassing any organ system and any age of onset. Genetic diagnosis is improving markedly, as we start to utilise new technologies, such as Whole Exome Sequencing, to sequence all our 20,000 genes at once rather than relying on single gene analyses. We have used these approaches to identify mutations in many known genes and in 10 novel disease genes in the last four years.

Primary OXPHOS disorders cause a range of symptoms relevant to Otorhinolaryngology. Hearing impairment is common, can be one of the first symptoms and can remain isolated or be syndromic. In patients with isolated deafness, the most common cause is the mtDNA m.1555A>G mutation, in which hearing loss is often recognised or exacerbated after aminoglycosides. A surprising finding of recent years is that about 1 in 250 people in the general population carry either the m.1555A>G mutation or another mtDNA mutation, m.3243A>G, associated with deafness, diabetes or MELAS. Only a small fraction of these carriers are being identified with mitochondrial disease and while some may be asymptomatic, it is likely that many additional cases are being missed. Mitochondrial hearing loss is usually due to cochlear or auditory nerve dysfunction and often responds well to hearing aids or cochlear implants.

Bulbar weakness is relatively common in mitochondrial disease and may predispose to excessive snoring, obstructive sleep apnoea, swallowing difficulties and aspiration pneumonia. Many patients with mitochondrial disease walk a metabolic tightrope and are prone to severe decompensation following infections, so may be referred for management of recurrent otitis media.

About a third of paragangliomas in the head and neck region may be familial. Many of these are caused by mutations in subunits or assembly factors for OXPHOS complex II (SDH), which are thought to drive a pseudohypoxia response.

AUDITORY SYSTEM PLASTICITY IN ADULTS

Professor Dexter Irvine
BIONICS INSTITUTE OF AUSTRALIA

In the adult auditory system, plasticity has been demonstrated experimentally in association with, or as a consequence of, a number of variables - partial hearing loss, behavioural conditioning (i.e. learning and memory), perceptual learning, environmental enrichment, cortical microstimulation, direct activation of neuromodulatory systems, cochlear electrical stimulation in profoundly deaf animals and blindness (i.e. cross-modal plasticity). Some of these experimentally demonstrated forms of plasticity have clinical implications and clinical observations provide evidence of plasticity. Perhaps most dramatically, it is widely recognised that the remarkable success of cochlear implants is in part due to the brain's ability to adapt to the input provided by the device. Those forms of plasticity with the clearest clinical implications will be considered in more detail.

Partial hearing loss, associated with damage to a restricted region of the cochlea, results in a reorganisation of the frequency (tonotopic) "maps" in auditory cortex and thalamus, and also in hyperactivity (increased spontaneous activity) in central auditory nuclei. These changes are essentially "bottom-up", in that they are driven by the changes in afferent input. Although plasticity is commonly thought of as adaptive or compensatory, this form of plasticity is not adaptive, in that it in no way compensates for the hearing loss. In fact, there is growing evidence that it is maladaptive - tinnitus has been related to both hyperactivity in auditory brainstem centres and to cortical map reorganisation, and hyperacusis has also been related to hyperactivity.

Severe/profound neonatal deafness results in numerous changes in the central auditory system, one of which is a loss of cortical tonotopic organisation. We have shown in neonatally deafened cats that cochlear electrical stimulation derived from a clinical implant, whether initiated shortly after deafening or after an extended period of deafness, can restore normal tonotopicity. Others have found that degraded temporal processing in the auditory cortex as a consequence of long-term deafness can also be partially restored by cochlear electrical stimulation. It is likely that these forms of plasticity contribute to the improvements in speech perception exhibited by cochlear implantees over an extended period post-implantation. The plasticity underlying improvements in speech perception by post-lingually deaf implantees also involves "top-down" processes, however, in that it depends on lexical, syntactic and semantic knowledge.

There is evidence from both animal and human studies that profound deafness can result in auditory cortical areas being recruited or "taken over" by visual processing. There is also some evidence that this cross-modal plasticity can limit the efficacy of a cochlear implant, presumably because the input from the implant has reduced access to auditory cortical processing mechanisms.

Perceptual learning refers to the improvement in sensory discriminative performance with practice. There is evidence that such learning involves plasticity in primary and secondary sensory cortical areas. This form of plasticity has engendered interest in the development of training regimes for cochlear implantees.

Professor Irvine completed a BA (Hons) degree in psychology at The University of Sydney in 1966 and a PhD in auditory neuroscience at Monash University in 1971.

After postdoctoral training at The University of Western Australia and the University of California at Irvine, he joined the Department of Psychology at Monash University, where he held a Personal Chair from 1994 until his retirement in 2005. He currently holds a part-time position as a Professorial Research Fellow at the Bionics Institute of Australia.

His research focuses on a number of aspects of central auditory processing, notably the mechanisms of sound localisation and the functional organisation of the auditory cortex.

THURSDAY
31 JULY 2014

SESSION 3: 2.00 – 2.15 pm

THE AVIAN SYRINX

Dr David Hogan
ROYAL BRISBANE AND WOMEN'S HOSPITAL

Dr Hogan completed his undergraduate studies with a BSc at The University of Queensland, majoring in biomedical science and anatomy. He then went on to complete his medical training, graduating with a MBBS in 2006. He is currently a senior registrar at the Royal Brisbane and Women's Hospital.

Together with colleagues at the Princess Alexandra Hospital, he has been involved in a number of research projects, most recently investigating pharyngo-oesophageal fistula rates with differing closure techniques.

His clinical interests include both head and neck surgery and otology.

Like humans, songbirds learn complex vocalisations early in life. Sensory exposure results in internalisation of sensory experience with sensorimotor learning that, when combined with auditory feedback from self-generated vocalisation, results in song development. Unlike humans, songbirds are not generally limited with respect to early neural plasticity associated with language development in children.

Generally speaking, songs are usually long and complex, and produced spontaneously by males. However, the females of some species do sing, and sometimes sing in duet with the male, for example, in certain tropical species.

The primary sound source in birds is the syrinx. The syrinx can be located at the junction of the two primary bronchi and the trachea (tracheobronchial in songbirds) or located entirely in the trachea or bronchi. This arrangement varies considerably between different orders or even within families of the same order.

In songbirds, two sound sources are produced by their bipartite syrinx. It consists of modified tracheal and bronchial cartilaginous rings making up the skeletal framework to form the tympanum. At the cranial end of each bronchus sits a pair of vibratory structures made up of the medial and lateral labia, producing sound when adducted and set into vibration by an expiratory airstream. A dorso-ventrally oriented cartilage bridge, the pessulus, supports the junction of the primary bronchi. At its apex, the semilunar membrane forms the bronchial septum. The rostral end of the medial labia attaches to the semilunar membrane, while the caudal end attaches to the medial tympaniform membrane (MTM).

A mass of connective tissue in the lateral wall of each bronchus forms the lateral labia. This is covered by four external syringeal muscles. Innervation of the syringeal muscles is supplied by the ipsilateral tracheosyringeal branch of the hypoglossal nerve. Each side of the syrinx being under independent control of the ipsilateral motor neurons situated in the hypoglossal nucleus in the brainstem.

Considerable overlap exists between left and right sides of the syrinx with respect to production of mid frequency sounds. However, they are otherwise specialised to produce low frequency sounds on the left and high frequency sounds on the right with some exceptions.

Birds with a tracheobronchial or bronchial syrinx are able to sing in internal duet, otherwise known as the 'two-voice' theory. With independent vibrating membranes, two very independent carrier waves can be produced. Sound can be produced by either membrane alone, by both membranes acting together or by switching the sound source from one membrane to the next. Sound generated in the syrinx is modulated and filtered by the vocal tract.

The classical theory of sound production, first published by Miskimen in 1951, and then tested experimentally by Greenwalt in 1968, was centred on vibrations produced by the MTM set into vibration via the Bernoulli Effect. This was questioned by Goller and Larsen in 1997, who suggested that sound was produced by the medial and lateral labia after endoscopic visualisation of the vibrating labia. It may still be possible that this theory of sound production is correct in some species, particularly given the large diversity of syringeal anatomy.

RADICAL VERSUS FUNCTIONAL TECHNIQUES IN SINUS SURGERY

Professor Anders Cervin
DEPARTMENT OF OTOLARYNGOLOGY, THE UNIVERSITY OF QUEENSLAND

Comparison of surgical techniques in Chronic Rhinosinusitis (CRS) is marred by lack of standardised outcome measurements, small series (with a few exceptions) and the obscure definition of CRS that lend itself to the inclusion of a wide array of different CRS patient subgroups.

The largest study to date is the English national comparative audit of surgery for nasal polyposis and chronic rhinosinusitis, in total 3,128 patients. Eight hundred and forty-four patients received simple polypectomy and 1,004 patients received polypectomy with additional surgery. There were no differences in SNOT-22 outcome scores at 12 and 36 months. The revision rate at 36 months was slightly higher in the simple polypectomy group (13.3% vs. 10.4%, p=0.12). The postoperative bleeding rate was lower in the simple polypectomy group (6.0% vs. 8.6%, p=0.04).

Middle turbinate (MT), to resect or preserve? Several studies comparing middle turbinate conservation vs. resection suggests that there is no difference in overall patient satisfaction. However, a study by Soler et al compared 195 sinus surgery cases with preservation of MT against 47 with MT resection. In spite of the fact that the MT resection group had higher baseline disease burden, they had a better smell identification score (p=0.047) and a better endoscopic score at 12 months.

Balloons sinuplasty or surgery in CRS without polyps? Koskinen compared 45 sinus surgery patients with 40 balloon sinuplasty patients. Patient satisfaction was identical with 64% of patients satisfied in both groups, however, the balloon sinusotomy group reported a statistically significant higher number of maxillary sinus punctures and antibiotic courses at 12 months.

A recent study from Bikhazi *et al* compared the effect on maxillary CRS by endoscopic balloon dilation (n=50) or endoscopic sinus surgery (n=42). Both groups showed similar improvement in SNOT-20 outcome scores, as well as significant reductions in rhinosinusitis episodes (mean decrease, 4.2 for balloon dilation and 3.5 for FESS). Overall, work productivity and daily activity impairment were significantly improved ($p < 0.001$) in both groups. Revision surgery in the first year was 2% in each group, suggesting that balloon dilatation is as effective as surgery.

Further radical surgery in patients with recalcitrant CRS? Fokkens et al have performed a Denkers procedure in a select group of patients with persisting symptoms after endoscopic sinus surgery with an approximately 70% response rate regarding rhinorrhoea, feeling of congestion and nasal obstruction. No effect on olfaction nor asthma (n=23, follow up 2 years).

Overall, more extensive surgery in nasal polyposis may lead to better results regarding olfaction and an extended recurrence free interval. Resection of middle turbinate can be done without causing harm to either patient related outcomes or olfaction. Whereas, a minimal invasive procedure may be sufficient in CRS patients without polyps. However, further studies are warranted and, ideally, they would include well defined patient groups, patient related outcome measurement tools, olfaction, healthcare utilisation and productivity.

Professor Cervin is the inaugural Professor of Otolaryngology Head and Neck Surgery (Rhinology) at The University of Queensland (Royal Brisbane and Women's Hospital) and Associate Professor at Lund University, Sweden.

He has a longstanding interest in sino-nasal disorders, endoscopic sinus surgery, as well as endoscopic anterior skull base surgery.

His research interests include mucociliary function in the upper airways, the role of nitric oxide in chronic sinusitis, the use of macrolide antibiotics as an immune modulator in chronic sinusitis, health economic perspectives on sino-nasal disease, and the role of probiotics in airway infection and inflammation.

SESSION 3: 2.30 – 2.45 pm

TRACKING THE COURSE OF ACUTE HUMAN VESTIBULAR COMPENSATION

Dr Hamish MacDougall
SCHOOL OF PSYCHOLOGY, THE UNIVERSITY OF SYDNEY

Dr MacDougall completed his PhD at The University of Sydney on eye movements to galvanic vestibular stimulation (GVS) in 2003, followed by a 3-year postdoctoral fellowship in the United States to work on artificial gravity countermeasures, head-eye coordination during simulated Orbiter landing and GVS augmented training.

Since returning to Australia in 2006, Dr MacDougall has been working on head-eye coordination during driving, incomplete vestibular compensation, the effect of motion on human performance and operator proficiency following long-duration spaceflight.

His research interests include acute human vestibular compensation, video head impulse testing, and the development of educational modelling tools for smart-phones and tablet computers.

Some 30% of patients with unilateral vestibular loss (UVL) compensate poorly to their peripheral sensory problems, such that serious symptoms including vertigo, nystagmus, oscillopsia, postural instability and locomotor dysfunction persist indefinitely, whereas many other similar patients compensate well.

Objective markers of vestibular function that distinguish between these well- and poorly-compensated groups are, therefore, required in order to predict the outcome of individuals and find ways to encourage more complete and effective compensation.

We have focused on new exact measures of vestibular and oculomotor function during testing and during normal activities to see whether well-compensated patients actually regain vestibular function, or, as we hypothesise, they learn new oculomotor strategies, such as saccades to conceal their vestibular inadequacy. To this end, we have developed new vestibular indicators.

The most promising development towards our understanding of the process has come from our video head impulse system for the evaluation of the vestibular ocular reflex during video head impulse testing (vHIT). The rapid international acceptance of our vHIT method of testing semicircular canal function was demonstrated at the recent meeting of the Barany Society in Buenos Aires, where many of the presentations used our vHIT method.

In order to apply vHIT to track the course of acute human vestibular compensation, we needed to establish several features of the method, including the sensitivity and specificity and diagnostic accuracy of vHIT, the repeatability of test results, the comparability of results from different operators, the degree to which normal ageing affects results and the influence of cerebellar dysfunction.

Our results show that vHIT is a very stable and sensitive test, and that saccades rather than VOR calculated from slow phase eye velocity, are the best indicator of compensation. The gain results indicate that, rather than use a single value, it would be better to consider gain at various velocities in each plane. Horizontal gain displays a tight cluster around unity at low speeds, with a small drop off in gain as velocity increases. Variability is much greater in the vertical planes, with a more rapid drop-off as velocity increases. Results, however, vary less with age than other balance patient data would suggest.

The vHIT, if carried out correctly, is a simple, fast, robust and reliable method of assessing semicircular canal function at all ages using the physiological stimulus of rotation. We have developed, firstly, a new saccadic indicator of residual vestibular function that is the perfect complement to the present standard vHIT measure of VOR gain and, secondly, a sensitive new paradigm to measure vestibular loss and its recovery.

CORTICAL CHANGES FOLLOWING ACUTE LOWER MOTOR NEURONE FACIAL NERVE PARALYSIS

Dr Susan Coulson
DISCIPLINE OF PHYSIOTHERAPY, THE UNIVERSITY OF SYDNEY

Facial nerve disorders may significantly affect the sufferer's quality of life. These disorders occur after Bell's palsy or nerve damage during the removal of an acoustic neuroma.

Currently, diagnosis and treatment decisions depend on judgment by the human eye for application of facial grading systems and for assessing lack of facial movement information from standard static imaging testing, as well as by EMG recordings of peripheral muscular activity. In addition, these measures do not account for any changes in the dynamic neural representation of the main essential function of the human face, that of facial expression.

By measuring facial movements through changes in 'blood-oxygenation level dependent functional magnetic resonance imaging' (BOLD fMRI), the extent of neural representation and cortical reorganisation during recovery after facial paralysis can be investigated. This fMRI technology provides a measure that can then be used to examine the effectiveness of future treatment interventions.

Cortical reorganisation describes the capacity of the cerebral cortex to change its reactivity to various stimuli, resulting in changes to somatotopic representations. Human cortical representations are continuously modified by experience, as occurs in the processes of learning, training and skill acquisition. This is demonstrated by the ability of the brain to preferentially allocate cortical area to better represent specific peripheral input sources that are proportionally the most used. Injury-induced cortical reorganisation with representation area shrinkage has been documented to occur for both sensory and motor representations following central nervous system injuries, such as stroke, and similar processes have been found to occur following peripheral nerve injuries, such as facial nerve paralysis. Cortical changes occurring in the facial motor cortex and surrounding areas following facial nerve paralysis are influenced by surgical repair and may be modified with facial physiotherapy rehabilitation.

Dr Coulson holds a BAppSc (Physiotherapy), MAppSc (Exercise and Sport Science) and a PhD (Physiotherapy), all of which were obtained from The University of Sydney.

She is a clinical and academic physiotherapist.

Her research focuses on the assessment and treatment of people following disorders of the facial nerve. She is currently investigating treatments specifically designed to improve control and quality of the smile after long-term facial nerve injury.

FRIDAY
1 AUGUST 2014

SESSION 6: 8.30 – 9.00 am

AGE RELATED EFFECTS ON THE LABYRINTH AND ITS CENTRAL CONNECTIONS

Dr Americo Migliaccio
NEUROSCIENCE RESEARCH AUSTRALIA

Dr Migliaccio is a Senior Research Fellow and Group Leader at Neuroscience Research Australia, where he has been head of the Balance and Vision Laboratory since 2008. He is also a conjoint Senior Lecturer at The University of New South Wales and an Adjunct Associate Professor at Johns Hopkins University, United States.

He has a broad range of skills, including basic (animal) science, clinical studies and biomedical engineering.

His research focuses on vestibular treatment and rehabilitation that increases or restores vestibular function.

The vestibular system detects and initiates responses to changes in sensations of equilibrium. Hypofunction in any part of this system, typically due to ageing or injury, results in dizziness and imbalance, which contributes to an increased risk of falls. Injury to the vestibular system due to trauma, disease or ototoxic drugs is often localised, for example, to the peripheral component, whereas injury through ageing is thought to affect the vestibular system as a whole.

Structurally, ageing brings about degeneration in most, if not all, areas of the vestibular system. This degeneration is most pronounced within the cristae ampullares of the semicircular canals, where there is a 40% average decrease in hair cells for all canals. More recently, similar results have been obtained in research conducted by Merchant *et al*, as well as Rauch *et al*, into hair cell populations within the elderly. Startlingly, within the ageing hair cells themselves, an aggregation of lipofuscin pigments, as well as an accumulation of lysosome-like granules, has been observed in post-mortem specimens.

Given the profound anatomical degeneration exhibited with age, the question which consequently arises is how these changes manifest themselves functionally, that is, whether or not vestibular degeneration corresponds to reduced physiological vestibular function. It has been postulated previously that within the normal population, there are adaptive and plastic characteristics that may be able to compensate partially, if not completely, for this structural degeneration. Additionally, given the interactions between other input systems involved in equilibrium maintenance, it is possible that as a consequence, subtle physiological degenerations are unable to be identified.

One component of the vestibular system is the angular vestibulo-ocular reflex (VOR), which stabilises vision during head motion by rotating the eyes in the opposite direction to maintain gaze and images stationary on the retina. The semicircular canals, which sense angular head rotations, display the most profound degeneration in the vestibular end organ. However, previous studies examining the effect of ageing on the angular VOR have been conflicting in their findings. For example, during unidirectional rotation testing of the VOR in order to ascertain the dominant time constant (time taken for eye velocity to decay to 63% of its peak velocity under constant velocity head rotation), some report decreased time constants (from a mean of 15.1s to a mean of 11.7s) in older participants, whilst others reported decreased time constants in younger participants, whereas others report no age related changes. Therefore, for those within the healthy population, who do not experience noticeable balance problems, it is still unclear whether the anatomical changes described in the literature relate to functional changes.

THE NEUROSCIENCE AND NEUROPSYCHOLOGY OF MUSIC

Associate Professor Neil McLachlan
SCHOOL OF PSYCHOLOGICAL SCIENCES, THE UNIVERSITY OF MELBOURNE

Since classical times, music in the west has been considered a "high art", a behavior that requires high levels of abstract cognition and emotional sensitivity.

However, this idea conflicts with the long held belief that the perception of pitch and harmony are innate products of the harmonic relationships found in the human voice and many musical instruments. This conundrum has led to the idea that the ability to hear pitch and harmony are inherited talents that vary across the population. In contrast, we have found that within the physiological limits of the auditory system, the ability to hear pitch and harmony is largely learnt. Furthermore, in direct contradiction to widely accepted theories of pitch, we have shown that people can even learn to accurately pitch inharmonic sounds.

The adaptability of pitch perception points to plasticity in sub-cortical auditory pathways. We propose that sound recognition initiates early in the auditory pathway and uses long-term memory templates of familiar sounds to segregate and integrate afferent auditory information according to previously established source identities and feature maps. For example, a human voice can be recognised and associated with pitch height by its harmonics, as well as being associated with a verbal meaning by its formants. We also propose that failure to recognise an unfamiliar sound disrupts pitch processing and leads to high arousal in musicians and the experience of dissonance.

The speed at which sound recognition occurs and the ability of primitive reptiles to learn to recognise pitch contours in bird song, suggests that the early stages of sound recognition (template matching) occur in the auditory brain stem. The ponto-cerebellar pathways are well developed in reptiles and mammals, and have been shown to be involved in auditory conditioned behaviors. We present a new model of the auditory pathways that includes these well-documented cortico-cerebellar networks and can account for rapid plasticity of sub-cortical auditory processing and the implicit learning of musical abilities. We then show how these networks interact with the limbic system to produce strong emotional responses to music that either matches or violates long-term memory for musical timbre and grammar. Finally, we show a range of neurophysiological evidence for the involvement of ponto-cerebellar networks in music perception.

Associate Professor McLachlan has broad professional experience in music, acoustic design, engineering and auditory neuroscience.

In 2000, he designed the world's first harmonic bells and, more recently, a new harmonic percussion ensemble for use in educational and a range of community contexts. He also developed the first end-end neurobiological model of auditory processing.

His research interests include design optimisation, human psycho-acoustical modelling, neuro-psychologically inspired machine sensing systems, and human cognitively based representations of music and acoustical events.

FRIDAY
1 AUGUST 2014

SESSION 6: 9.30 – 10.00 am

WEIRD EARS: THE STRUCTURE AND FUNCTION OF INSECT AUDITORY SYSTEMS

Associate Professor David Merritt
SCHOOL OF BIOLOGICAL SCIENCES, THE UNIVERSITY OF QUEENSLAND

Associate Professor Merritt gained a PhD in Entomology in 1989 and, after several postdoctoral positions in the United States and in Australia, he joined The University of Queensland in 1996.

He teaches courses in entomology and developmental biology, and specialises in on-line delivery and the use of innovative techniques for teaching entomology.

His research focuses on the development and physiology of insect nervous systems. Specific projects include the development of the sensory system and axonal path-finding in embryos of the genetic model organism *Drosophila melanogaster* and the investigation of possible developmental and genetic links in the formation of the nervous system and dermal glands of *Drosophila*.

Given their evolutionary distance from humans, it would not be surprising if the auditory systems of insects and vertebrates showed no similarities at all. However, recent work on the genetic model organism, the fruitfly, *Drosophila melanogaster*, has revealed deep evolutionary similarities in the hearing systems of humans and insects.

Searching for genes that affect hearing is relatively simple in the fruitfly, by mutagenising and testing (screening) for loss of hearing or vibration sensitivity. In fact, a number of mutants were isolated in a screen that involved playing a recorded version of the fruitfly mating song - a buzzing sound that males produce by vibrating the wings - to groups of males and observing whether it caused them to initiate courting behaviour.

Similar approaches have been used to identify a number of ion channel-encoding genes that are essential for insect hearing. An important developmental gene, called *atonal*, was first identified in *Drosophila* because it was required for the formation of sensory neurons called chordotonal organs. Chordotonal organs are the sensory units that are required for hearing in *Drosophila*, where they are clustered around the base of the antenna. *Drosophila atonal* has an ortholog in vertebrates that is similarly required for auditory function. It is named MATH, the mammalian atonal homolog. The conservation of function in this gene family suggested that hearing systems across much of the animal kingdom could have ancient evolutionary similarities, meaning that the genetic and mutant approaches, plus the cell biological and electrophysiological approaches used in *Drosophila*, might help identify additional key genes used in the auditory pathway. Like vertebrate hair calls, insect auditory receptor cells possess a ciliated process that detects sound. Unlike vertebrate hair cells, the insect auditory cells are neurons with long axons that enter the CNS and make synaptic connections in auditory neuropil.

Despite the recognisable genetic and cellular similarities between insects and humans, insects have many surprises in store when it comes to how they hear and where their "ears" are located. Moths have ears located on the thorax near the base of the wings that appear to be primarily involved in detecting the sounds of hunting bats. In crickets, where chorusing between males and females is an essential component of the mating system, the ears can be located on the fore-legs. Such diverse modifications in the location and structure of insect ears can be related to evolution changing the function of pre-existing chordotonal organs from a proprioceptive function to an auditory one.

FLUID DYNAMICS OF THE INNER EAR

Dr Daniel Brown
BRAIN & MIND RESEARCH INSTITUTE, THE UNIVERSITY OF SYDNEY

We have a reasonable understanding of how cells regulate their volume and ionic composition during an osmotic challenge, however, the same cannot be said for extracellular fluid spaces in sensory organs, such as the eye or inner ear. Given that cochlear and vestibular hair cells are sensitive to nanometre displacements of the labyrinth, there is a need to homeostatically regulate fluid volumes and pressures to avoid non-acoustic stimulation.

Evidence is emerging that fluid regulation involves extracellular matrix molecules and epithelial channels, such as ENaC, Na^+/K^+-ATPase, Cl^-/HCO_3^- and aquaporins. In addition to the epithelial secretion and absorption of salt and water content of endolymph and perilymph, we also need to understand the dynamics of fluid transport through the various ducts, valves and leaky tissues of the ear. Beyond underlying disorders, such as endolymphatic hydrops, these mechanisms play a pivotal role in the pharmacokinetics of the inner ear and are likely of primary importance to current pharmacotherapies in otology.

Whilst it is clear that the endolymphatic duct and sac play an important role in the regulation of endolymph, the theory that endolymph is simply produced in the cochlea and absorbed in the sac is an oversimplification on the basis of direct experimental findings and the complex morphology of the labyrinth. Additionally, it is still unclear how the rate of endolymph absorption in the duct or sac is regulated, although morphological valves inherent to the membranous labyrinth may play a role. As an example of the function of these ducts, we have recently demonstrated that the utriculo-saccular duct provides a protective barrier during elevated endolymph pressure in the pars inferior, at least up to a three-fold increase in endolymph volume. Further, perilymph regulation is unlikely to be a passive process despite directly communicating with the cerebrospinal fluid via the cochlear aqueduct. Evidence suggests that perilymph can be pressurised slightly due to the presence of the cochlear aqueduct valve, which may also play a role in cochlear pharmacokinetics.

Ultimately, the inner ear is far from a leaky chicken-wire like environment, with active epithelial regulation of inner ear fluids and with membranous barriers impeding the flow of fluids and ions between compartments. Progress in our understanding of inner ear fluid dynamics is likely to be driven partly by disorders, such as Meniere's Disease, but also so by the need to deliver drugs to the inner ear more effectively.

Dr Brown is a Research Fellow at the Brain & Mind Research Institute.

He developed the first laboratory fully devoted to researching Meniere's Disease (MD). Whilst this mainly involves *in vivo* experimentation in animal models, he has a broader interest in sensory electrophysiology, neuroscience and homeostasis.

His research focuses on the cause and clinical diagnosis of MD. Specific projects include investigating the regulation of endolymphatic fluid, emulating endolymphatic hydrops in guinea pigs at the same time as monitoring cochlear and vestibular function, and developing new imaging techniques for demonstrating the morphological changes that occur within the inner ear during hydrops development.

FRIDAY
1 AUGUST 2014

SESSION 7: 11.00 – 11.40 am

EVALUATING THYROID NODULES USING MOLECULAR GENETIC TECHNIQUES

Professor Robert Ferris
INTERNATIONAL KEYNOTE SPEAKER

Recent advances in research on thyroid carcinogenesis have yielded applications of diagnostic molecular biomarkers and profiling panels in the management of thyroid nodules. The specific utility of these novel, clinically available molecular tests is becoming widely appreciated, especially in perioperative decision-making by the surgeon regarding the need for surgery and the extent of resection.

Clinical scenarios by cytologic category are reviewed in which the surgeon could find molecular profiling test results useful, particularly for cases with indeterminate fine needle aspiration (FNA) cytology. Distinct strengths of each ancillary test are highlighted to convey the current status of this evolving field, which has already demonstrated potential to streamline surgical decision-making and reduce unnecessary surgery, with the accompanying benefits.

However, the performance of any diagnostic test, that is, its positive predictive value (PPV) and negative predictive value (NPV), are exquisitely influenced by the prevalence of cancer in that cytologic category, which is known to vary widely at particular institutions. Thus, it is crucial for the surgeon to know the prevalence of malignancy in each indeterminate cytologic category, at one's own institution. Without this information, the performance of the diagnostic tests may vary substantially.

Professor Ferris is leading a task force convened by the Surgical Affairs Committee of the American Thyroid Association and was tasked with writing a consensus statement on this topic to guide perioperative decision-making, which he will outline in this presentation, showing specific case scenarios and how the University of Pittsburgh has implemented a molecular testing strategy for routine reflexive testing.

SESSION 7: 11.40 – 12.20 pm

FRIDAY
1 AUGUST 2014

THE ETIOLOGY AND PATHOGENESIS OF CHRONIC RHINOSINUSITIS: IMPLICATIONS FOR THERAPY

Professor Robert Kern
INTERNATIONAL KEYNOTE SPEAKER

Chronic rhinosinusitis (CRS) is a broad clinical syndrome defined by persistent symptomatic inflammation of the mucosa of the nose and paranasal sinuses. The majority of cases are idiopathic, with only a very small subset occurring in association with a discrete event (e.g. trauma) or as a local manifestation of a known systemic disease.

At present, factors that have been associated with the etiology and pathogenesis of idiopathic CRS include fungi, resistant bacteria, superantigens, biofilms, environmental irritants, acquired sinonasal obstruction (especially of the osteomeatal complex or OMC), as well as genetic or epigenetic variation of the host. This list includes both environmental agents and host factors, and though the relative importance of each remains a matter of rigorous debate, consensus has emerged on two points, firstly, specific factors likely vary in importance in individual patients and, secondly, CRS is an antegrade process wherein the mucosal inflammation is typically triggered by exogenous agents inhaled through the nose.

Overall, this leads to the concept that CRS pathogenesis is best described as a dysfunctional interaction that occurs at the site of interface between the host and the environment (i.e. the sinonasal mucosa). In other words, a dysfunctional immune response to exogenous factors at the sinonasal mucosal border leads to the mucosal inflammation, radiographic changes and the symptoms that broadly characterise CRS. The working hypothesis is that a combination of genetic factors and environmental events creates a predisposition to the development of chronic inflammation when the nasal mucosa is subsequently challenged by otherwise innocuous exogenous agents.

The CRS syndrome actually consists of multiple clinical phenotypes driven by one or more biologic pathways. The most widely accepted classification system divides CRS phenotypes into chronic rhinosinusitis without nasal polyps (CRSsNP) and chronic rhinosinusitis with nasal polyps (CRSwNP) based on nasal endoscopy. CRSwNP is closely associated with Th2 inflammation and eosinophilic infiltration in the polyp tissue while CRSsNP has much less Th2 skewing, less eosinophilia and relatively more prominent neutrophilia in the sinus mucosa. These statements are only generally true and provide no insight into the mechanisms or biological processes that take place.

This presentation will highlight the current research from our laboratory and others. Firstly, evidence for an innate immune barrier defect that broadly predisposes to the development of CRS will be presented. Secondly, evidence will be presented demonstrating an exaggerated B cell and immunoglobulin response in the polypoid form of CRS. Third, remodelling changes associated with the deposition of fibrin in the sinus mucosa will be shown to be associated with the Th2 skewed form of CRS. Finally, remodelling changes associated with the deposition of collagen will be shown to be associated with the non-Th2 skewed form of CRS.

In summary, a CRS model begins to emerge wherein multiple, possibly overlapping, biological pathways translate environmental stimuli into tissue damage.

FRIDAY
1 AUGUST 2014

SESSION 7: 12.20 – 1.00 pm

THE INTRA-OPERATIVE ASSESSMENT OF OSSICULAR FUNCTION: RESEARCH AND CLINICAL IMPLICATIONS

Professor Magnus von Unge
INTERNATIONAL KEYNOTE SPEAKER

A variety of conditions, such as otosclerosis, malformations and sequels of chronic otitis media (e.g. tympanosclerosis and adhesions), can cause more or less fixation of the middle ear ossicles, which leads to hearing impairment. In order to intra-operatively determine the best course of surgical treatment, knowledge of the degree of ossicular mobility is useful. Ossicular assessment is routinely done by manual palpation during surgical exploration, however, it is subjective and imprecise. Furthermore, manual pressing tests the quasi-static mechanical properties, which do not necessarily coincide with acoustic properties. An objective method to assess mobility would be helpful.

Laser-Doppler vibrometry allows non-contact measurements on the nanometre scale and is a standard tool to measure ossicular motion in experimental situations. During surgery with the tympanic membrane elevated, the middle ear mechanics cannot be driven by acoustic stimulation. Devices with a physical actuator have been developed but suffer from risk of overloading or hampering of ossicular motion and are not in use.

We developed a novel non-contact method to assess ossicular fixation during surgery. A small magnet and coil are used to vibrate the umbo. The method has been evaluated in measurements on eight fresh human temporal bones.

A calibrated sound was used to stimulate the tympanic membrane and data on the vibration response of the umbo was measured with the vibrometer. A piece of reflective tape was used to improve the signal strength. The tympanic membrane was then elevated and the magnet was attached near the umbo with a small drop of glass ionomer cement. A custom built pancake coil was placed over the ear, with its opening over the ear canal. A signal was put to the coil to vibrate the magnet and the vibrometer was used to measure the response of the umbo. The stimulation was adjusted to produce a response matching within 1dB that of the acoustic stimulation. Repeated measurements were made at the umbo, at the tip of the long process of incus and at the posterior crus of stapes. Subsequently, in one group of temporal bones, the incus was artificially fixated with ionomer cement and in another group, the stapes was fixated. Fixations were followed by repeated measurements.

The natural variation in ossicular velocity between individuals is 10dB or more, which makes defining a base velocity impossible and, therefore, limits the use of simple velocity measurements in detecting partial fixations. However, measuring the ratio between different points seems to provide an opportunity to define a baseline.

In the normal condition, the incus-umbo ratio in the mid frequency range was -4 to -6 dB in 75% of ears and -12 dB in the remaining 25%, and the stapes-incus ratio zero. The most clear cut data was obtained in the mid frequency region, where the average variation in repeated measurements was <1dB. After incus fixation, the ratio fell to -20 to -40 dB (partial to full fixation), which gives a useful range for intra-operative diagnostics. After partial stapes fixation, the stapes-umbo ratio fell from around -6dB to -30 to -40dB. In conclusion, ratios <0 for stapes-incus and <-12 for incus-umbo is abnormal.

SESSION 8: 2.00 – 2.30 pm

FRIDAY
1 AUGUST 2014

EVOLUTION AND DEVELOPEMENT: EPIGENETICS AND OTORHINOLARYNGOLOGY

Professor Susan Clark
GARVAN INSTITUTE OF MEDICAL RESEARCH

Professor Clark completed her BSc (Hons) degree at the Australian National University in 1978 and graduated with a PhD in Biochemistry (mapping and sequencing human histone genes) from The University of Adelaide in 1982. She spent her postdoctoral years at Biotechnology Australia from 1983 to 1988, leading studies on recombinant vaccine development and eukaryotic expression of human inhibin, Il-3 and GMCSF.

In 1992, she returned to basic research as Group Leader of the Gene Regulation Unit at Kanematsu Laboratories, Royal Prince Alfred Hospital, where she developed and implemented bisulphite sequencing for DNA methylation analysis. In 2000, she established and headed the Epigenetics Group at the Sydney Cancer Centre, Royal Prince Alfred Hospital and, in 2004, moved her group to the Garvan Institute of Medical Research, where she initiated and led the growth of the Epigenetics Research Program in the Cancer Research Division.

Professor Clark's DNA methylation studies over the last twenty years have instigated profound questions about the importance of epigenetics in early development and in disease, especially in cancer. She has made extensive ground-breaking discoveries relating to DNA methylation patterns in normal and cancer genomes that have led to the commercialisation of new methylation-based tests for early cancer detection. The techniques she pioneered in the early 1990s, including bisulphite sequencing, have revolutionised and now underpin the new era in epigen"omic" research.

She was founding member of IHEC (International Human Epigenome Consortium) and led the formation of AEpiA (Australian Epigenetics Alliance). She has a number of awards, including the RPAH Research Medal in 2002, Julian Wells Medal in 2003, and "Biochemisch Analytik Preis" for outstanding contribution for Methylation analysis in 2004. In 2006, she was elected a Fellow of the World Technology Network for Biotechnology and, in 2009, was awarded one of Australia's "Top Ten" National Health and Medical Research (NHMRC) Project Scientists.

FRIDAY
1 AUGUST 2014

SESSION 8: 2.30 – 2.45 pm

DEVELOPING A BIONIC VOICE PROSTHESIS

Dr Farzaneh Ahmadi
SCHOOL OF ELECTRICAL AND INFORMATION ENGINEERING, THE UNIVERSITY OF SYDNEY

Dr Ahmadi completed her PhD at Nanyang Technological University of Singapore and is currently working at The University of Sydney.

She has a background in electrical engineering with expertise in signal processing, computational neuroscience, brain dynamics and bionic systems design.

Her research focuses on bionic technologies to assist individuals with various impairments. Specific projects include investigating how the human larynx is controlled by its neural signals and the development of a bionic voice prosthesis.

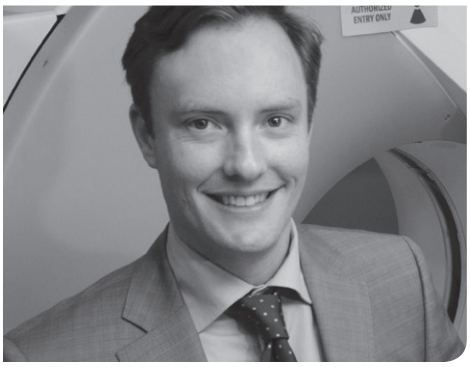
Despite the advancement in many subfields of bionics, the development of a bionic voice prosthesis for voice-loss patients has not really progressed.

A bionic voice prosthesis replaces the function of a missing larynx and generates natural voice for patients, who retain a functional vocal tract but have lost their voice because of surgical removal of the larynx. The individuals likely to receive this prosthesis are laryngectomy patients, who lose their voice-box surgically because of larynx cancer or swallowing disorders. This presentation introduces the latest achievements in developing a solution for these patients.

The proposed bionic voice prosthesis has been implemented as a simulated version of the human larynx and is controlled using the same physiological cues that contribute to generating natural voice. Designing the prosthesis has involved components of neural control, respiratory control and a simulated model of the human larynx. The neural control unit interfaces the nerve signals sent by the laryngeal motor cortex of the brain on their path to control the activity of the missing larynx. The respiratory interface employs the natural role of respiration to drive and regulate voice generation. A precise model of the vocal folds is also implemented in the context of this solution as a software unit, and is driven by respiratory and neural control mechanisms. The resulting bionic sound source is implanted on a denture unit inside the mouth.

This presentation describes the process of developing the experimental bionic voice prototype and testing it in pre-clinical trials on laryngectomy patients. The design of the prototype involved a denture-based housing for electronics and transducers, optimisation of neural/neuromuscular recording electrodes and sensing respiratory pressure variations, and current performance in terms of controlling the pitch and onset/offset of the resulting voice is discussed. The pitch (i.e. fundamental frequency) is the highest contributor of generating natural voice for laryngectomy patients. Precise control of the onset/offset of voice is the most important requirement for generating intelligible speech. Using these parameters, the resulting speech signal is compared against the gold standard of tracheo-esophageal speech in terms of intelligibility and naturalness.

On a parallel line of research, the neuro-muscular activity of the extrinsic laryngeal muscles is analysed using advanced signal processing to provide a natural mechanism of controlling the pitch of the bionic voice prosthesis. The result has been a significant improvement on the state of the art of using neuro-muscular cues for generating natural voice.



NUCLEAR THERANOSTICS AND RADIOIMMUNOTHERAPY

Dr Timothy Marr
SCHOOL OF SURGERY, THE UNIVERSITY OF WESTERN AUSTRALIA

Personalised medicine is rapidly evolving and establishing credibility as part of the management of a diverse range of malignancies. An underlying hypothesis of personalised medicine is the notion that every patient's cancer is unique and, therefore, management should be individualised.

Emerging best practice in the management of breast cancer is an example of how variability in molecular expression of oestrogen and progesterone receptors, as well as genetic expression of the key proto-oncogene ERBB2 (HER2) and mutation of BRACA genes, have directed and personalised targeted treatment with agents, such as Tamoxifen and Trastuzumab. Indeed, government subsidisation of such treatments in Australia is now restricted to patients in whom such molecular and genetic pathways are proven. In a climate of ever increasing cost pressures and budgetary health constraints, this trend is set to continue.

Whilst personalised medicine holds much promise to improving the care of patients with cancer, there has been little work done to develop personalised targeted therapies for patients with head and neck malignancy. Indeed, for advanced-stage patients, refractory to all known efficacious treatments, no standard treatment option exists and this represents a significant deficit, particularly given the large number of patients who relapse following primary treatment.

As part of a personalised approach to cancer management, the concept of nuclear theranostics has evolved. Nuclear theranostics epitomises a personalised approach to cancer management by combining pre-targeting of cancer therapy using diagnostic molecular radionuclide imaging with rapid progression to molecular targeted radioimmunotherapy if the pre-targeted diagnostic imaging is positive.

In this presentation, the concept of nuclear theranostics and its utility in head and neck malignancy is discussed, and its potential utility explained with a presentation of preliminary results from an ongoing single centre prospective, pragmatic phase 2 theranostic clinical trial based at Fremantle Hospital. For this study, we have adopted a novel theranostics-radioimmunotherapeutic approach in the clinical setting of adjuvant and salvage treatment of head and neck squamous cell carcinoma coupled with receptor targeted PET/CT localisation of residual tumour sites. Consecutive eligible patients were recruited between the period September 2013 and June 2014, enrolling 35 patients for diagnostic molecular PET/CT imaging with Gallium-68-DOTATATE. To be eligible for recruitment, patients require a pathological diagnosis of squamous cell carcinoma involving the head and neck, and a comparison 18F-FDG PET/CT study completed at the time of diagnosis. In select patients with a positive diagnostic study, we have progressed to a world first in human theranostic trial of pre-targeted Lutetium-177-DOTATE with tumour uptake confirmed on SPECT/CT.

Dr Marr is a surgeon-scientist currently undertaking a PhD at The University of Western Australia.

His PhD is titled *Molecular Surgery: Novel biomarker development for a personalised genetic approach to the management of head and neck cancer*. A translational research programme has been established in conjunction with this research for the development of new molecular diagnostic imaging methods and targeted radioimmunotherapy.

Dr Marr has set up the first Head and Neck Cancer Biobank in Western Australia to strengthen the research effort for the treatment of head and neck cancer.

FRIDAY
1 AUGUST 2014

SESSION 9: 3.00 – 4.00 pm

THE SURGEON, THE SCIENTIST AND THE ACADEMIC SURGEON/SCIENTIST

Professor John Windsor
DEPARTMENT OF SURGERY, THE UNIVERSITY OF AUCKLAND

Professor Windsor holds a personal Chair in Surgery at The University of Auckland and is a consultant surgeon at Auckland City Hospital.

He founded the Pancreas Research Group (1992), Surgical Skills Centre (1993), HPB/UGI Unit (1994), the Surgical Research Network (2007), which now encompasses ASML (Applied Surgery and Metabolism Laboratory) and SCORE (Surgical Centre for Outcomes Research and Evaluation). He recently completed a five-year term as Chair of the Section of Academic Surgery, RACS (2013).

His surgical interests include the management of acute and chronic pancreatitis, pancreatic cancer, and gastro-oesophageal reflux, malignancy and the development of medical devices.

"The future of surgery is academic surgery" according to a former President of the Royal Australasian College of Surgeons (RACS) when reflecting on the successful *Developing a Career in Academic Surgery* course recently prefixed to the Annual Scientific Congress. Such a statement is not widely accepted.

The RACS was established in 1920 with two mandates - the training of surgeons and the promotion of research in surgery. In the former, it flourished and the training program is held in high regard throughout the world. In the latter, it never truly flourished and is now more challenged than ever.

The American Surgical Association reported recently that "research training in surgery is regarded almost as an afterthought and the surgical profession has not placed a premium on its development and support. It lacks the structure, organisation and oversight that are so well developed in clinical training." It went on to say that "the future of surgery as an academic and professional discipline that continues to contribute to the discovery and clinical translation of new knowledge, technology and surgical therapeutic innovation will depend on how high research is on the priority scale of surgical education and practice."

The recently deceased Irish academic, Professor Gerry O'Sullivan put it this way in a presidential address that when "faced with the complexities of the delivery of modern surgery, research and training, academic surgeons will assume even greater importance in providing leadership. The principal difficulty facing the academic surgeon is the acquisition and the maintenance of both clinical and academic competencies." In the New England Journal of Medicine, Julie Dienstag made the case for greater scientific literacy in saying that "we should expect a higher standard from our trainees who wish to pursue (surgery) in an era in which genomics and informatics will revolutionise biomedical science and health care. To fulfil expectations (surgical trainees) need to foster scholastic rigor, analytical thinking, quantitative assessment and analysis of complex systems in human biology. Our goal should be to help trainees acquire a different, more molecularly orientated and scientifically sophisticated knowledge base."

A number of strategies have been implemented to respond to these challenges, to lift the profile of academic surgery, promote the training of more academic surgeons and assist the output of established academic surgeons. We have had considerable success in developing future surgeon-scientists through the Surgical Research Network in Auckland and some of the reasons for this will be unpacked. The RACS has also been responding to this challenge. Two major projects will be discussed - the first is to elevate the minimum training requirements in surgical research, across all specialties, and, the second is to explore the establishment of a deliberate training pathway for academic surgeons.

1

TINNITUS IMPROVEMENT AFTER VERY LOW FREQUENCY SOUND STIMULATION

P Winkler[1]

[1] Macquarie Street Tinnitus Clinic, Sydney, Australia

BACKGROUND

Residual inhibition is the absence or reduction of tinnitus that occurs after a tinnitus masking signal ceases. Although this phenomenon is well known, the duration of inhibition produced by conventional masking was only 30 to 60 seconds and, therefore, not considered to be therapeutically useful. A new series of non-sinusoidal low frequency sounds below 30 Hz (TIPA) and playing for 12 minutes has been developed and produces prolonged residual inhibition that may last from hours to days.

OBJECTIVES

Tinnitus theory suggests that if tinnitus is repeatedly suppressed, induced development of brain plasticity will produce longer-term reduction of the tinnitus. This study was, therefore, designed to determine whether repeated residual inhibition induced by TIPA would induce longer-term tinnitus suppression.

METHODS

Patients were selected on the basis of having demonstrated positive residual inhibition of tinnitus following an initial single test exposure to the 12-minute TIPA sound. 36 patients who responded were then provided with a digital player and fully enclosed headphones. The player contained 50 copies of the TIPA signal. Patients were instructed to listen to the sound signal daily at a comfortable volume above the Minimum Masking Level. The stimulus was applied to both ears simultaneously. Tinnitus Handicap Inventory (THI) scores were recorded at the commencement of treatment and on completion of the 7-week program. The THI is a standard measure of tinnitus severity with scores ranging from 0 to 100, with higher scores indicating greater tinnitus handicap. A reduction of 7 points in the THI is regarded as the minimum clinically important improvement resulting from treatment.

RESULTS

19 (53%) of the 36 patients in the trial reported improvement resulting from the treatment. The average reduction in THI score was 27 points with a range of 8 to 62 points, including two patients recording a reduction of 58 points. The greater the reduction in the THI score, the greater is the improvement in tinnitus. Three patients reported absence of tinnitus after treatment.

CONCLUSION

Low frequency sound stimulation has a demonstrable effect on tinnitus and the duration of treatment producing this result has been short. In several cases, the THI change (58, 58 and 62 points) has been significantly greater than the 7-point minimum required to demonstrate clinical improvement. Stimulation of inhibitory cells in central auditory pathways is a neurophysiologic mechanism that may explain this tinnitus suppression.

2

THE VIDEO HEAD IMPULSE TEST (vHIT) OF SEMICIRCULAR CANAL FUNCTION: TRUE SENSITIVITY, SPECIFICITY AND AGE DEPENDENT NORMS IN HEALTHY SUBJECTS

L McGarvie[1]
H MacDougall[2]
E Chiarovano[3]
C de Waele[4]
I Curthoys[5]

[1] Royal Prince Alfred Hospital, Sydney, Australia
[2] School of Psychology, The University of Sydney, Australia
[3] University of Paris Descartes, Paris, France
[4] Hopital Salpetriere, Paris, France
[5] School of Psychology, The University of Sydney, Australia

BACKGROUND

Our team has developed a new test of semicircular canal function - the video Head Impulse Test (vHIT). It is a fast and simple test, which is replacing the caloric test. There have been reports comparing vHIT with calorics, however, these cannot give the sensitivity and specificity of vHIT. Further, the caloric is not a definite indicator of vestibular loss, since healthy people may have poor or even absent caloric responses.

OBJECTIVES

To measure the true sensitivity and specificity of vHIT, and to obtain normative values of vestibulo-ocular reflex (VOR) gain in healthy subjects.

METHODS
Eye movement during small, abrupt, passive and unpredictable head turns is recorded by a high-speed video camera together with measures of head velocity and software that objectively quantifies VOR gain for natural stimuli in real time (MacDougall *et al* 2009; 2013).

RESULTS
Sensitivity and Specificity of vHIT: We tested 20 patients within the first year after surgery for unilateral vestibular schwannoma (at Hopital Salpetriere, Paris, France), so they have known section of the vestibular nerve, together with 37 healthy people, to identify just how well vHIT can differentiate between patients and normals. The results show that vHIT is 100% accurate for detecting patients with known unilateral vestibular loss - sensitivity 1.0, specificity 1.0 - i.e. it is diagnostically accurate. Since vHIT gives a continuous measure of vestibular function, it allows measurement of partial vestibular loss e.g. in patients after systemic gentamicin. Normative data: We have measured VOR gain using vHIT on 85 healthy subjects aged between 20 and 93, and we report normative values for VOR gain (means +/- 2 standard deviations) of 10 people in each decade of life. The clear result is that VOR gain to these natural values of head acceleration remains close to 1.0, even into the 80s and 90s.

CONCLUSION
The vHIT is an excellent test of semicircular canal function, which is replacing the caloric test; vHIT sensitivity and specificity is 1.0; in healthy people, VOR gain stays close to 1.0, even in the 9th decade of life; and VOR gain is close to 1.0 at all head velocities, except the highest velocities.

3

E-GROUP (EFFERENT) VESTIBULAR NEURONS FORM A HOMOGENEOUS POPULATION IN THE MOUSE BRAINSTEM

M Mathews[1]
V Tung[2]
A Murray[3]
L Zhang[4]
A Camp[5]

[1] Discipline of Biomedical Science, The University of Sydney, Australia
[2] Discipline of Biomedical Science, The University of Sydney, Australia
[3] Discipline of Biomedical Science, The University of Sydney, Australia
[4] Discipline of Biomedical Science, The University of Sydney, Australia
[5] Discipline of Biomedical Science, The University of Sydney, Australia

BACKGROUND
Our sense of balance is fundamental to our ability to interact with our environment, yet we still know little about the central control of the peripheral balance system.

OBJECTIVES
To confirm the location and characterise the discharge properties of mouse e-group (efferent) vestibular nucleus neurons *in vitro*.

METHODS
Immunohistochemistry: Transverse serial sections (40 µm) were sliced through the 4 week old mouse brainstem and labelled with antibodies against CGRP (n = 7) and ChAT (n = 4). Electrophysiology: Transverse slices (200 µm) were used to characterise intrinsic action potential and discharge properties of visualised e-group neurons (n = 22) in whole-cell current-clamp mode at room temperature.

RESULTS
Small clusters of both CGRP and ChAT immunopositive neurons were identified dorsolateral to the genu of the facial nerve (VII). Spontaneous (n = 9) and non-spontaneous (n = 12) neurons show homogeneous passive membrane properties, including input resistance that differ from neighbouring MVN neurons ($p < 0.05$). In response to both hyperpolarising and depolarising steps, all e-group neurons respond with a short burst of high frequency (ISI < 5 ms) AP's at the cessation of the inhibitory stimulus or the onset of an excitatory stimulus.

CONCLUSION
E-group vestibular neurons are homogeneous in their discharge output suggesting that central control of peripheral vestibular structures may be related more to the inputs that these neurons receive.

4

NEAR INFRARED LIGHT (NIr) UPREGULATES THE EXPRESSION OF ANTIOXIDANT GENES IN THE VESTIBULAR SENSORY EPITHELIUM

L Zhang[1]
M Mathews[2]
P Witting[3]
V Tung[4]
A Camp[5]

[1] Discipline of Biomedical Science, The University of Sydney, Australia
[2] Discipline of Biomedical Science, The University of Sydney, Australia
[3] Discipline of Biomedical Science, The University of Sydney, Australia
[4] Discipline of Biomedical Science, The University of Sydney, Australia
[5] Discipline of Biomedical Science, The University of Sydney, Australia

BACKGROUND

While balance performance declines with age, previous work has shown no significant loss of balance receptors (i.e. vestibular hair cells) with age, at least until the ninth decade of life. As such, subtle subcellular changes may underlie observed age-related balance decline.

OBJECTIVES

Markers of cellular response to oxidative stress (a common feature of ageing) are used to assess the impact of age on the vestibular sensory epithelium (VSE).

METHODS

The sensory epithelium of individual mice was excised in ice-cold glycerol-based artificial cerebrospinal fluid. mRNA was then isolated using a commercially available kit. rtPCR was then used to produce a cDNA library that was subsequently probed for two ubiquitous age-related antioxidants (superoxide dismutase; SOD1 and SOD2). In addition, a novel treatment regime of transcranial near infrared light (NIr; 90s/day for 5 continuous days) was used to protect against the impact of oxidative damage to the mouse vestibular sensory epithelium.

RESULTS

Antioxidants (SOD-1 and SOD-2) are slightly decreased in the VSE of older (9 month old) mice when compared with young (1 month old) mice. In response to brief NIr treatment, both young and older mice showed an increase in the expression of both genes when compared with sham-treated counterparts ($p < 0.05$; SOD-2).

CONCLUSION

These results suggest that oxidative stress may be higher in the VSE of older mice and that NIr light is a potential strategy to protect the VSE from age-related oxidative damage.

5

THE VESTIBULAR MEMBRANOUS LABYRINTH RECONSTRUCTED FROM MICRO-CT SCANS OF FIXED TEMPORAL BONES

P Mukherjee[1]
C Wong[2]
I Curthoys[3]

[1] The University of Sydney, Australia
[2] The University of Sydney, Australia
[3] School of Psychology, The University of Sydney, Australia

BACKGROUND

The spatial organisation of the complex interconnected ducts and sacs of the inner ear is still poorly understood. We sought to extend the use of our new microCT method of the temporal bone (Uzun *et al* 2007), using osmium to stain the membranous labyrinth, to show the spatial organisation of these structures in the inner ear.

OBJECTIVES

The present study set out to use high-resolution microCT scans of human and guinea pig temporal bones to visualise exactly how the membranous structures are organised, with a focus on ductus reuniens, the utriculo-saccular duct and membrana limitans.

METHODS

Guinea pig or human temporal bones were fixed with 3 - 5% paraformaldehyde and glutaraldehyde or just 5% paraformaldehyde and then en bloc stained in 2% osmium tetroxide, which attaches to the membranes of the inner ear, and in microCT allows visualisation of the spatial organisation of these structures and their 3-d spatial relationships. The specimens were scanned by an XRadia high-resolution microCT scanner at very high resolution (down to 2 microns) to visualise these very thin membranes and their interconnections. Other stains do not show inner ear membranes as well. The data were reconstructed using Aviso or VGstudio Max.

RESULTS
Images from the reconstructions show the spatial characteristics of ductus reuniens, the utriculo-saccular duct and membrana limitans, as well as the different character of the perilymphatic space close to the stapes (around the utricle), compared to the perilymphatic space in the canals. The membrana limitans supports the utricular macula and, in one human specimen, was attached to the footplate of the stapes.

CONCLUSION
The use of osmium stained specimens with very high resolution X-ray microCT allowed us to visualise the spatial relationships of membranous structures vital to inner ear functioning.

6

THE DIAGNOSTIC TEST ACCURACY OF THE KUDUWAVE AUTOMATED AUDIOMETER IN HEARING-IMPAIRED ADULTS

C Brennan-Jones[1]
R Eikelboom[2]
D Swanepoel[3]
P Friedland[4]
M Atlas[5]

[1] Ear Science Institute Australia and Ear Sciences Centre, The University of Western Australia, Australia
[2] Ear Science Institute Australia; Ear Sciences Centre, The University of Western Australia, Australia and Department of Communication Pathology, University of Pretoria, South Africa
[3] Department of Communication Pathology, University of Pretoria, South Africa; Ear Science Institute Australia and Ear Sciences Centre, The University of Western Australia, Australia
[4] Ear Science Institute Australia and Ear Sciences Centre, The University of Western Australia, Australia
[5] Ear Science Institute Australia and Ear Sciences Centre, The University of Western Australia, Australia

BACKGROUND
Previous research providing clinical validation of automated audiometers has focused on normal hearing participants. Inclusion of participants without the target condition introduces bias into diagnostic accuracy studies. It is, therefore, essential that the accuracy of automated audiometry is examined in hearing-impaired populations.

OBJECTIVES
To examine the diagnostic test accuracy of automated audiometry in hearing-impaired adults using the KUDUwave automated audiometer.

METHODS
Participants: 45 study participants (20 male, 25 female) were recruited from audiology and otolaryngology clinics at Sir Charles Gairdner Hospital, Perth, Australia. Procedure: Manual audiometry was performed by an audiologist either before or after automated audiometry. The audiologist was blinded to the results of automated audiometry. The KUDUwave is designed to be used outside conventional sound-treated audiological test environments and, as such, testing was conducted in a quiet room. Level of hearing loss was classified according to WHO criteria (normal 0 - 25 dB; mild 26 - 40 dB; moderate 41 - 60 dB; severe 61 - 80 dB; profound >=81 dB) and a conductive hearing loss was identified with a four-frequency average (0.5, 1, 2 and 4 kHz) air-bone gap of >20 dB.

RESULTS
For diagnostic accuracy, the sensitivity for identifying conductive hearing loss was 90.9% in the right ear and 60.0% in the left ear, with specificity at 96.9% in the right ear and 96.7% in the left ear. For diagnosing the level of hearing impairment, sensitivity was 95.2% in the right ear and 77.8% in the left ear, with specificity at 93.4% in the right ear and 94.4% in the left ear. Absolute mean differences for air-conduction thresholds at 0.25, 0.5, 1, 2, 4 and 8 kHz ranged between 5.39 dB - 9.09 dB. Absolute mean differences for bone-conduction thresholds at 0.5, 1, 2 and 4 kHz ranged from 12.12 dB - 16.82 dB.

CONCLUSION
The KUDUwave in automated audiometry mode is highly specific, correctly identifying patients without a conductive hearing loss in environments that are not sound treated. Sensitivity was lower in the left ear across both domains. However, 70% of unilateral losses in the study cohort affected the left ear, with a number of participants reaching maximum testable limits, which may account for some of the variation in addition to known calibration errors at 4 kHz. The KUDUwave, and automated audiometry as a whole, shows potential to be a sensitive and highly specific measure for determining the type and level of hearing loss.

7

SENSITIVITY AND SPECIFICITY OF SELF-REPORTED HEARING DIFFICULTY IN ADULTS OVER 60 YEARS OF AGE

C Brennan-Jones[1]
D Taljaard[2]
S Safstrom[3]
R Bennett[4]
R Eikelboom[5]

[1] Ear Science Institute Australia and Ear Sciences Centre, The University of Western Australia, Australia
[2] Ear Science Institute Australia and Ear Sciences Centre, The University of Western Australia, Australia
[3] Ear Science Institute Australia and Ear Sciences Centre, The University of Western Australia, Australia
[4] Ear Science Institute Australia and Ear Sciences Centre, The University of Western Australia, Australia
[5] Ear Science Institute Australia; Ear Sciences Centre, The University of Western Australia, Australia and Department of Communication Pathology, University of Pretoria, South Africa

BACKGROUND
Screening for hearing loss often involves audiological measures, such as pure-tone audiometry or otoacoustic emissions. However, these methods require specialised equipment and training, and are generally not available in rural and remote regions. Self-reported hearing difficulty has been proposed as a cost-effective way of identifying patients requiring a diagnostic audiological assessment.

OBJECTIVES
This study evaluated the results from the Lions Hearing Foundation mobile hearing-screening unit and examined whether self-reported hearing difficulty is a reliable indicator of hearing loss.

METHODS
Participants were a convenient sample of 2,090 adults presenting for hearing screenings between March 2010 and July 2013. Self-reported hearing difficulty was assessed using the Hearing Handicap in the Elderly-Screening (HHIE-S) validated questionnaire. Ears were examined by otoscopy and screening audiometry was conducted at 0.5, 1, 2 and 4 kHz, with hearing loss considered a four-frequency average of >= 25 dB in the better ear.

RESULTS
The self-report measures from validated questionnaires (HHIE-S score >8) for identifying hearing loss in adults aged over 60 were sensitive (89.88%; 95%CI 87.59, 91.79) but not specific (10.34%; 95%CI 0.03, 28.50). Prevalence of hearing loss in this population was very high (96.66%; 95%CI 95.18, 97.71).

CONCLUSION
Self-reported hearing difficulty, established via a validated questionnaire, appears to be a sensitive but not a specific indicator of actual hearing impairment for adults aged over 60 years. Due to the high prevalence of hearing loss in this age group, self-reported hearing loss from patients should be considered justifiable cause for referral for a full diagnostic assessment.

8

PREVALENCE AND CONFIGURATION OF HEARING LOSS IN BABY BOOMERS

R Eikelboom[1]
D Swanepoel[2]
P Friedland[3]
M Hunter[4]
M Atlas[5]

[1] Ear Science Institute Australia; Ear Sciences Centre, The University of Western Australia, Australia and Department of Communication Pathology, University of Pretoria, South Africa
[2] Department of Communication Pathology, University of Pretoria, South Africa; Ear Science Institute Australia and Ear Sciences Centre, The University of Western Australia, Australia
[3] Ear Science Institute Australia and Ear Sciences Centre, The University of Western Australia, Australia
[4] Busselton Health Study, Busselton and School of Population Health, The University of Western Australia, Australia
[5] Ear Science Institute Australia and Ear Sciences Centre, The University of Western Australia, Australia

BACKGROUND
Baby Boomers, people born between 1945 and 1965, form a large section of the population that is currently progressing to become intensive users of the health care system. Studies of this population are important towards understanding the demands for services and developing public health policies.

OBJECTIVES
This study aimed to determine the prevalence and configuration of hearing loss in Baby Boomers, and compare results with those of previous population studies.

METHODS
Pure-tone air and bone conduction

audiometry was conducted on 1,996 Baby Boomers in the Busselton Baby Boomer Study. A significant hearing loss (HL) was indicated if the four-frequency average in the better ear was greater than 25 dB and a significant high frequency hearing loss was indicated if the mean of 2,000 and 4,000 Hz was greater than 30 dB.

RESULTS
53.7% of the cohort was female and 42% reported occupational noise exposure. The prevalence of HL was 2.5% in 45 to 49 year olds, 2.2% in 50 to 54 year olds, 5.2% in 55 to 59 year olds, and 11.3% in over 60 year olds. HL increases significantly after 50 years of age, more in males than in females. High frequency hearing loss (mean of 4,000 and 8,000 Hz) in these age groups increased from 10.3% to 42.4%. Prevalence of HL was significantly greater in males (OR=1.95; CI:1.32 - 2.87, p=0.001). Less than 3% of ears had moderate, severe or profound HL. 83.7% of HLs for males have a sloping configuration and 8.9% a flat configuration; for females, the rates are 59.9% and 24.0% respectively.

CONCLUSION
There is a significant gender difference in the severity and configuration of HL. These results show a lower prevalence of hearing loss than in previous studies, suggesting inter-generational changes in the prevalence of hearing loss in the population.

9

REMOTE MAPPING FOR COCHLEAR IMPLANT RECIPIENTS AND THE DEVELOPMENT AND VALIDATION OF A REMOTE COCHLEAR IMPLANT TELEHEALTH SERVICE: OBJECTIVE AND SUBJECTIVE OUTCOMES

R Eikelboom[1]
D Jayakody[2]
D Swanepoel[3]
S Chang[4]
M Atlas[5]

[1] Ear Science Institute Australia; Ear Sciences Centre, The University of Western Australia, Australia and Department of Communication Pathology, University of Pretoria, South Africa
[2] Ear Science Institute Australia and Ear Sciences Centre, The University of Western Australia, Australia
[3] Department of Communication Pathology, University of Pretoria, South Africa; Ear Science Institute Australia and Ear Sciences Centre, The University of Western Australia, Australia
[4] Ear Science Institute Australia and Ear Sciences Centre, The University of Western Australia, Australia
[5] Ear Science Institute Australia and Ear Sciences Centre, The University of Western Australia, Australia

BACKGROUND
Distance, mobility and availability of time make it difficult for people with a cochlear implant to access mapping and rehabilitation services. Telehealth technologies offer opportunities to change the way services are delivered to address some of these challenges.

OBJECTIVES
To develop a system to remotely map a cochlear hearing implant, and to validate technical and patient aspects.

METHODS
A web-based system was developed to incorporate video, voice, text and user feedback. Med-El cochlear implant recipients participated in a conventional and a remote fitting session. Fitting was confirmed by open sentences and the Ling six sound test administered by a facilitator. The preferred map was recorded, as were maximum comfort levels (MCLs). Participants were surveyed regarding technical aspects and satisfaction with the session.

RESULTS
Eleven recipients were tested (average age 67.8 +/- 6.2 years) with an average experience of 2.7 (+/- 1.9) years with an implant. MCLs were not statistically different between sessions. All patients scored perfect on the Ling test and ten answered all six open-sentence questions, compared to eight and nine people respectively for conventional mapping. Six participants reported no preference between the maps, two preferred the map from the conventional method and three preferred the map from the remote session. Time for remote mapping was five minutes longer. The most common technical issue raised was video and voice dissynchrony. Ten participants indicated that they would be willing to use a remote mapping service in the future and all indicated that they would recommend it for others.

CONCLUSION
The remote mapping system is a reliable method of mapping and has excellent recipient acceptance.

10

DOES HEARING INTERVENTION IMPROVE DOMAINS OF COGNITIVE FUNCTION? A SYSTEMATIC REVIEW

D Taljaard[1]
C Brennan-Jones[2]
R Bucks[3]
M Olaithe[4]
R Eikelboom[5]
M Atlas[6]

[1] Ear Science Institute Australia and Ear Sciences Centre, The University of Western Australia, Australia
[2] Ear Science Institute Australia and Ear Sciences Centre, The University of Western Australia, Australia
[3] School of Psychology, The University of Western Australia, Australia
[4] School of Psychology, The University of Western Australia, Australia
[5] Ear Science Institute Australia; Ear Sciences Centre, The University of Western Australia, Australia and Department of Communication Pathology, University of Pretoria, South Africa
[6] Ear Science Institute Australia and Ear Sciences Centre, The University of Western Australia, Australia

BACKGROUND
There have been many recent reports on the linkages between hearing loss intervention and cognitive factors. Cognitive factors appear to be at play in outcomes from hearing aids and hearing implants. However, sweeping statements have also been made suggesting that hearing rehabilitation will arrest cognitive decline.

OBJECTIVES
To systematically review the level and quality of the evidence supporting cognitive outcomes following hearing intervention. The review aimed to summarise the evidence, comment on the rigour of the research methodologies of included studies and discuss avenues for future research.

METHODS
Level 1 and 2 studies were included, based on the Oxford-Centre for Evidence-Based Medicine Levels of Evidence. The review followed guidelines proposed by the Cochrane Handbook for Systematic Reviews of Interventions and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. To identify studies published as of 2013, a structured search strategy, which combined relevant controlled vocabulary terms (such as MEDLINE's Medical Subject Headings), with additional non-index terms was developed. Terms included 'cognitive risk', 'hearing loss', 'hearing', 'dementia' and 'cognitive'. The search strategy was applied to the following major biomedical bibliographic databases from inception September 2013: Pubmed, CINAHL, EMBASE (Ovid), PsycINFO, Scopus, Academic Search Premier, The Cochrane Library, The Centre for Reviews and Dissemination.

RESULTS
The electronic search revealed 35 relevant articles and was supplemented by manual searches of the references from articles. Only seven papers met the inclusion criteria of being at least a Level 2b study. Two studied the impact of hearing loss intervention on cognitive factors, with opposing findings. A meta-analysis of the data showed a very small positive effect. The other five studied the influence of cognitive factors on hearing intervention. A meta-analysis did not provide any conclusive outcomes.

CONCLUSION
There is a lack of evidence on which to base statements that hearing loss intervention will have a positive impact on cognitive factors. More research studies in this field are required.

11

APOPTOSIS IN THE MOUSE MIDDLE EAR AND EUSTACHIAN TUBE USING BROMODEOXYURIDINE

A Cecire[1]
R Cursons[2]
C Barnett[3]

[1] Anglesea Clinic, Hamilton, New Zealand (formerly Waikato Hospital, Hamilton, New Zealand)
[2] Molecular Genetics Laboratory, Waikato University, New Zealand
[3] Royal Brisbane and Women's Hospital, Brisbane, Australia (formerly Molecular Genetics Laboratory, Waikato University, New Zealand)

BACKGROUND
The epithelium of the Eustachian tube is similar to tracheobronchial epithelium. Previous studies have shown that cell

nuclei of the lining epithelium of the Eustachian tube migrate from the basal level to its lumen over a period of approximately one week, reflecting the natural apoptosis of this epithelium. Apoptosis can be accelerated in middle ear infection. Bromodeoxyuridine (BrdU) is an analogue of thymidine and is taken up by cells in the S-phase of the cell division cycle. This allows nuclei of cells to be followed over set times and so measures the life span of epithelial cells.

OBJECTIVES
To identify the rate at which the epithelium of the middle ear and Eustachian tube replaces itself.

METHODS
23 BALB/c mice received intraperitoneal bromodeoxyuridine and were sacrificed at 0, 6, 24, 48 and 72 hours, and at 7 days. Immunohistochemical staining was performed using antibodies based upon an indirect immunoperoxidase technique using a monoclonal antibody to BrdU. Two control animals were injected with saline and positive and negative control tissues were used.

RESULTS
Between 0 and 24 hours, there was a gradual uptake of BrdU by simple cuboidal epithelium of the middle ear cells and isolated basal cells in the pseudo-stratified epithelium of the nasopharynx and Eustachian tube. At 48 hours, labelling was still sporadic but pairs of cell nuclei in the Eustachian tube were staining positive indicating recent cell division. Intermittent staining was seen in the tympanic membrane. At 72 hours, labelling was absent from most cells lining the middle ear cavity, but present at the luminal borders of respiratory epithelium in the Eustachian tube and nasopharynx. This represents the stage just prior to final apoptosis. We also identified clusters of macrophages in the middle ear cavity, which are analogous to pulmonary macrophages of the lung.

CONCLUSION
The replication of the epithelium of the middle ear and Eustachian tube is a rapid process with different time frames for the various cell types present in this modified respiratory epithelium. Apoptosis of the ciliated epithelium in mouse middle ear is relevant to otitis media, as there is evidence that apoptosis is accelerated by bacteria in middle ear infection. The presence of macrophages, in otherwise normal murine middle ear cavities, has been confirmed and possibly means that these macrophages remove the apoptotic cells, as occurs in lung alveoli.

12

TARGETED GENTAMICIN ONTO THE STAPES FOOTPLATE OR ROUND WINDOW MEMBRANE: RAMIFICATIONS FOR THE TREATMENT OF MENIERE'S DISEASE

E King[1]
A Salt[2]
R Shepherd[3]
S O'Leary[4]
J Fallon[5]

[1] Bionics Institute of Australia and Department of Otolaryngology, The University of Melbourne, Australia
[2] School of Medicine, Washington University, United States
[3] Bionics Institute of Australia; Department of Otolaryngology, The University of Melbourne and Department of Medical Bionics, The University of Melbourne, Australia
[4] Department of Otolaryngology, The University of Melbourne, Australia
[5] Bionics Institute of Australia; Department of Otolaryngology, The University of Melbourne and Department of Medical Bionics, The University of Melbourne, Australia

BACKGROUND
Meniere's Disease (MD) is a debilitating disease originating from a problem in the vestibular system. Symptoms include severe vertigo attacks, temporary hearing loss and tinnitus. When other treatments are ineffective, symptoms are clinically controlled by suppressing vestibular function with gentamicin, an antibiotic that is toxic to inner ear sensory cells, and, therefore, the treatment carries a risk of permanent hearing loss. Gentamicin is commonly administered via a simple injection through the eardrum into the middle ear space, which is then absorbed into the inner ear, resulting in varied therapeutic outcomes due to variable drug concentration in contact with the round window membrane (RWM) and stapes footplate. We have shown in previous studies that substances can be absorbed into inner ear fluid in the vestibule directly in the vicinity of the stapes footplate. We are now quantifying gentamicin absorption in this region compared to absorption through the RWM into the cochlea to

enable improved treatment protocols to be developed that reduce the risk of permanent hearing loss.

OBJECTIVES
To establish the inner ear pharmacokinetics of gentamicin delivered to the middle ear space.

METHODS
2 microlitres of gentamicin (40 or 337 mg/ml) or saline were applied to the stapes footplate or RWM of guinea pigs. Hearing thresholds and short latency vestibular evoked potentials were recorded to assess cochlear and vestibular function respectively at T=0, 1 week and 2 weeks after gentamicin treatment. Histological analysis of sensory cells in the cochlea and vestibule were compared.

RESULTS
Topical gentamicin administration onto the stapes footplate resulted in greater functional losses and abnormal cellular morphology compared to RWM delivery or saline controls.

CONCLUSION
Greater functional losses and abnormal sensory cellular morphology is consistent with higher drug concentration reaching the sensory cells. The results suggest gentamicin readily enters inner ear fluids when delivered to the stapes footplate. This implies that the vestibule can be treated directly with topical gentamicin application onto the stapes footplate, which could be beneficial for the treatment of MD.

13

ABSENCE OF SERPINB6 CAUSES SENSORINEURAL HEARING LOSS WITH MULTIPLE HISTOPATHOLOGIES IN THE MOUSE INNER EAR: IMPLICATIONS FOR NON-SYNDROMIC HEARING LOSS IN HUMANS

J Tan[1]
D Kaiserman[2]
M Prakash[3]
P Bird[4]

[1] The University of Melbourne, Australia
[2] Monash University, Australia
[3] Monash University, Australia
[4] Monash University, Australia

BACKGROUND
Serpins are a large family of structurally related inhibitors of serine and cysteine proteases. The first case of a protease inhibitor associated with hearing loss in humans was reported in 2010 and this inhibitor was identified as SERPINB6 (Sirmaci *et al* 2010). Humans with homozygous deficiency of SERPINB6 show hearing loss when they reach adulthood. Affected individuals noticed a progressive loss in hearing but no audiograms were performed to follow the extent of their hearing loss with age. It is unknown how SERPINB6 deficiency causes hearing loss.

OBJECTIVES
To use mouse models to help us understand this deafness syndrome in humans by analysing mutant mice in which the orthologous Serpinb6a gene is replaced by enhanced green fluorescent protein.

METHODS
We exposed mutant and wild type control mice to tones varying from 4 to 32 kHz to determine the hearing thresholds. Cochleae of these mice were dissected and decalcified to produce frozen sections of 10-µm thickness. Representative sections of each cochlea were stained with eosin and haematoxylin, and examined for pathological changes. Remaining sections were incubated with an anti-serum against SERPINB6 to localise its expression in the cochlea.

RESULTS
SERPINB6 is present in the neurosensory epithelium, lateral wall and spiral limbus of the cochlea, with highest levels in the inner and outer hair cells of the organ of Corti, cells lining the inner sulcus, and supporting cells distributed along the epithelial gap junction layer to the outer sulcus. Measurements of hearing thresholds in these mice demonstrated age-related hearing loss in all homozygous null, but not heterozygous, mice. The defect is associated with progressive cellular degeneration within the cochlea. This begins with the hair cells then involves the primary auditory neurons and finally the fibrocytes in the lateral wall.

CONCLUSION
SERPINB6 is a protease inhibitor that is essential for protecting cochlear

cells from degeneration. A deficiency of SERPINB6 can lead to progressive hearing loss in both humans and mice. We have generated a mouse model that can potentially be used to screen candidate drugs targeting the cognate protease of SERPINB6.

14

VERTIGO AND WOMEN: A SIGNIFICANTLY HIGHER PREVALENCE IN A COHORT OF OVER 2,000 BABY BOOMERS

V Yau[1]
P Friedland[2]
R Eikelboom[3]
C Brennan-Jones[4]
M Hunter[5]
M Atlas[6]

[1] Ear Science Institute Australia and Ear Sciences Centre, The University of Western Australia, Australia
[2] Ear Science Institute Australia and Ear Sciences Centre, The University of Western Australia, Australia
[3] Ear Science Institute Australia; Ear Sciences Centre, The University of Western Australia, Australia and Department of Communication Pathology, University of Pretoria, South Africa
[4] Ear Science Institute Australia and Ear Sciences Centre, The University of Western Australia, Australia
[5] Busselton Health Study, Busselton and School of Population Health, The University of Western Australia, Australia
[6] Ear Science Institute Australia and Ear Sciences Centre, The University of Western Australia, Australia

BACKGROUND

Dizziness is one of the most common presentations to general practitioners. However, its prevalence has not been fully documented. The only major Australian study was the Blue Mountains Hearing Study conducted between 1997 to 2000 on >49 years olds.

OBJECTIVES

This study aimed to document the prevalence and nature of dizziness of Baby Boomers (45 to 65 years of age) and investigate links to various demographic and health metrics.

METHODS

Self-reported data on dizziness was collected from 2,023 participants in the Busselton Baby Boomer Study. Participants were asked to fill in a questionnaire about the nature, onset, frequency, duration and effect on daily activities of dizziness and imbalance, and details of their medical history. Participants reporting dizziness were differentiated into two groups: those with vertigo and those without. A decision matrix (Kentala, 2003) was used to assign a diagnosis of BPPV, vestibular neuritis, Meniere's Disease (MD) and Labrynthitis.

RESULTS

Data from 927 males and 1,063 females were included in the study. 22.6% reported episodes of dizziness or imbalance. Of these 36.7% reported spinning sensations i.e. vertigo. In 41.2% of cases, episodes occurred at least monthly and over 50% of people reported it affected with daily activities. In this cohort, the prevalence of BPPV was 6.7%, 0.85% for vestibular neuritis, 0.70% for MD, and there was one case of Labyrinthitis. Females were more likely ($p<0.01$) than males to have general dizziness, vertigo and BPPV; the odds ratios were 1.94, 2.27 and 2.21 respectively. Age was found to have no association with dizziness or dizziness disorders in this population. MD was found to be associated with Type 1 Diabetes (OR 10.78, $p<0.01$) and hypercholesterolaemia (OR 4.53, $p<0.01$).

CONCLUSION

The results of this study are generally in agreement with other studies, confirming too that there is greater prevalence in females. The reason for this is still unknown. The Epley manoeuvre is known to be an effective treatment of BPPV in 80% of cases. Therefore, 29.3% of 45 to 65 year olds with dizziness are potentially treatable with non-pharmacological methods, representing 1 in 20 Baby Boomers.

15

BACTERIAL BIOFILMS AND THE DEVELOPMENT OF CHRONIC TYMPANIC MEMBRANE PERFORATIONS

R Marano[1]
H San Wong[2]
R O'Handley[3]

[1] Ear Science Institute Australia and Ear Sciences Centre, The University of Western Australia, Australia
[2] School of Animal and Veterinary Sciences, The University of Adelaide, Australia
[3] School of Animal and Veterinary Sciences, The University of Adelaide, Australia

BACKGROUND

Bacterial infection of the middle ear

may lead to chronic suppurative otitis media (CSOM), which may rupture the tympanic membrane (TM). Once the infection clears, the perforation heals spontaneously in most cases. Those that do not heal become chronic and may lead to further complications. While there are effective surgical treatments for chronic TM perforations (cTMPs), little is known regarding the cause of their development.

OBJECTIVES
We have hypothesised that biofilms associated with bacterial infections of the middle ear may play a role in the development of a chronic TM perforation (CTMP) through the secretion of anti-wound healing compounds. We aim to demonstrate that biofilm conditioned media (BCM) is capable of affecting several aspects of cell growth, including proliferation, migration and viability.

METHODS
BCM was obtained from two common bacterial species associated with infection, *Pseudomonas aeruginosa* and *Staphylococcus aureus*. Both pathogens were cultured using MBEC® biofilm culture plates in tryptic soy broth (TSB). Once the biofilm was established, fresh media was added to the culture vessels and incubated for a further 24 hours to obtain the BCM. This was freeze dried and resuspended in an equal volume of tissue culture media. The BCM was diluted to various concentrations in tissue culture media for proliferation and migration assays using human TM keratinocyte (hTMK) cells. Similar conditioned media was also obtained from the bacteria grown in planktonic form and is referred to as planktonic conditioned media (PCM).

RESULTS
Proliferation assays have revealed that BCM from *P. aeruginosa* significantly reduced the proliferative capability of hTMKs. Furthermore, an increase in cellular metabolism was also observed, indicating a stress load on the cells. For *S. aureus*, proliferation did not seem to be affected. However, similar to *P. aeruginosa*, metabolism was significantly elevated. Conversely, PCM appeared to have no significant effect on proliferation or metabolic rate.

CONCLUSION
Culturing hTMKs in the presence of BCM from *P. aeruginosa* had a deleterious effect on cellular proliferation and placed the cells under stress as seen using a metabolic assay. *S. aureus* produced a similar stress response without affecting proliferation. If similar responses were translated *in vivo* under disease conditions, it may be possible for bacterial secretions, whilst in biofilm mode, to prevent effective wound closure leading to a CTMP.

16

SEARCHING FOR AN ANIMAL MODEL OF CHRONIC TYMPANIC MEMBRANE PERFORATION

A Wang[1]
Y Shen[2]
L Liew[3]
M Atlas[4]
R Dilley[5]

[1] Ear Sciences Centre, The University of Western Australia, Australia
[2] Ear Sciences Centre, The University of Western Australia, Australia
[3] Ear Sciences Centre, The University of Western Australia, Australia
[4] Ear Science Institute Australia and Ear Sciences Centre, The University of Western Australia, Australia
[5] Ear Sciences Centre, The University of Western Australia, Australia

BACKGROUND
Chronic perforation of the tympanic membrane (TM) is a significant source of morbidity worldwide. Establishing chronic tympanic membrane perforations (TMP) in animal models in a laboratory setting will have value if they replicate many of the properties of the human clinical condition and can thus be used for the investigation of novel grafting materials. Various methods to create TMP in animals have been used, including infolding, thermal injury, reperforation and topical agents, such as chemicals and growth factor receptor inhibitors. However, a review of the existing literature has not found an ideal chronic TMP animal model available.

OBJECTIVES
To develop a rat model for chronic TMP with the novel technique of paper insertion into middle ear cavity (MEC). To validate and compare against previous chronic TMP animal model techniques (i.e. reperforation, topical application of mitomycin C + dexamethasone).

METHODS
Forty male Sprague Dawley rats underwent perforation of the right TM and were randomly divided into four experimental groups (n=10): (i) allowed to heal spontaneously (control), (ii) topical application of mitomycin C + dexamethasone, (iii) paper insertion into MEC and (iv) repetitive reperforation, if healed. Patency of TMP of each group was evaluated post-operatively by otomicroscopy at 1, 3, 5, 7, 9, 11, 14, 21, 28, 35, 42, 49 and 56 days. All rats were sacrificed at day 56 and TMs surgically harvested for evaluation of structure by histology.

RESULTS
The mean time of TMP patency in control, mitomycin C + dexamethasone and paper insertion were 7.2, 19.6 and 12.0 days respectively. The maximum time of TMP patency in the control, mitomycin C + dexamethasone and paper insertion were 9, 56 and 35 days respectively. Only 1 of 10 rats from the mitomycin C + dexamethasone group had a chronic TMP staying patent at 56 days. In the reperforation group, TMP continued to heal rapidly with no sign of delayed healing despite repetitive perforations in which all rats necessitated multiple reperforations. The mean number of reperforation required per animal was 6.6.

CONCLUSION
We conclude that paper insertion into MEC and reperforation does not produce chronic TMP in the rat. Topical application of mitomycin C + dexamethasone could create chronic TMP but with a sub-optimal success rate of only 10%. Despite these various animal models and techniques employed, an ideal chronic TMP animal model is yet to be found.

17

NOVEL METHOD OF ISOLATING EPIDERMAL CELLS FROM RAT TYMPANIC MEMBRANE

L Liew[1]
A Wang[2]
R Dilley[3]

[1] Ear Sciences Centre, The University of Western Australia, Australia
[2] Ear Sciences Centre, The University of Western Australia, Australia
[3] Ear Sciences Centre, The University of Western Australia, Australia

BACKGROUND
Cells with epidermal stem cell-like properties have been localised to focal areas of high cell turnover in the tympanic membrane (TM), specifically at the umbo and annulus where they are thought to contribute to both epidermal homeostasis and wound repair. While these locations have been identified and stem cells partially characterised, their isolation, regulation and role in the repair and regeneration of TM have not previously been described. This study aims to isolate and characterise stem cell populations of the TM utilising a rat model, and to explore their potential in tissue engineering of TM.

OBJECTIVES
To isolate cells with substantial regenerative capabilities from the rat TM (rTM) and to evaluate them for stem cell characteristics *in vitro*.

METHODS
Six male Sprague Dawley rats weighing 250 - 300 g were sacrificed under general anaesthesia with isoflurane. External ears were separated bilaterally at the osteocartilaginous junctions, and the TMs, along with its bony annulus, harvested from the tympanic bulla. Isolation of rTM cells in primary culture from fresh TM (n=12) was optimised using various enzymatic digestion and explant methods. Thereafter, the cells were culture-expanded in either DMEM/10% serum (Life Technologies, Mulgrave VIC) or keratinocyte growth medium (Life Technologies), purified using magnetic separation and characterised based on rapid attachment to Collagen IV, immunocytochemistry and PCR.

RESULTS
Explants from rTM yielded fibroblast-like cells, which grew rapidly and could be

passaged after one week to generate stable subcultures in DMEM. Fibroblast cultures developed more rapidly after partial digestion of the TM with trypsin or collagenase prior to explant culture. By contrast, primary cell cultures with predominantly epithelial-like cobblestone morphology were obtained from explants after overnight treatment of the rTM in Dispase II. The epithelial cultures proliferated rapidly in keratinocyte growth medium and maintained their phenotype after passage, thus providing stable cultures for further study. Furthermore, rTM explants treated with this method remained stable in culture and, after 2 weeks, could be transferred to a new culture dish to generate further cultures.

CONCLUSION

Explant culture of Dispase II-treated rTM appears to be a superior method for the isolation of epidermal-like cells from rTM. Further studies are currently underway to characterise the cell biology of this system.

18

MOLECULAR, PHYSIOLOGICAL AND SYNAPSE-FORMING CHARACTERISTICS OF STEM CELL-DERIVED SENSORY NEURONS

B Nayagam[1]
N Gunewardene[2]
T Hyakumura[3]
K Needham[4]
M Dottori[5]

[1] Department of Otolaryngology, The University of Melbourne, Australia
[2] Department of Otolaryngology, The University of Melbourne, Australia
[3] Department of Otolaryngology, The University of Melbourne, Australia
[4] Department of Otolaryngology, The University of Melbourne, Australia
[5] Department of Otolaryngology, The University of Melbourne, Australia

BACKGROUND

In severe cases of sensorineural hearing loss where auditory neurons (ANs) are significantly depleted, stem cell-derived neurons may provide a potential source of replacement cells. The success of such a therapy relies, among other things, upon producing an appropriate population of physiologically functional sensory neurons, which can both innervate the sensory tissues of the inner ear and relay the precise sound information to the brainstem.

OBJECTIVES

To direct the differentiation of various human stem cell types into bipolar, sensory, auditory-like neurons with biochemical, electrophysiological and synapse-forming properties that would make them suitable for a neural cell replacement therapy for hearing loss.

METHODS

An established neural induction protocol was used to differentiate two human induced pluripotent stem cell (hiPSC) lines (IPS1 and IPS2) and one human embryonic stem cell (hESC) line (H9) towards a neurosensory lineage *in vitro*. Immunocytochemistry and qPCR were used to examine the expression of a cohort of relevant AN developmental markers at defined time points of differentiation. Whole-cell patch-clamp electrophysiology was used to determine whether stem cell-derived neurons were physiologically functional. Stem cell-derived sensory neurons were then co-cultured with either cochlear hair cell explants or auditory brainstem slices for up to two weeks *in vitro*, to determine their ability to make new synapses on appropriate tissues.

RESULTS

Both hiPSCs- and hESCs-derived neurons expressed a cohort of relevant lineage markers, including Pax7, Pax2, Sox2, NeuroD1, Islet1, Brn3a, GATA3, Neurofilament 160kDa, ßIII-Tubulin, Peripherin and VGLUT1, illustrated by immunocytochemistry. These data were then confirmed using qPCR. All stem cell-derived neurons were similarly electrically active, with action potential profiles akin to embryonic mammalian auditory neurons. Inward and outward currents were eliminated by the application of appropriate sodium and potassium blockers respectively. In cochlear explant co-cultures, both hiPSC- and hESC-derived neurons made widespread synapses on inner and outer hair cells with varying degrees of efficiency (hESC>IPS2>IPS1). In brainstem co-cultures, hESC-derived neurons made extensive glutamatergic synapses on neurons in the cochlear nucleus.

CONCLUSION

The described studies address a critical step in the development of a stem cell therapy for hearing loss, by determining whether appropriate functional sensory

neurons can be derived from different human stem cell sources, and whether these neurons can make functional connections with relevant cell types in the peripheral and central auditory nervous system. Results of these studies directly inform our *in vivo* cell transplantation studies.

19

CHRONIC RHINOSINUSITIS AS A WINDOW INTO THE BACTERIA AND MUCOSAL IMMUNITY OF CYSTIC FIBROSIS

R Kim[1]
T Yin[2]
A Wood[3]
R Jain[4]
R Douglas[5]

[1] Department of Surgery, The University of Auckland, New Zealand
[2] Department of Surgery, The University of Auckland, New Zealand
[3] Department of Surgery, The University of Auckland, New Zealand
[4] Department of Surgery, The University of Auckland, New Zealand
[5] Department of Surgery, The University of Auckland, New Zealand

BACKGROUND

Chronic rhinosinusitis (CRS) is highly prevalent in cystic fibrosis (CF) patients, where a close correlation exists between upper and lower respiratory tract microbiology. We have reported intramucosal bacterial microcolonies in the sinus mucosa from idiopathic CRS patients and have made observations suggesting that these may result from mucosal immunotolerance secondary to altered macrophage function.

OBJECTIVES

To determine whether intramucosal microcolonies exist in the mucosa of CF patients with CRS and to investigate the mucosal immunology.

METHODS

Mucus swabs and tissue biopsies were taken from 9 patients with CF undergoing functional endoscopic sinus surgery (FESS) for CRS, 11 with idiopathic CRS undergoing FESS and 9 with normal sinuses having transnasal pituitary surgery. Swabs were cultured and intramucosal microcolonies sought using Gram staining and fluorescence *in situ* hybridization. Mucosal immune cells were identified using fluorescent immunohistochemistry.

RESULTS

Swab culture rates were similar between CRS patients and controls, however, there were significantly more intramucosal microcolonies in the CRS groups (8/9 CF-CRS, 7/11 idiopathic CRS) compared to the controls (1/9). Furthermore, the bio-volume of intramucosal microcolonies was significantly higher in CF-CRS than idiopathic-CRS. Mirroring the microbiological observations, the number of CD163+ macrophages was significantly increased in CF-CRS compared to idiopathic CRS ($p = 0.03$).

CONCLUSION

Intramucosal bacteria exist within the sinus mucosa of patients with CF and in significantly greater numbers than in patients with idiopathic CRS. We suspect that intramucosal microcolonies exist in the lower respiratory tract mucosa in CF and may play a role in disease recalcitrance.

20

THE EFFECT OF TOPICAL AGENTS ON PARANASAL SINUS MUCOSA HEALING: A RABBIT STUDY

R Jain[1]
R Kim[2]
S Waldvogel-Thurlow[3]
J Cornish[4]
R Douglas[5]

[1] Department of Surgery, The University of Auckland, New Zealand
[2] Department of Surgery, The University of Auckland, New Zealand
[3] Department of Surgery, The University of Auckland, New Zealand
[4] Department of Surgery, The University of Auckland, New Zealand
[5] Department of Surgery, The University of Auckland, New Zealand

BACKGROUND

Currently a number of topical applications are used intra-operatively in an attempt to improve postoperative mucosal recovery. However, the histological effects of these treatments have not been well characterised. We have investigated the impact of topical mometasone, acitretin, lactoferrin and Silastic on the healing of sinus mucosa in a rabbit model.

OBJECTIVES

To characterise the effect of topical mometasone 0.1%, acitretin 0.25% and 0.5%, lactoferrin, Silastic sheet, no

treatment and our placebo gel on sinus mucosal healing. Outcomes include measurements of mucosal thickness, epithelial thickness, density of collagen, number of goblet cells and recovery of cilia.

METHODS
Forty-eight New Zealand white rabbits underwent defined, localised stripping of a bilateral region of maxillary sinus mucosa via an external approach. Immediately after wounding, one of six treatments was placed in one maxillary sinus and the treatment carrier applied to the contralateral sinus (mometasone 0.1%, acitretin 0.25% and 0.5%, lactoferrin, Silastic sheet, no treatment, n=8 for each group). Rabbits were euthanised after 2 weeks and examined by light microscopy.

RESULTS
Rabbit sinuses treated with acitretin 0.25% and acitretin 0.5% had significantly improved cilial recovery over the contralaterally applied placebo ($p < 0.01$ and $p < 0.05$ respectively). Rabbits treated with 0.25% acitretin were also found to have significantly less collagen in healing mucosa ($p < 0.05$). Conversely, rabbits treated with mometasone 0.1% had more regions of denuded bone than any other treatment or control group. Intergroup comparisons demonstrated a significant improvement in cilial recovery with both acitretin doses over 0.1% mometasone ($p < 0.05$) and less scarring in the rabbits treated with placebo gel over Silastic ($p < 0.05$).

CONCLUSION
This study demonstrates that intra-operatively used agents have the potential to affect wound healing, particularly cilial recovery and collagen deposition. These data suggest that topical low dose acitretin may facilitate post-surgical mucosal recovery by improving cilial regrowth and reducing collagen deposition.

21

EVALUATION OF A NOVEL MAGNETOSTRICTIVE BONE CONDUCTOR FOR ASSESSING INNER EAR FUNCTION IN A GUINEA PIG MODEL

M Bergin[1]
S Vlajkovic[2]
P Bird[3]
P Thorne[4]

[1] Department of Physiology, The University of Auckland, New Zealand
[2] Department of Physiology, The University of Auckland, New Zealand
[3] Department of Surgery, University of Otago, New Zealand
[4] Department of Physiology, The University of Auckland, New Zealand

BACKGROUND
Evaluation of cochlear sensorineural reserve following middle ear surgery in small animals is challenging. Air-conducted stimulation is confounded by possible disruption of the middle ear transformer by surgical manipulation of the tympanic membrane and/or ossicles. Useful bone-conducted stimulation is possible only at frequencies at which the transducer can produce satisfactory power output and conventional bone conductors for humans have an upper limit of 4 - 6 kHz. In small animals, these frequencies are in the lowest region of their hearing frequency spectrum. Unfortunately, these low frequencies are much less sensitive to cochlear injury than the higher frequencies and are, therefore, unsatisfactory for evaluating cochlear sensorineural reserve. Other bone conduction techniques are needed for small animal studies.

OBJECTIVES
To assess the utility of a novel high frequency magnetostrictive bone conductor in a small animal model.

METHODS
Commercially available bone-conducting headphones (HP-F200, TEAC, Tokyo, Japan) were modified to allow the magnetostrictive transducer to be connected with a TDT 3 auditory electrophysiology stimulus and acquisition system (Alachua, FL). Various coupling techniques and sites were investigated on adult Duncan Hartley guinea pigs. A calibration voltage of 80 dB (SPL) = 5 V (peak) was used for all frequencies. Amplitude and latency input-output functions of waves I and II of the auditory brainstem responses were

assessed at 8, 12, 16, 20 and 24 kHz and then compared with air-conducted stimuli from a calibrated electrostatic transducer.

RESULTS
Optimal magnetostrictive transducer location and coupling was the postero-inferior bulla. Optimal transducer performance was seen at 12 kHz where wave I and II amplitudes were nearly identical to those elicited with air-conduction. 8 and 16 kHz performance was within 5 - 10 dB SPL, while differences of 20 - 25 dB SPL were observed at the higher frequencies. Neither transducer had any notable roll-off at the upper intensities of stimulation. At frequencies where amplitudes approximated, magnetostrictive transducer-evoked latencies were reduced by 0.2 - 0.3 milliseconds.

CONCLUSION
We have shown our modified magnetostrictive transducer is capable of stimulating the cochlea at frequencies consistent with hearing range studies in small animals. The calibration voltage selected for this study closely approximates cochlear stimulation with a calibrated air-conduction transducer <20 kHz. The lack of roll-off at the highest intensity suggests that higher voltages may be tolerated by the transducer at all frequencies, which would allow for further calibration fine-tuning. This approach is now being used to evaluate the impact of middle ear surgery on inner ear function in rodents and guinea pigs.

22

THE INFLUENCE OF CURRENT FOCUSING ON HEARING WITH A COCHLEAR IMPLANT

J Marozeau[1]
H McDermott[2]
B Swanson[3]
C McKay[4]

[1] Bionics Institute of Australia and Department of Medical Bionics, The University of Melbourne, Australia
[2] Bionics Institute of Australia and Department of Medical Bionics, The University of Melbourne, Australia
[3] Cochlear Ltd, Sydney, Australia
[4] Bionics Institute of Australia and Department of Medical Bionics, The University of Melbourne, Australia

BACKGROUND
Hearing with a cochlear implant remains difficult when listening in background noise and when listening to music. Such difficulties may be due in part to channel interactions whereby overlapping populations of neural activity are evoked by adjacent electrodes, leading to poor place specificity of neural activation and the smearing of important temporal information related to pitch.

OBJECTIVES
To evaluate the effect of using highly focused electrical fields on different aspects of hearing using an experimental implant with multiple current sources. It was hypothesised that the focused current would result in more place-specific neural activity, less temporal smearing between channels and improved ability to distinguish different vowel sounds.

METHODS
Five patients were implanted with an experimental implant with a percutaneous connector that allowed simultaneous activation of all 22 electrodes of the array. By selecting the current levels on each electrode appropriately, the resulting neural activation pattern was spatially restricted. Psychophysical experiments were performed to measure spread of current, place specificity, temporal channel interactions and vowel recognition.

RESULTS
It was confirmed that the method of simultaneously activating currents achieved a more focused electrical field. However, measures of channel interactions (place specificity and temporal interactions) showed minimal benefit on average. The ability to distinguish and identify vowel sounds was improved in three subjects compared to the standard monopolar mode of stimulation.

CONCLUSION
Current focusing may lead to improved speech understanding in some cochlear implant users. However, its benefit may be limited in some subjects possibly due to density of surviving ganglion cells being insufficient to take advantage of current focusing.

23

VESTIBULAR-MEDIATED BALANCE PERFORMANCE DECLINES WITH INCREASING AGE IN MICE

V Tung[1]
T Burton[2]
A Camp[3]

[1] Discipline of Biomedical Science, The University of Sydney, Australia
[2] Discipline of Biomedical Science, The University of Sydney, Australia
[3] Discipline of Biomedical Science, The University of Sydney, Australia

BACKGROUND

It is well known that adults aged over 65 have an increased risk of falls. Despite this, the underlying causes of imbalance remain unknown. While falls are multifactorial, presumably declines in the vestibular system, which is the most important system responsible for maintaining postural stability, contribute significantly.

OBJECTIVES

To assess age-related changes in balance performance and whether environmental enrichment mitigates these changes using a murine model.

METHODS

Vestibular-mediated balance performance of C57BL/6 mice aged 1 (n=9), 8 - 9 (n=6) and 12 - 13 (n=5) months were assessed using the inclined balance beam test before and after a vestibular stimulus. The stimulus was a horizontal rotation accelerating from zero to 3 revolutions per second over 20 seconds delivered using a custom-built rotator. Measurements of time to traverse (TTT) and time to start (TTS) were used to assess performance. In addition, 11 month old environmentally enriched mice (n=7) were also tested using the protocol described above and compared to age-matched controls without enrichment (n=4).

RESULTS

The balance beam performance of 1 month old mice were the least affected by the vestibular stimulus with lower measurements of TTT than 12 - 13 month old mice ($p<0.01$) and also lower measurements of TTS compared to 8 - 9 month old mice ($p<0.05$). Environmentally enriched mice were also affected by the vestibular stimulus with higher measurements of TTT post-challenge ($p<0.001$). While no TTS was observed in environmentally enriched mice, a TTS was observed in 50% of standard-housed mice post-vestibular challenge.

CONCLUSION

The effect of the vestibular stimulus on balance beam performance was greater in older mice possibly reflecting age-related deteriorations in vestibular function. In addition, environmental enrichment reduced aversion to the balance beam task post-vestibular challenge.

24

DEVELOPING HUMAN HAIR CELLS: STRUCTURE AND FUNCTION

R Lim[1]
H Drury[2]
M Tadros[3]
R Callister[4]
A Brichta[5]

[1] School of Biomedical Sciences and Pharmacy, The University of Newcastle, Australia
[2] School of Biomedical Sciences and Pharmacy, The University of Newcastle, Australia
[3] School of Biomedical Sciences and Pharmacy, The University of Newcastle, Australia
[4] School of Biomedical Sciences and Pharmacy, The University of Newcastle, Australia
[5] School of Biomedical Sciences and Pharmacy, The University of Newcastle, Australia

BACKGROUND

The majority of studies investigating the development of peripheral vestibular function have focused on animal models. In this study, we describe anatomical and physiological characteristics of developing human hair cells during a critical period of maturation.

OBJECTIVES

We have established a semi-intact preparation of human vestibular organs to investigate the functional development of human hair cells and afferent terminals.

METHODS

Human tissue was collected according to regulatory requirements. Inner ears from electively terminated human fetuses (11 to 18 weeks gestation; WG) were isolated. Tissue was used for either anatomical characterisation or physiological recordings. The vestibular triad, including semicircular canal cristae and utricle, were excised in ice-cold glycerol-based Ringer's solution. For

recordings, tissue was transferred to a recording chamber perfused with oxygenated L15 cell culture medium. Whole-cell patch-clamp recordings using potassium fluoride internal solution were made from embedded hair cells. For anatomical studies, the tissue was fixed using 4% paraformaldehyde and later sectioned. A number of different antibodies were used to label hair cells, stereocilia and afferent fibres.

RESULTS

We have recorded and intracellularly labelled human hair cells that display inward and outward rectifying conductances. Throughout the period examined (11 - 18 WG), approximately 20% of immature hair cells exhibit sodium conductances. The remaining cells that lacked a specific type I conductance (GK,L), and were classified as type II hair cells, showed a significant increase in maximal conductance (GMAX) between 11 - 14 WG and 15 - 18 WG (3.5 ± 0.2 nS versus 11.9 ± 1.5 nS, $p<0.05$). The earliest expression of the mature type I hair cell conductance (GK,L) was observed at 15 WG. This approximately coincided with our first recordings from calyx afferent terminals (15 WG). Our anatomical results show that there is a variety of morphological characteristics (cylindrical versus amphora shape) of developing human hair cells by 13 WG.

CONCLUSION

Our data show that while human vestibular hair cells are beginning to show distinctions in morphology by 13 WG, functionally the 11 - 14 WG age group, are still immature. By 15 WG, hair cells begin to express more mature conductances, including those typically seen in either mature type I or type II human hair cells. In addition, there is a concomitant maturation of calyx afferent terminals contacting putative type I hair cells.

25

MODULATION OF HAIR CELL ACTIVITY BY THE CHOLINERGIC EFFERENT VESTIBULAR SYSTEM

L Poppi[1]
H Tabataee[2]
R Callister[3]
R Lim[4]
A Brichta[5]

[1] School of Biomedical Sciences and Pharmacy, The University of Newcastle, Australia
[2] School of Biomedical Sciences and Pharmacy, The University of Newcastle, Australia
[3] School of Biomedical Sciences and Pharmacy, The University of Newcastle, Australia
[4] School of Biomedical Sciences and Pharmacy, The University of Newcastle, Australia
[5] School of Biomedical Sciences and Pharmacy, The University of Newcastle, Australia

BACKGROUND

The function of the mammalian efferent vestibular system (EVS) has remained a mystery. Our limited understanding of the EVS has come from either isolated mammalian vestibular hair cells or studies of afferent discharge following electrical activation of the EVS. However, afferent discharge is an indirect measure of cellular activity and isolation of hair cells results in the unavoidable destruction of the microarchitecture of the vestibular neuroepithelium. The contribution of cholinergic transmission in the EVS is yet to be determined.

OBJECTIVES

Recently, we have developed a semi-intact preparation that preserves the cellular microarchitecture and allows us to record from the three major neuroepithelial components: type I hair cells, type II hair cells and calyx afferent terminals. Thus, this preparation provides a means of investigating efferent action in the mammalian periphery. We investigated the cholinergic contribution to EVS activity in all three peripheral components by using immunolabelling techniques and recording the cellular response to exogenously applied acetylcholine (ACh).

METHODS

A semi-intact preparation of vestibular organs comprising the horizontal and anterior cristae and utricle were dissected from the mouse inner ear. This preparation was used for all experiments. Immunofluorescent labelling: Mouse vestibular organs were fixed (4% paraformaldehyde), sectioned (20 μm), and incubated in primary (VAChT, ChAT

and calbindin) and secondary (Texas Red and FITC) antibodies. Patch-clamp electrophysiology: Recordings from hair cells and calyx afferent terminals were done during brief application of ACh (300 µm) to evoke cholinergic responses.

RESULTS

Emerging evidence from our semi-intact preparation indicate that the EVS has a much more complex and heterogeneous effect than previously thought. During ACh exposure, type II hair cells display a biphasic current response - (i) a current carried by the ACh receptor subunit (alpha-9/10) and (ii) a current carried by calcium-activated potassium channel (SK-type). In some cases, an additional cholinergic response was also detected and was identified as containing alpha4-beta2 acetylcholine receptor subunits. Approximately 25% of type II hair cells did not respond to ACh exposure. We have also recorded long-lasting ACh-induced responses in calyx afferent terminals and type I hair cells, which suggests the presence of muscarinic receptors.

CONCLUSION

Combining our electrophysiological and immunohistochemical results, we are building a more comprehensive picture of how EVS functions within the vestibular periphery. Preserving the critical cellular milieu, by using the semi-intact neuroepithelial preparation, we are able to define peripheral cholinergic EVS function in ways that were not possible previously.

26

OPTOGENETICS: SHINING LIGHT ON BALANCE AND THE BRAINSTEM

T Wellings[1]
B Graham[2]
R Callister[3]
A Brichta[4]
R Lim[5]

[1] School of Biomedical Sciences and Pharmacy, The University of Newcastle, Australia
[2] School of Biomedical Sciences and Pharmacy, The University of Newcastle, Australia
[3] School of Biomedical Sciences and Pharmacy, The University of Newcastle, Australia
[4] School of Biomedical Sciences and Pharmacy, The University of Newcastle, Australia
[5] School of Biomedical Sciences and Pharmacy, The University of Newcastle, Australia

BACKGROUND

Optogenetics is an emerging technique that uses light to excite or inhibit targeted neurons. To do this, light-activated ion channels, called channelrhodopsins (usually expressed in the retina), are inserted into the membranes of specific neurons. These channelrhodopsins may be linked to the expression of proteins that have a discrete function, such as calcium binding proteins (e.g. calretinin and parvalbumin). Light can then be used to selectively activate channelrhodopsins in targeted subsets of neurons to determine their specific contribution within a complex circuit. This precise cell-specific light-activation technique will enable us to probe complex vestibular networks and tease out their functional connections with visual, proprioceptive and cerebellar neuronal circuits. By targeting neuronal subgroups in vestibular nuclei, optogenetics could be used to investigate their explicit role. Two discrete subgroups within the medial vestibular nucleus (MVN) express different calcium binding proteins - calretinin (CR) and parvalbumin (PV). The activity patterns of these two neuron types suggest that they have discrete functional roles. Therefore, it is proposed that using optogenetics, we will be able to establish the role of neurons expressing CR and PV within vestibular circuits.

OBJECTIVES

To assess the feasibility of using an *in vitro* optogenetic model to study central vestibular networks.

METHODS

We used transgenic mice that co-express channelrhodopsin-2 (ChR2) conjugated to a reporter protein, yellow-fluorescent protein (YFP), in either CR or PV neurons. Brain sections containing MVN were used for immunohistochemistry or electrophysiology. Immunohistochemistry: Primary antibodies against YFP, PV and CR together with secondary antibodies were used to determine co-expression levels of YFP with either CR or PV. Electrophysiology: We used patch-clamp recordings from MVN sections (300 µm) to investigate the effects of high intensity LED light (470 nm) under controlled exposure. Light activation was recorded from individual CR and PV MVN neurons.

RESULTS
Under current clamp conditions, light exposure triggered trains of action potential discharge in neurons expressing ChR2-YFP. The frequency and duration of action potential trains were directly proportional to intensity and duration of the light exposure. In voltage clamp, the amount of inward current was proportional to the light intensity.

CONCLUSION
We have shown optogenetic light activation of subpopulations of MVN neurons can be used to selectively stimulate neurons and their connections. This technique will provide us with a valuable new tool with which to explore the complex vestibular network connectivity.

27

IDENTIFYING FUNCTIONALLY DISTINCT SUBGROUPS IN THE MEDIAL VESTIBULAR NUCLEUS

T Wellings[1]
B Graham[2]
R Callister[3]
A Brichta[4]
R Lim[5]

[1] School of Biomedical Sciences and Pharmacy, The University of Newcastle, Australia
[2] School of Biomedical Sciences and Pharmacy, The University of Newcastle, Australia
[3] School of Biomedical Sciences and Pharmacy, The University of Newcastle, Australia
[4] School of Biomedical Sciences and Pharmacy, The University of Newcastle, Australia
[5] School of Biomedical Sciences and Pharmacy, The University of Newcastle, Australia

BACKGROUND
The medial vestibular nucleus (MVN) integrates multiple inputs, including those from vestibular, visual and proprioceptive systems. The MVN plays an essential role in the vestibulo-ocular reflex (VOR) and other functions, such as vestibular adaption and vestibular compensation. Therefore, understanding how this nucleus modulates these important activities has been a major goal in vestibular research. While distinct MVN subgroups have been determined neurochemically or electrophysiologically, few studies have combined these methodologies to functionally characterise MVN subgroups.

OBJECTIVES
Two neurochemically discrete subpopulations of MVN neurons have been identified by their expression of specific calcium binding proteins (CBPs) - calretinin (CR) and parvalbumin (PV). Our aim was to functionally characterise these two groups using transgenic mice that co-expressed enhanced green fluorescent protein (eGFP) and either CR or PV.

METHODS
Electrophysiology: Whole-cell patch-clamp technique was used to record from fluorescently labelled eGFP-CR or eGFP-PV neurons in the MVN. Action potential profile, discharge properties and spontaneous miniature post-synaptic currents were assessed in both populations of neurons.
Immunolabelling: Paraformaldehyde-fixed brains were labelled using antibodies against GFP, calretinin, parvalbumin and calbindin to determine co-expression levels and density of cerebellar inputs.

RESULTS
CR-neurons are located in the juxtaventricular parvocellular MVN. They have a type B action potential profile, consisting of double after-hyperpolarisation (AHP). They also have reduced excitability in response to depolarising current steps compared to control neurons (104 Hz/nA, n=31 vs 146 Hz/nA, n=30, $p<0.005$), and show only small changes in discharge rate following hyperpolarising current steps (0.66 ± 0.22Hz, n=25 vs 5.98 ± 0.84Hz, n=23, $p<0.0005$). Synaptic inputs to CR neurons were both GABAAergic and glutamatergic, with very few glycinergic inputs. PV-neurons are located in the rostrolateral parvocellular MVN. They also have a type B action potential profile. They are less excitable than surrounding control neurons (124 Hz/nA, n=39 vs 170 Hz/nA, n=42, $p<0.05$), however, in contrast to their CR counterparts, PV neurons show a small increase in discharge rate after hyperpolarising current steps no different to control (3.81 ± 0.46, n=33 vs 13.3 ± 4.7, n=35, NS). Inputs to PV neurons were similar to CR neurons.

CONCLUSION
We identified two distinct subgroups within the MVN. Not only do they differ in their calcium binding expression but also in their functional properties. This suggests separate roles for these two MVN subgroups. Since CR-neurons maintain AP discharge, even after hyperpolarisation, this suggests an

important regulatory role in the MVN. The role of PV-neurons, however, is unclear.

28

EVIDENCE FOR PERTURBATIONS IN ION AND ENERGY HOMEOSTASIS IN THE INNER EAR VESTIBULAR (BALANCE) SYSTEM OF THE AGED MOUSE AND RAT

M Bigland[1]
A Brichta[2]
D Smith[3]

[1] School of Biomedical Sciences and Pharmacy, The University of Newcastle and Hunter Medical Research Institute, Australia
[2] School of Biomedical Sciences and Pharmacy, The University of Newcastle and Hunter Medical Research Institute, Australia
[3] School of Biomedical Sciences and Pharmacy, The University of Newcastle and Hunter Medical Research Institute, Australia

BACKGROUND
Vestibular system dysfunction in the elderly is common, resulting in dizziness, vertigo and loss of balance. Impairment of the peripheral vestibular organs is thought to be a contributing factor, however, little is known about the effects of age on this structure. Inner ear, vestibular hair cells detect head motion by precisely regulating ionic fluxes across their membranes, a process that is energy demanding. The effects of ageing on the mechanisms that maintain the ionic gradients are yet to be fully characterised. Changes in the ability to control ion homeostasis, and indeed mitochondrial energy metabolism of the inner ear, could be associated with impaired vestibular organ function with ageing.

OBJECTIVES
To characterise the effect of ageing on gene expression in the inner ear vestibular balance organs in the F344 rat and C57Bl6 mouse, with a particular emphasis on those genes involved in energy metabolism and ion homeostasis.

METHODS
Genome-wide gene expression comparisons were carried out between young (3 - 6 months) and old (23 - 30 months) animals using Affymetrix Gene Arrays. Genes of interest were then confirmed using quantitative polymerase chain reaction (qPCR).

RESULTS
We found over 30 genes that were differentially expressed in both species with age. A number of these are involved in ion transport. For instance, the expression of the chloride ion channel cystic fibrosis transmembrane conductance regulator (CFTR; the gene that is mutated in cystic fibrosis) was increased in aged animals. An unexpected finding was the reduction in expression of four genes associated with mechanotransduction in aged mice. These genes are involved in the opening of mechanically gated channels that allow influx of charged ions into the cell thus turning head movement into an electrical signal.

CONCLUSION
These data indicate possible perturbations in vestibular ion homeostasis, whether through mechanotransduction and/or plasma membrane ion channels with age, and has identified age-related changes in molecular pathways in two species. This gives us increased confidence that the changes are likely to be seen in other mammals, including humans.

29

TRAUMATIC TENSION PNEUMOCEPHALUS

T Loh[1]
R Chin[2]

[1] St Vincent's Hospital, Sydney, Australia
[2] Nepean Hospital, Sydney, Australia

BACKGROUND
Tension pneumocephalus is a rare neurosurgical emergency that can present in various contexts in the practice of Otorhinolaryngology, especially in anterior cranial fossa and functional endoscopic sinus surgery. It occurs as a complication of dural violation, especially the cranial dura, by instrumentation, trauma or infections. Delayed intervention results in permanent neurological sequelae.

OBJECTIVES
To present a case of traumatic tension pneumocephalus secondary to base of skull fractures.

METHODS
A 69-year-old man was admitted to

ICU after a motor vehicle accident secondary to syncope. He had extensive craniofacial fractures (Bilateral Le Fort I, II and III, orbital floor, roof, cribiform plate and frontal sinus fractures), intracranial haemorrhage and CSF rhinorrhea. There was an acute deterioration in his level of consciousness five days after his admission to ICU. An urgent CT scan showed bilateral bulging ventricles, consistent with tension pneumocephalus. He subsequently underwent an urgent decompression and transnasal endoscopic nasal septal flap repair of his skull base.

RESULTS

Our case demonstrates the importance of having a high index of suspicion in diagnosing tension pneumocephalus. This is even more so in the obtunded patient with base of skull fractures and CSF rhinorrhea. Emergent intervention with the insertion of an external ventricular drain and/or craniotomy is life saving. In this case, an endoscopic reconstruction of the skull base prevented further occurences of pneumocephalus. The patient was subsequently transferred to a brain rehabilitation unit after a prolonged recovery. Tension pneumocephalus occurs rarely. It has been described after endoscopic sinus and skull base surgeries, especially with the use of a perioperative lumbar drain. It usually occurs within one week of the surgery but can present in a delayed fashion. It is diagnosed by a peaked appearance of the frontal lobes (Mount Fuji sign) on a non-contrast CT scan. In our case, the air collected within the ventricles.

CONCLUSION

Tension pneumocephalus is a rare life-threatening complication of trauma to the skull base, iatrogenic or otherwise. Repair of the skull base defect should be carried out promptly after an emergent decompression procedure.

30

ANIMAL MODEL OF LARYNGEAL INJURY AND WOUND HEALING

J Allen[1]

[1] Waitemata District Health Board, Auckland and Department of Surgery, The University of Auckland, New Zealand

BACKGROUND

Vocal fold injury in humans results in severe voice alteration that is often permanent. This limits occupational function and social interaction. Insights into mechanisms of vocal fold scar development are needed to identify therapeutic targets. Animal models offer a controlled environment for assessment of tissue behaviour. Sheep were selected as a laryngeal model due to similarities in anatomic characteristics of the larynx.

OBJECTIVES

To examine wound healing in the ovine vocal fold and subglottis.

METHODS

An ovine laryngeal model was utilised to study controlled right vocal fold and subglottic injury and healing. 24 sheep were divided into four groups. Each group consisted of a control sheep and 5 sheep exposed to a novel collagen type 1-A inhibitor - halofuginone. Sheep underwent controlled injury preceded or followed by administration of halofuginone. Biopsies were taken at commencement, at one month and then sheep were euthanised and larynges explanted at three months. Specimens were examined using histological staining, particularly for elastin, epithelial thickness and collagen density.

RESULTS

All sheep tolerated halofuginone. One sheep death occurred due to bacterial pneumonia. Increased elastin density is seen in subglottic tissue compared to true vocal fold superficial lamina propria. Sheep vocal fold and subglottic tissues demonstrated a predictable histological response to injury. Significant loss of elastin at the injury zone was followed by replacement with thin and non-cohesive elastin fibrils. Collagen density in the superficial lamina propria of the vocal fold was decreased following injury. Epithelium regenerated in the majority of injuries.

CONCLUSION
An ovine model of laryngeal injury demonstrates predictable histological changes over three months following injury. Loss of elastin and reduction in collagen density may suggest that loss of vocal fold pliability following injury is influenced more strongly by lack of elastin rather than collagen stiffening as previously suggested. Changes in collagen may reflect reduced collagen production or increased collagen turnover.

31

RESPONSE OF OVINE LARYNGEAL INJURY MODEL TO SELECTIVE COLLAGEN TYPE IA INHIBITOR

J Allen[1]

[1] Waitemata District Health Board, Auckland and Department of Surgery, The University of Auckland, New Zealand

BACKGROUND
Vocal fold injury in humans results in severe voice alteration that is often permanent. This limits occupational function and social interaction. Insights into mechanisms of vocal fold scar development are needed to identify therapeutic targets. An ovine model of laryngeal injury has been developed to examine vocal fold and subglottic wound healing and allow testing of therapeutic agents.

OBJECTIVES
To examine wound healing in the ovine vocal fold and compare wound healing response between sheep treated with an inhibitor of fibrosis (halofuginone) vs untreated sheep.

METHODS
An ovine laryngeal model was utilised to study controlled vocal fold and subglottic injury and healing. 24 sheep were divided into four groups. Each group contained a control sheep and 5 sheep exposed to a novel collagen type 1-A inhibitor - halofuginone. Sheep underwent controlled injury preceded or followed by administration of halofuginone orally or by topical/intralesional injection. Biopsies were taken at commencement, at one month and then sheep were euthanised and larynges explanted at three months. Specimens were examined histologically. Elastin and collagen density were compared and epithelial changes documented. Pearson correlation statistics were used to assess inter-relationships.

RESULTS
All sheep tolerated halofuginone. One sheep death occurred due to bacterial pneumonia (untreated sheep). Sheep vocal fold and subglottic tissues demonstrated a predictable histological response to injury. Elastin was significantly reduced post-injury in both the glottis and subglottis. Halofuginone administration showed no effect on elastin profile. Administration of halofuginone demonstrated a trend of reducing collagen density post-injury in both the glottis and subglottis.

CONCLUSION
In an ovine laryngeal injury model, administration of a specific type 1A collagen inhibitor resulted in no appreciable effect on elastin behaviour but a trend to reduced collagen deposition after injury in both the glottis and subglottis. Further investigation is warranted to correlate drug pharmacokinetics with tissue effects and vocal fold dynamics.

32

EFFECT OF BDNF DRUG DELIVERY ON THE INNER EAR OF NORMAL-HEARING GUINEA PIGS

P Sale[1]
S O'Leary[2]
D Rowe[3]
L Winata[4]
D Sly[5]

[1] Department of Otolaryngology, The University of Melbourne, Australia
[2] Department of Otolaryngology, The University of Melbourne, Australia
[3] Department of Otolaryngology, The University of Melbourne, Australia
[4] Department of Otolaryngology, The University of Melbourne, Australia
[5] Department of Otolaryngology, The University of Melbourne, Australia

BACKGROUND
Recent studies suggest that neurotrophic factors may be useful agents for reducing the damage associated with progressive hearing loss resulting from surgery, noise and ageing.

OBJECTIVES
In prior studies, we discovered that brain-derived neurotrophic factor (BDNF) could prevent ongoing hearing loss associated with middle/inner ear surgery. In these studies, we sought to determine if this effect would last for a prolonged period of time after BDNF treatment.

METHODS
Normal-hearing guinea pigs received surgery to the left ear and a cannula placed onto the round window niche. This cannula allowed the slow dripping of drug solutions onto the round window membrane through a connected mini-osmotic pump. Animals received either (i) BDNF in an artificial perilymph (AP) solution, (ii) a vehicle solution of AP alone or (iii) an empty cannula placed over the round window niche. The osmotic pump delivered the solutions continuously for four weeks after which the mini-osmotic pump ceased delivering solution. The auditory brainstem response (ABR) thresholds of these animals were followed over the course of 16 weeks from pre-implantation until 12 weeks following treatment cessation.

RESULTS
We found that in animals receiving BDNF and AP, there was an increase in auditory brainstem response thresholds two weeks after surgery, however, the increase was significantly smaller in the animals receiving BDNF, suggesting a protective effect of BDNF. This protective effect lasted until at least 10 weeks after surgery, where the thresholds in the animals receiving AP remained elevated, and the BDNF threshold were similarly elevated. The empty cannula control group did not show an elevation of thresholds at any stage, suggesting that the initial increase in ABR thresholds after AP treatment may have been due to toxicity of this treatment rather than the surgery itself.

CONCLUSION
The findings suggest a transient protective effect of BDNF in a similar vein to the protective effects that other agents have shown against otological surgery but not an ongoing protective effect. The mechanism for this is unclear. Importantly, AP treatment, not an empty cannula, increased ABR thresholds, suggesting that the AP solution itself was detrimental to hearing thresholds. This is an important otological finding in light of other recent findings where other surgical and drug delivery perturbations to the round window membrane were also detrimental to hearing.

33

INITIAL RESULTS OF A PILOT TRIAL OF TISSUE ENGINEERED MYRINGOPLASTIES IN WESTERN AUSTRALIA

H Coates[1]
A Acharya[2]
F Lannigan[3]
S Rodrigues[4]
P Bumbak[5]
G Rajan[6]

[1] Department of Otolaryngology, The University of Western Australia and Princess Margaret Hospital for Children, Perth, Australia
[2] Fremantle Hospital, Perth, Australia
[3] Department of Otolaryngology, The University of Western Australia and Princess Margaret Hospital for Children, Perth, Australia
[4] Princess Margaret Hospital for Children, Perth, Australia
[5] Princess Margaret Hospital for Children, Perth, Australia
[6] Department of Otolaryngology, The University of Western Australia and Fremantle Hospital, Perth, Australia

BACKGROUND
A traumatic tympanic membrane perforation (TMP) often regenerates spontaneously but only heals in two layers, where the absence of the central, firm and elastic layer can lead to retraction pockets and cholesteatoma. The currently available myringoplasty requires theatre time, sophisticated equipment and general anaesthetic. Furthermore, outcomes are variable and inconsistent. Thus, new strategies in reconstruction are desperately needed.

OBJECTIVES
To evaluate the safety and efficacy of new tissue engineering myringoplasty techniques using basic fibroblast growth factor (b-FGF) alone or in combination with a variety of scaffolds in adults and children.

METHODS
This is a prospective cohort study, designed into four groups - (i) topical use of b-FGF alone; (ii) topical use of b-FGF in combination with gelatin sponge (Gelfoam®); (iii) topical use of b-FGF in combination with silk fibroin scaffold (TymPaSil®); and (iv) topical use of b-FGF in combination with collagen scaffold (Celgro®). To date, 18 adults and 12

children have been recruited from the otolaryngology departments of two major hospitals in Western Australia. Patients were randomised in the first three groups, being the latter (i.e. Celgro®) in final stage of safety assessment. The procedure is a modification of the technique devised by Kanemaru *et al*. The surgeries were performed under local anaesthesia in adults and under general anaesthesia in children. Serial video otoscopy and audiometry was performed postoperatively, and outcomes and results determined. Inclusion suitability for the study involved the application of defined inclusion and exclusion criteria together with informed consent.

RESULTS

Overall, there was a success rate in patient terms of 83%, with the success rate in children similar. However, in terms of treatment, the children required 1.3 treatments, on average, and the adults, 1.0. The major reason for the reduction in the success rate in children was related to post-operative infection or non-compliance with water precautions. In those patients with pre-operative hearing loss, there was a 90% improvement in hearing. There were no safety issues related to the procedure.

CONCLUSION

The safety and efficacy of b-FGF combined with different scaffolds is an effective and short procedure with comparable success to conventional myringoplasty in both adults and paediatric patients.

34

ANTIBODY RESPONSES TO CONSERVED BACTERIAL PROTEINS DIFFER BETWEEN INDIGENOUS AND NON-INDIGENOUS AUSTRALIAN CHILDREN WITH OTITIS MEDIA: IMPLICATIONS FOR VACCINATION

R Thornton[1]
J Hillwood[2]
S Toster[3]
P Edminston[4]
G Zhang[5]
S Vijayasekaran[6]
K Corscadden[7]
H Coates[8]
P Richmond[9]

[1] School of Paediatrics and Child Health, The University of Western Australia and Telethon Institute for Child Health Research, Perth, Australia
[2] School of Paediatrics and Child Health, The University of Western Australia, Australia
[3] School of Paediatrics and Child Health, The University of Western Australia, Australia
[4] School of Paediatrics and Child Health, The University of Western Australia, Australia
[5] School of Paediatrics and Child Health, The University of Western Australia and Princess Margaret Hospital for Children, Perth, Australia
[6] School of Paediatrics and Child Health, The University of Western Australia and Princess Margaret Hospital for Children, Perth, Australia
[7] School of Paediatrics and Child Health, The University of Western Australia and Telethon Institute for Child Health Research, Perth, Australia
[8] School of Paediatrics and Child Health, The University of Western Australia; Telethon Institute for Child Health Research and Princess Margaret Hospital for Children, Perth, Australia
[9] School of Paediatrics and Child Health, The University of Western Australia; Telethon Institute for Child Health Research and Princess Margaret Hospital for Children, Perth, Australia

BACKGROUND

Some children are prone to recurrent and severe otitis media (OM), particularly Indigenous Australian children.

OBJECTIVES

To investigate differences in naturally acquired serum antibody responses to nontypeable *Haemophilus influenzae* (NTHi) and *Streptococcus pneumoniae* proteins in Indigenous and non-Indigenous otitis-prone children.

METHODS

Serum samples from 32 healthy non-Indigenous children, 64 Caucasian children and 55 Indigenous children undergoing surgery for OM were tested for specific IgG and IgA antibodies against pneumococcal proteins Ply, CbpA and PspA1 and 2, and, NTHi proteins PD, P6 and P4, using a multiplex bead-based assay.

RESULTS

Indigenous children had higher levels of IgA than their non-Indigenous counterparts with OM (PspA1, CbpA, Ply and P6). No differences were observed for most IgG (Ply, CbpA, PspA 1 and 2, P6 and P4) between healthy controls, Indigenous OM children and non-Indigenous OM children. Despite high levels of NTHi exposure, Indigenous children had the lowest geometric mean concentration of PD IgA and IgG (10,927AU and 92,967AU respectively), when compared to both non-Indigenous otitis-prone children (16,399AU, 168,384AU) and healthy non-Indigenous controls (11,464AU, 335,709AU).

CONCLUSION
Despite increased susceptibility to severe recurrent OM, Indigenous children mount similar or increased antibody responses to most conserved NTHi and pneumococcal antigens tested when compared to their non-Indigenous otitis-prone children and healthy controls. Indigenous children with OM and their non-Indigenous counterparts, appear to have deficient PD IgA and IgG responses. This could have major implications when considering vaccination with the new PD containing pneumococcal conjugate vaccine.

35

COMBINING DRUG DELIVERY WITH COCHLEAR IMPLANTS: DEVELOPING AND EVALUATING NEW APPROACHES

R Shepherd[1]
J Fallon[2]
J Tan[3]
F Caruso[4]
A Wise[5]

[1] Bionics Institute of Australia and Department of Medical Bionics, The University of Melbourne, Australia
[2] Bionics Institute of Australia and Department of Medical Bionics, The University of Melbourne, Australia
[3] Bionics Institute of Australia and Department of Otolaryngology, The University of Melbourne, Australia
[4] Department of Chemical and Biomolecular Engineering, The University of Melbourne, Australia
[5] Bionics Institute of Australia and Department of Medical Bionics, The University of Melbourne, Australia

BACKGROUND
Cochlear implants provide significant improvements in speech perception for the severe-profoundly deaf. However, their clinical performance in noisy conditions can be significantly reduced. A major reason for this reduced performance is the limited number of independent stimulation channels available owing to extensive current spread in the highly conductive, fluid-filled cochlea. This produces far broader neural activation of SGNs than natural hearing, leading to a reduction in the fidelity of neural input to the auditory system. One method to improve the performance of these devices is to promote growth of auditory neurites towards the electrode array in order to improve the electrode-neural interface.

OBJECTIVES
To evaluate the use of drug-based therapies to improve the electrode-neural interface in cochlear implants.

METHODS
Using three species of deafened animals, we have delivered brain-derived neurotrophin (BDNF) and neurotrophin 3 (NT-3) to the inner ear using chronically implanted pumps and, in concert, have developed and evaluated alternate delivery methods for long-term (weeks - months) drug delivery. These techniques include viral vectors, cell-based therapies and slow-release nanotechnology-inspired applications. In many of these studies, we combined long-term drug delivery with electrical stimulation via a cochlear implant.

RESULTS
Delivery of exogenous neurotrophins rescues auditory neurones from the gradual degenerative changes observed following loss of hair cells. These rescue effects are typically greater during the period of drug delivery, when associated with greater drug loads (e.g. via a pump or nanotechnology-inspired applications rather than cell based therapies), and when delivered in association with cochlear implant use. Importantly, the delivery of neurotrophins evokes a regeneration of auditory neurite projections towards the electrode array resulting in a reduction in electrical thresholds.

CONCLUSION
Neurotrophin delivery to the deafened cochlea can prevent ongoing degeneration of auditory neurones, promote neurite growth towards the cochlear implant and improve the electrode-neural interface. Importantly, a number of the technologies described can deliver a wide variety of therapeutic drugs in a controlled manner and have the potential for treating other pathologies associated with the inner ear.

36

USE OF MAGNETIC RESONANCE IMAGING TO QUANTITATIVELY ASSESS INFLAMMATION AND BLOOD-LABYRINTH BARRIER INTEGRITY IN INNER EAR DISEASE

P Thorne[1]
J Le Floc'h[2]
J Plumat[3]
R Telang[4]
S Vlajkovic[5]

[1] Department of Physiology and Centre for Brain Research, The University of Auckland, New Zealand
[2] Department of Physiology and Centre for Brain Research, The University of Auckland, New Zealand
[3] Department of Physiology and Centre for Brain Research, The University of Auckland, New Zealand
[4] Department of Physiology and Centre for Brain Research, The University of Auckland, New Zealand
[5] Department of Physiology and Centre for Brain Research, The University of Auckland, New Zealand

BACKGROUND

Hearing loss is a major health problem, affecting one in six of the New Zealand population, and is mostly caused by diseases of the inner ear. Some of these conditions may be due to or exacerbated by inflammation of the inner ear leading to sensory cell and neural degeneration. However, the inner ear is difficult to study non-invasively because of its location within the temporal bone.

OBJECTIVES

To develop methods to apply Dynamic Contrast Enhanced (DCE) MRI to quantify cochlear inflammation and changes in vascular permeability of the guinea-pig inner ear, and to apply these approaches to study the blood-labyrinth barrier in human inner ear conditions, such as Meniere's Disease.

METHODS

In order to investigate the inflammatory changes in the inner ear, guinea pigs were inoculated intratympanically with bacterial lipopolysaccharide (LPS, 0.8mg/kg) and DCE-MRI was performed at 4, 7 and 10 days using a 4.7T MRI system. A control group comprised saline-treated animals studied at the same time after saline injection. A two-compartment pharmacokinetic (PK) model was used to determine the rate constant (K^{trans}) characterising gadolinium based contrast agent (GBCA) leakage from the vascular space into the extravascular, extracellular space of the cochlear tissues. To assess the use of this technique in humans, participants with normal hearing underwent a DCE-MRI study using a 3T clinical MRI system (GBCA administered as a bolus at a dose of 0.1mmol/kg).

RESULTS

PK modelling showed that the vascular permeability K^{trans} of the GP cochlea increased substantially 4 days after LPS injection and was about three fold greater than values 7 - 10 days after LPS injection. No significant GBCA uptake was observed in the normal human inner ear until 4 hours after the GBCA injection, suggesting a very tight blood-labyrinth barrier in human inner ear.

CONCLUSION

It is possible to quantitatively assess inner ear vascular permeability in normal and inflamed animal cochleae. The results establish DCE-MRI as a promising diagnostic tool for human hearing conditions.

37

CEREBELLAR ATAXIA WITH NEUROPATHY AND VESTIBULAR AREFLEXIA SYNDROME (CANVAS), A NOVEL VESTIBULO-CEREBELLAR ATAXIA: CLINICAL PHENOTYPE, PATHOLOGY, IMAGING ABNORMALITIES, DIFFERENTIAL DIAGNOSES AND A QUANTITATIVE BEDSIDE TEST

D Szmulewicz[1]
H MacDougall[2]
C McLean[3]
L Roberts[4]
E Storey[5]
I Curthoys[6]
G Halmagyi[7]

[1] Department of Otolaryngology, The University of Melbourne, Australia
[2] School of Psychology, The University of Sydney, Australia
[3] Department of Anatomical Pathology, Alfred Hospital, Melbourne, Australia
[4] Department of Neuroscience, St Vincent's Hospital, Melbourne, Australia
[5] Department of Neuroscience, Monash University, Australia
[6] School of Psychology, The University of Sydney, Australia
[7] G Halmagyi, Institute of Clinical Neurosciences, The University of Sydney, Australia

BACKGROUND
As neuro-otological investigative modalities evolve, it has become increasingly apparent that a greater number of patients with imbalance have a multifactorial cause for their dizziness. Whilst a number of these patients may have accrued multiple independent causes of their imbalance, our improved diagnostic methods have highlighted the possibility of further single diseases with multiple underlying foci of pathology.

OBJECTIVES
To elucidate the underlying pathology and clinical phenomenology in patients presenting with a combination of a bilateral vestibulopathy, cerebellar impairment and peripheral sensory loss. Furthermore, we sought to construct a diagnostic algorithm to aid identification of these patients in clinical practice.

METHODS
Prospective examination and investigation of 80 patients identified with idiopathic cerebellar ataxia and bilateral vestibulopathy, who were also found to have a somatic sensory loss. Investigation included quantitative neuro-otologic oculomotor evaluation, MRI brain and spine imaging, and peripheral somatic neurophysiology.

RESULTS
We describe a novel balance disorder, CANVAS, which is characterised by the triad of bilateral peripheral vestibulopathy, cerebellar ataxia and somatic sensory deficit. The bilateral peripheral vestibulopathy has been quantified using rapid video-oculography and has been pathologically demonstrated to be a vestibular neuronopathy (ganglionopathy). The characteristic pattern of cerebellar atrophy has been elucidated (on MRI and validated by three post-mortem samples), whilst the sensory deficit has been shown to be a neuronopathy, with marked dorsal root ganglia neuronal loss. We have also designed an objective clinical test of compound cerebellar and bilateral vestibular impairment - the abnormal video visually enhanced vestibulo-ocular reflex - present in only a very limited number of diseases, CANVAS being the most common.

CONCLUSION
CANVAS is a newly described balance disorder with clear pathoclinical correlations, diagnostic criteria and, given the existence of 13 kindred amongst the 80 patients described, is most likely autosomal recessive.

38

A QUANTITATIVE BEDSIDE TEST OF BALANCE FUNCTION: THE VIDEO VISUALLY ENHANCED VESTIBULO-OCULAR REFLEX (VVOR)

D Szmulewicz[1]
H MacDougall[2]
E Storey[3]
I Curthoys[4]
G Halmagyi[5]

[1] Department of Otolaryngology, The University of Melbourne, Australia
[2] School of Psychology, The University of Sydney, Australia
[3] Department of Neuroscience, Monash University, Australia
[4] School of Psychology, The University of Sydney, Australia
[5] G Halmagyi, Institute of Clinical Neurosciences, The University of Sydney, Australia

BACKGROUND
Initially utilised to investigate the visual-vestibular interaction, the visually enhanced vestibulo-ocular reflex (VVOR) has only recently found clinical utility in the form of a qualitative bedside test. We outline the next increment in the evolution of the clinical application of the visual-vestibular interaction by describing the quantitative bedside VVOR, which employs rapid video-oculographic (VOG) diagnosis of vestibulo-cerebellar disease. Portable VOG is a new field of diagnostic eye movement quantification, whose utility has been facilitated by the recent development of a lightweight, minimum-slip high-speed video eye tracking system. Underlying the efficacy of the VVOR as a robust and sensitive clinical sign, is the knowledge that its perturbation represents a compromise in all three compensatory oculomotor reflexes - smooth pursuit (SP), optokinetic nystagmus (OKN) and vestibulo-ocular reflex (VOR). The clinical utility of the VVOR sign is its unique ability to simultaneously test for the co-existence of vestibular and cerebellar pathology. Conditions with this compound deficit include spinocerebellar ataxia 3 and 6, Friedreich's ataxia, cerebellar ataxia with neuropathy and vestibular areflexia syndrome (CANVAS), multiple system atrophy predominantly of the cerebellar

subtype and idiopathic cerebellar ataxia with bilateral vestibulopathy.

OBJECTIVES
To identify a robust and easily performed quantitative bedside clinical test of vestibular and cerebellar function.

METHODS
A prospective observational study.

RESULTS
We present data on 131 patients with combined vestibular and cerebellar pathology; 61 with cerebellar ataxia with neuropathy and vestibular areflexia syndrome; 23 with Friedreich's ataxia; 16 with spinocerebellar ataxia type 6 (SCA6); 7 with spinocerebellar ataxia type 3 (SCA3); 15 with multiple system atrophy of the cerebellar subtype; and 9 with idiopathic cerebellar ataxia with bilateral vestibulopathy.

CONCLUSION
The video VVOR test readily allows identification and quantification of combined vestibular and cerebellar pathology at the time of consultation. This process previously involved referral for specialised neuro-otology testing and so, improves clinical pathway efficiency and directs the diagnostic algorithm.

39

A SALIVA-BASED TEST FOR THE DETECTION OF HPV-ASSOCIATED ORAL CANCERS

R Chai[1]
D Lambie[2]
I Frazer[3]
C Punyadeera[4]

[1] The University of Queensland Diamantina Institute, Australia
[2] The School of Medicine, The University of Queensland, Australia
[3] Translational Research Institute, Australia.
[4] The University of Queensland Diamantina Institute, Australia

BACKGROUND
Human papilloma virus (HPV) infection is a major risk factor for a distinct subset of head and neck squamous cell carcinoma (HNSCC). The incidence of HPV-associated HNSCC is increasing and there are no early detection methods with most cases at an advanced stage upon diagnosis.

OBJECTIVES
To develop a saliva-based assay for the detection of oncogenic HPVs in patients with oral squamous cell carcinoma (OSCC).

METHODS
Salivary rinse was collected from OSCC patients recruited from the Head and Neck Clinic at Princess Alexandra Hospital, Brisbane, Australia. Briefly, genomic DNA and RNA were extracted from rinse samples using a commercial kit and phenol-chloroform method respectively. PCR amplification was performed using MY11/MY09 primers that target >25 HPV strains as well as primers specific to oncogenic HPV16 and HPV18. HPV16-related transcripts (p16, E6 and E7) were detected using reverse transcription PCR (RT-PCR).

RESULTS
Oncogenic HPV-16 DNA was detected in the salivary rinse of 18/22 patients diagnosed with HPV-positive OSCC and 0/16 in the salivary rinse of patients with HPV-negative tumour. In addition, the presence of HPV-related mRNA was correlated with high viral load in patient rinse samples.

CONCLUSION
Salivary rinse is a promising diagnostic medium for the detection of oncogenic HPV in the oral cavity. The current study will aid in the detection of HPV infection in people at a high risk of developing HPV-associated HNSCC in a non-invasive and cost effective way. Early detection and intervention will significantly reduce the mortality and morbidity associated with HNSCC.

40

HEAD AND NECK CANCER DETECTION IS A SPITTING DISTANCE AWAY

Y Lim[1]
Y Wan[2]
D Ovchinnikov[3]
W Coman[4]
C Perry[5]
P Slowey[6]
C Punyadeera[7]

[1] The University of Queensland, Australia
[2] The University of Queensland, Australia
[3] Australian Institute for Bioengineering and Nanotechnology, The University of Queensland, Australia
[4] School of Medicine, The University of Queensland, Australia

[5] School of Medicine, The University of Queensland, Australia
[6] Oasis Diagnostics® Corporation, Vancouver, United States
[7] The University of Queensland Diamantina Institute, Australia

BACKGROUND
Head and neck squamous cell carcinoma (HNSCC) encompasses a diverse group of aggressive tumours. HNSCC is the most distressing and disfiguring tumour for the patient to endure, for health workers to manage and families to cope with. HNSCC patients, particularly those with a history of smoking, often develop secondary tumours. Currently, there are no diagnostic tests to detect these cancers at an early stage and, as such, most patients present with metastatic disease at the time of diagnosis (regional nodal involvement in 43% and distant metastasis in 10%), leading to 5-year survival rates of less than 60%.

OBJECTIVES
With an increasing recognition of the link between oral and systemic disease, attention has turned to saliva as an alternative diagnostic medium for a diverse array of health conditions. Compared with blood, saliva collection is non-invasive, easy sampling with multiple sampling opportunities, does not need pre-processing and is ideal for third world countries. It is well established that tumour cells secrete biomolecules into the saliva. DNA methylation and microRNAs (miRNAs) are the most extensively studied epigenetic biomarkers in HNSCC.

METHODS
We collected saliva (resting saliva and buccal swabs; DNA•SAL™) from HNSCC patients and healthy controls, and interrogated CpG hypermethylation events in tumour suppressor genes using a sensitive methylation-specific PCR (MSP) assay.

RESULTS
RASSF1a, DAPK1 and p16, showed an overall specificity of 87% and sensitivity of 80%. The test panel performed extremely well in the detection of the early stages of HNSCCs, with a sensitivity of 94% and specificity of 87%, and a high κ value of 0.8, with an excellent overall agreement between the presence of HNSCC and a positive MSP panel result. In addition, miR-9 and miR-191 provided a good discriminative ability with AUC values of 0.76 and 0.73 respectively ($p<0.01$) for distinguishing between HNSCC patients from healthy controls.

CONCLUSION
In conclusion, we demonstrate that salivary DNA methylation and miRNA biomarkers are clinically useful in detecting HNSCC in a non-invasive manner.

41 THE SCENT OF A WOMAN: WHY ARE OLFACTORY RECEPTORS EXPRESSED IN THE MALE REPRODUCTIVE SYSTEM?

A Cunningham[1]
Y Makeyeva[2]

[1] Developmental Neurosciences Program, The University of Medicine, Australia
[2] Developmental Neurosciences Program, The University of Medicine, Australia

BACKGROUND
Ectopic expression of olfactory receptors (ORs) has been widely reported in non-chemosensory tissues since the large gene family was isolated from olfactory epithelium twenty years ago. This expression has been determined mostly by PCR or fluorescence *in situ* hybridization, as the proteins have been difficult to study due to lack of appropriate antibodies. The earliest reports of ectopic expression identified ORs in testis and sperm, in dogs, humans and mice (Parmentier *et al*, 2002; Spehr *et al*, 2003; and Fukuda *et al*, 2004). It was proposed that ORs might play the same role in both sperm and the nose, as psychophysical and physiological experiments in humans displayed that a single OR expressed in the nose, also mediated directed chemotactic movement of sperm to the ligand bourgeonal (Spehr *et al*, 2004).

OBJECTIVES
To explore further the question of whether ORs function in sperm chemotaxis and are essential to normal fertility, we used a novel antibody to the family of rat ORs, fOR-AC1 and antibodies to G_{olf} and Type 3 cyclase in immunohistochemistry of rat male reproductive tissues. We proposed that finding co-expression of the three signalling components would provide evidence of true chemosensory function of sperm ORs.

METHODS
A degenerate peptide corresponding to a conserved c-terminal region of the rat OR-gene super family was produced in rabbits, purified on an Affigel antigen column and designated fOR-AC1. This antibody labelled rat olfactory cilia in a nearly continuous manner and recognised a band of apparent molecular weight 55kDa on immunoblot of olfactory epithelium and testes. Commercially available antibodies included rabbit pAb, A cyclase III and goat pAb G_{olf} (both Santa Cruz Biotechnology). Digital images were captured in brightfield and fluorescent modes using Axioplan cameras and a motorised Axioplan2 microscope (Zeiss) with AxioVision software. Confocal microscopy was performed with a Zeiss META LSM.

RESULTS
ORs, G_{olf} and Type 3 cyclase co-localised in a punctate pattern along the spermatozoa tail in the lumen of testes and in the cytoplasmic droplet of sperm in the epididymis. fOR-AC1 also labelled epididymal stereocilia.

CONCLUSION
Our findings strongly support the hypothesis that the olfactory signal transduction system may also function in mature spermatozoa. It is possible ORs are responding to chemotactic molecules in the seminiferous tubules or female oviduct system on their path to oocyte fertilisation. Future studies are needed to identify endogenous ligand(s) of ORs and potentially determine this receptor family's functional significance in sperm development and movement.

42

COCHLEAR IMPLANT FOR REHABILITATION OF UNILATERAL DEAFNESS IN CHILDREN: FIRST EXPERIENCES

D Tavora-Vieira[1]
R Marino[2]
A Acharya[3]
G Rajan[4]

[1] School of Surgery, The University of Western Australia, Australia
[2] School of Surgery, The University of Western Australia, Australia
[3] School of Surgery, The University of Western Australia, Australia
[4] School of Surgery, The University of Western Australia, Australia

BACKGROUND
In the paediatric population, unilateral deafness has been linked to delayed speech and language development, and poorer academic performance. Similarly, to the adult population, bone conduction devices have been used as a rehabilitation option for children older than five years of age. However, hearing rehabilitation encounters further challenge with young children, who are unlikely to wear CROS and/or FM systems. To date, there is very limited data regarding cochlear implantation for hearing rehabilitation of unilateral deafness in children.

OBJECTIVES
To investigate the implication of cochlear implantation in children with congenital and acquired unilateral deafness following "the earlier the better" intervention approach.

METHODS
This is an ongoing prospective study with 4 children (age 1.5 to 9 years old) implanted so far. All patients were implanted with a Flex Soft Med-El electrode and complete insertion. Localisation test and age appropriate speech perception in noise were performed on the two older children. For the younger child, behavioural observational testing in the soundproof room was performed with the normal-hearing ear masked with speech noise 65 dB. The sound-field hearing thresholds of 20 dB were obtained at 1,000 Hz and 4,000 Hz.

RESULTS
There is a good subjective acceptance of the implant and three children are full-time wearers. Localisation and lateralisation skills, as well as speech perception in noise scores, have improved through the first twelve months of CI usage.

CONCLUSION
Cochlear implantation may represent the only option that will fully assist children with unilateral deafness to make use of binaural hearing benefits. It is possible that "the earlier the better" approach is the most suitable path for cochlear implantation in the paediatric population.

43

THE BIMODAL BENEFITS OF COCHLEAR IMPLANTATION FOR UNILATERAL DEAFNESS

D Tavora-Vieira[1]
R Marino[2]
A Acharya[3]
G Rajan[4]

[1] School of Surgery, The University of Western Australia, Australia
[2] School of Surgery, The University of Western Australia, Australia
[3] School of Surgery, The University of Western Australia, Australia
[4] School of Surgery, The University of Western Australia, Australia

BACKGROUND

Patients with unilateral deafness lack the benefit of binaural hearing. They usually report difficulties understanding speech in the presence of background noise and speech coming from the side of the hearing loss, and have poor sound localisation. In addition, a large number of these patients suffer from tinnitus that cannot be treated by conventional masking devices.

OBJECTIVES

To investigate the benefit of cochlear implantation on speech perception, tinnitus suppression and sound localisation in these patients.

METHODS

Twenty-eight subjects with unilateral post-lingual sensorineural profound hearing loss, with and without tinnitus, were recruited for this study. The patients had unilateral hearing loss greater than a four-frequency pure-tone average (0.5 - 4 kHz) of 70 dB HL and contralateral hearing was ≤30 dB HL. All patients were implanted with a Flex Soft electrode array and received an Opus 2 speech processor (Med-El).

Speech perception was assessed using the BKB-SIN in various spatial configurations - speech and noise from the front; speech from the front and noise from the hearing ear; speech from the CI side; and noise from the hearing ear. Subjective benefits were assessed using the Speech, Spatial and Qualities of Hearing (SSQ) questionnaire and the APHAB (Abbreviated Profile of Hearing Aid Benefit). Localisation abilities were also evaluated. Tinnitus was assessed using the Tinnitus Reaction Questionnaire.

RESULTS

Analysis of the results reveal a significant improvement in signal to noise ratio in all spatial configurations, as well as on the localisation abilities, SSQ and APHAB scores.

CONCLUSION

Cochlear implantation is a viable treatment option for unilateral deafness, providing an improvement in hearing performance, decrease of tinnitus perception and high subjective acceptance of the implant. Auditory training appears to be a key factor for successful rehabilitation.

44

SPATIAL ACUITY AND LATERALISATION AFTER COCHLEAR IMPLANT IN UNILATERAL DEAFNESS: WHERE DOES THE AUDITORY CORTEX COME IN?

D Tavora-Vieira[1]
R Marino[2]
A Acharya[3]
G Rajan[4]

[1] School of Surgery, The University of Western Australia, Australia
[2] School of Surgery, The University of Western Australia, Australia
[3] School of Surgery, The University of Western Australia, Australia
[4] School of Surgery, The University of Western Australia, Australia

BACKGROUND

Sound localisation in the horizontal plane relies on two binaural cues - interaural level difference (ILDs) and interaural time difference (ITDs). The aforementioned cues help to localise high frequency and low frequency sounds respectively. Inability to localise a sound source is one of the major complaints of people with unilateral profound hearing loss. Improvement on localisation abilities can be the driving force for these patients to explore the possibility of cochlear implantation.

OBJECTIVES

To observe the localisation performance of patients with unilateral deafness, who received a cochlear implant (CI) within the last 24 months.

METHODS

Sixteen adults (9 male, 7 female) with post-lingual unilateral deafness were

included in this study. All subjects received the Med-El CI system and wear the speech processor on a full-time basis. Localisation testing was performed using the Auditory Speech Sounds Evaluation software (A§E®, P J Govaerts, Antwerp, Belgium). Each patient performed the localisation testing in two listening conditions - monaural hearing (normal acoustic hearing alone) and binaural hearing (acoustic hearing and CI activated). All patients had at least 6 months experience with their CI.

RESULTS
Analysis of the results showed that the group performed significantly better with CI on when compared with CI off. The majority of patients presented an RMS measure that was similar to those with normal hearing.

CONCLUSION
Cochlear implantation is effective in improving localisation abilities in patients with unilateral deafness.

45

TOWARDS A VESTIBULAR 'TRICORDER': SMART PHONE AND TABLET 'APPS' FOR VESTIBULAR TESTING

H MacDougall[1]
S Rogers[2]
L McGarvie[3]
I Curthoys[4]

[1] School of Psychology, The University of Sydney, Australia
[2] School of Psychology, The University of Sydney, Australia
[3] Royal Prince Alfred Hospital, Sydney, Australia
[4] School of Psychology, The University of Sydney, Australia

BACKGROUND
For many years, we have been developing our own research equipment and methods using laptop PCs and commercially available components (inertial sensors, analog-to-digital converters etc.). This strategy aimed to avoid the closed or black-box nature of many commercial solutions, as well as the considerable cost of turn-key research apparatus.

OBJECTIVES
To take advantage of the proliferation of current technology in the form of iPhones and iPads by developing the apps and associated hardware to assemble a basic neuro-otology testing kit. In the short term, we hope this project will influence the expectations of users and vendors and encourage the development of simpler, cheaper and more accessible testing equipment. In the medium term, we hope to provide free equipment to Australian and NZ ENT/ORL trainees. In the long term, we hope to facilitate the broad adoption of vestibular tests as part of the current wearable technology revolution.

METHODS
Our 'apps' are usually adapted from existing software written in the lab and previously validated in various research projects. Hardware accessories are made using inexpensive off-the-shelf components or fabricated using convenient new methods, such as 3D printing.

RESULTS
We have now finished a number of prototype apps and hardware accessories, including 'ImprovEyes': for eye movement recording and measurement; 'LocoMate': for gait, locomotion and movement analysis; 'OtoPotential': for cVEMP and oVEMP assessment of otolith function; 'BalanceRite': for posturography and balance rehabilitation; 'DynaVision' to assess dynamic visual acuity; 'BinocuLevel' a bucketless test of the subjective visual vertical; 'GalvaNice' a portable Galvanic vestibular stimulator; 'ViStim' virtual reality goggles for optokinetic stimuli and visual perturbation; and 'iOscope' a simple otoscope adapter for smart phone cameras.

We have previously demonstrated earlier versions of some of these apps at conferences, including *NOTSA 2012, Frontiers 2012, NOTSA 2013* and *Barany 2014*. Our efforts are sustained by significant interest, enthusiasm, encouragement and support from many potential end-users. At *Frontiers 2014*, we will show working proof-of-concept versions of all nine components of the prototype vestibular 'Tricorder' or basic neuro-otology testing kit in order to stimulate further suggestions, discussion and feedback.

CONCLUSION
While some of the 'apps' are significantly inferior to commercial grade solutions,

others produce data that compares favourably with commercial solutions which can cost hundreds of times more. We conclude that a vestibular 'Tricorder' using smart phone and tablet 'apps' for vestibular testing is feasible and has the potential for significant benefit.

46

VESTIBULAR MODELLING FOR EDUCATION AND PUBLIC OUTREACH

S Rogers[1]
L McGarvie[2]
I Curthoys[3]
H MacDougall[4]

[1] School of Psychology, The University of Sydney, Australia
[2] Royal Prince Alfred Hospital, Sydney, Australia
[3] School of Psychology, The University of Sydney, Australia
[4] School of Psychology, The University of Sydney, Australia

BACKGROUND

Smart phone and tablet devices offer unique opportunities to model the function of the vestibular system because they contain 3D sensors for rotation (gyroscopes) and linear acceleration/ tilt (accelerometers) that function like the semicircular canals and otoliths of the inner ear respectively (a 'bionic labyrinth'). iPads and iPhones also incorporate the screen required to show reflexive vestibular responses (eye movements) and the interface to make settings, import data files, network devices, record and analyse responses etc. The massive international iTunes app distribution system, Apple's user-friendly interface, and significant device availability and penetration, with ~600 million iOS devices in use, also offer new opportunities.

OBJECTIVES

To contribute to benefit of our students, colleagues and patients by providing free vestibular modelling tools that serve to educate and empower a broad range of end users in a friendly and intuitive manner.

METHODS

The first free app, called aVOR (angular Vestibulo-Ocular Reflex), demonstrates the stimulation of the balance sensors of the inner ear by rotation (angular velocity) and models the reflexive eye movement responses that serve to stabilise gaze (http://itunes.apple.com/app/avor/id497245573). The aVOR app allows manipulation of the functional state of the semicircular canals, the influence of cerebellar function, the type of visual fixation, saccade characteristics, the presence of canalithiasis etc. The user can interactively explore the consequences of these settings by moving the virtual subject's head (i.e. the device) and observing the displayed eye movement responses. A quiz mode introduces unknown settings.

Our second modelling app, called VOR (Vestibulo Ocular Reflex), will combine aVOR, lVOR and their complex interaction. This app will display the stimulation of the otoliths (utricle and saccade of the inner ear) by translation and tilt, and will generate reflexive eye movements, including ocular counter-roll, skew deviation, mergence etc. Users will be able to set the functional state of canals and otoliths to influence eye movement responses. Complex motion profiles, such as those during centrifugation, off vertical axis rotation (OVER) and unilateral radial acceleration, can be programmed easily and videos of the resulting simulations saved for use in lectures or conference presentations.

RESULTS

The aVOR app has been downloaded ~23,000 times from more than a hundred countries and in nine languages. The app consistently receives 5/5 star ratings and positive reviews on iTunes.

CONCLUSION

Significant positive feedback from around the world has reinforced the potential of mobile apps to benefit patients, students, researchers and clinicians.

47

EFFECTS OF ARTIFICIAL ENDOLYMPH INJECTION ON INNER EAR FUNCTION AND MORPHOLOGY IN GUINEA PIGS

D Brown[1]

[1] Brain & Mind Research Institute, The University of Sydney, Australia

BACKGROUND

Vertigo attacks in Meniere's Disease (MD) are often thought to be caused by

endolymphatic hydrops causing a rupture of the membranous labyrinth.

OBJECTIVES
To understand the details of changes in cochlear and vestibular function during hydrops development and how a sufferer may recover from a labyrinth rupture.

METHODS
We slowly (40 nl/minute) injected artificial endolymph into the membranous labyrinth of anaesthetised guinea pigs while continuously monitoring several objective measures of cochlear and vestibular function, including Compound Action Potential (CAP) thresholds, Summating Potential (SP) ratios, Cochlear Microphonic (CM), low-frequency biased DPOAEs, Endocochlear Potential (EP) and the Vestibular Evoked Potential (VsEP). Temporal bones were subsequently analysed using X-ray micro-tomography (Micro-CT).

RESULTS
Endolymph injection caused a slow decline in cochlear sensitivity, particularly to low frequency sounds, and a displacement of the hair cells towards scala tympani. After three microlitres of injection, cochlear sensitivity and hair cell displacement suddenly recovered, followed several minutes later by a transient change (usually a loss) in vestibular sensitivity to bone-conducted vibration. Vestibular sensitivity often recovered 30 - 40 minutes after the abrupt loss of function. Consecutive endolymph injections in the same animal produced multiple episodes of cochlear function loss with abrupt recovery and multiple episodes of sudden vestibular sensitivity loss. Micro-CT results demonstrated an increased endolymph volume during the injection, with a slight decrease in endolymph volume following the abrupt episodes of cochlear recovery. Micro-CT failed to demonstrate any labyrinth ruptures.

CONCLUSION
These results suggest that cochlear hydrops gradually increases endolymph pressure causing a displacement of the organ of Corti and a low frequency hearing loss, until some phenomenon suddenly alleviates the hydropic pressure. Given that this series of events occurred several times in the same acute animal experiment suggests either that the pressure-relief is not caused by a rupture of the labyrinth but rather by some other mechanism, or that a tear of the labyrinth is able to heal within 40 minutes to allow endolymph pressure to increase again with consecutive fluid injections. These results support the theory that hydrops causes the symptoms of MD. It is possible that differences in inner ear morphology between people may allow some people to develop hydrops but not experience the sudden relief of pressure, likely to underlie the vertigo attacks in MD.

48

DELAYED LOSS OF ACOUSTIC THRESHOLDS FOLLOWING COCHLEAR IMPLANTATION: CLINICAL OBSERVATIONS AND TRANSLATIONAL RESEARCH TO EXPLORE POTENTIAL MECHANISMS

S O'Leary[1]
H Smeds[2]
H Eastwood[3]
A Hampson[4]
M Moran[5]
P Sale[6]
L Campbell[7]

[1] Royal Victorian Eye and Ear Hospital and Department of Otolaryngology, The University of Melbourne, Australia
[2] Karolinska University Hospital, Stockholm, Sweden
[3] Department of Otolaryngology, The University of Melbourne, Australia
[4] Department of Otolaryngology, The University of Melbourne, Australia
[5] Royal Victorian Eye and Ear Hospital and Department of Otolaryngology, The University of Melbourne, Australia
[6] Department of Otolaryngology, The University of Melbourne, Australia
[7] Department of Otolaryngology, The University of Melbourne, Australia

BACKGROUND
Hearing loss that occurs months to years after otherwise successful hearing-preservation cochlear implantation (i.e. delayed hearing loss), occurs in approximately one third of patients and can compromise the functional utility of residual hearing. The cause(s) of delayed hearing loss is not known.

OBJECTIVES
To examine audiometric data followed for at least 12 months after cochlear implant (CI) surgery from Melbourne and other published series in order to determine the factor(s) influencing delayed hearing loss. Then, we consider a physiological mechanism that may

contribute to delayed hearing loss, namely endolymphatic hydrops (EH).

METHODS
Clinical observations and translational research.

RESULTS
Clinical data: The clinical studies revealed that pre-operative hearing thresholds and the hearing loss over the first 3 months after surgery (early hearing loss) were seldom correlated. Neither was there a relationship between pre-operative levels and hearing loss over the next 12 months (delayed hearing loss). Early and delayed hearing losses were positively correlated (r^2 0.7 - 0.9). It may be concluded that the main determinant of delayed hearing loss was the extent of the cochlear injury during surgery.

Experimental data: EH may follow cochlear injury and cause permanent hearing loss if it persists for extended periods of time. EH has been found in over 50% of cases in a human cadaveric study of CI recipients who had been implanted many years before (Handzel et al), suggesting that EH is a potential cause of delayed hearing loss.

In light of these observations, we have undertaken an experimental study in the guinea pig to assess the prevalence of hydrops early after CI surgery. Cohorts of animals survived for time intervals up to three months after surgery. On Micro-CT imaging of the inner ear, hydrops were seen in the majority of cochleae one day and one week after surgery; on electrocochleography, the SP/AP ratio was significantly higher one week after surgery.

CONCLUSION
These findings provide both morphological and functional evidence that EH is prevalent early but resolves in the majority of animals by one month after CI surgery. When it persists, it could potentially cause a delayed hearing loss.

49

ROLE OF WNT PATHWAY MEDIATORS IN REPAIR OF THE TYMPANIC MEMBRANE AFTER PERFORATION

R Dilley[1]
M Vinciullo[2]
S Redmond[3]
R Marano[4]
Y Shen[5]
A Dharmarajan[6]
M Atlas[7]

[1] Ear Science Institute Australia and Ear Sciences Centre, The University of Western Australia, Australia
[2] Ear Science Institute Australia and Ear Sciences Centre, The University of Western Australia, Australia
[3] Ear Science Institute Australia and Ear Sciences Centre, The University of Western Australia, Australia
[4] Ear Science Institute Australia and Ear Sciences Centre, The University of Western Australia, Australia
[5] Ear Science Institute Australia and Ear Sciences Centre, The University of Western Australia, Australia
[6] School of Biomedical Sciences, Faculty of Health Sciences, Curtin University, Perth, Western Australia
[7] Ear Science Institute Australia and Ear Sciences Centre, The University of Western Australia, Australia

BACKGROUND
Perforations of the tympanic membrane (TMP) are a frequent cause of conductive hearing loss worldwide. Research into why chronic TMP form, how they resolve and new therapeutic treatments are of significant interest. The role of Wnt signalling mediators have been broadly defined in the skin wound healing response, however, their role in TMP wound healing has not been identified.

OBJECTIVES
It is hypothesised that Wnt pathway mediators will be expressed and regulated in the TMP wound healing response. Furthermore, we propose that Wnt pathway regulators will have significant effects on wound healing mechanisms.

METHODS
This study examined the source and regulation of Wnt signalling mediators in rat acute TMP models using microarray analysis and immunohistochemistry. The role of Wnt signalling on TMP wound healing mechanisms was assessed *in vitro* using migration and proliferation assays in Wnt-treated human tympanic membrane keratinocytes (hTMT). The expression of Wnt mediators was also examined in hTMT cultures using polymerase chain reaction analysis.

RESULTS
It was found that rat tympanic membranes show measureable variation in levels of Wnt signalling mediators throughout the wound healing response, with the greatest changes being to Wnt 10 (increased 30 fold) in the inflammatory phase, Wnt 11 (increased 90 fold) in the proliferative phase, and Wnt 2, 7a and 11 (decreased 5 fold) in the remodelling phase. Wnt inhibitors were also regulated in inflammatory (SFRP4 50 fold increased), proliferative (SFRP4 110 fold increased; DKK3,4 10 fold increased) and remodelling phases (WIF1 increased 880 fold). WIF and β-catenin were most abundantly expressed, and their presence was confirmed and localised using immunohistochemistry. While the mediators were variously distributed through structures of the TM, staining predominantly was observed in the keratinocyte epithelial layer. Using a human tympanic membrane epidermal cell line (hTMt) in culture, we observed expression of Wnt ligands, inhibitors and beta catenin. Treatment of cells with the Wnt-agonist LiCl (0.1 mM -100 mM) produced dose-dependent inhibition of proliferation over a 48-hour period and of migration over a 6-hour period ($P<0.05$). The Wnt-antagonist Xav939 also produced a substantial inhibition of proliferation.

CONCLUSION
The present study confirmed that Wnt signalling pathway members are expressed and regulated during TMP wound healing and the pathway can significantly influence hTMT proliferation and migration. The Wnt pathway regulators may prove useful for exploration of pharmacological regulators for TMP wound healing.

50

A MICRO-POWER RADAR SYSTEM FOR CONTROLLING NEURO-PROSTHESES OF DYSPHAGIA

F Ahmadi[1]
F Yang[2]
C Jin[3]

[1]School of Electrical and Information Engineering, The University of Sydney, Australia
[2]School of Electrical and Information Engineering, The University of Sydney, Australia
[3]School of Electrical and Information Engineering, The University of Sydney, Australia

BACKGROUND
Dysphagia or swallowing disorder is the patient's inability to manage the transfer of food from the mouth to the stomach. Dysphagia may have possible catastrophic consequences, for example, the leakage of food to the respiratory system or choking, which is associated with a significant risk of death. The US Agency for Health Care Policy and Research estimates that each year, more than sixty thousand Americans die from complications associated with dysphagia - more than liver and kidney disease, as well as HIV/AIDS combined. An emerging research trend in dysphagia treatment has been designing neuro-prostheses, which can independently control the swallowing reflex by simultaneous excitation of malfunctioning muscles during swallowing. Despite the initial progress, the current stage of swallowing neuro-prostheses lacks a working solution for detecting food (bolus) location inside the swallowing tract. This "blindness", and having no information about the location of the bolus, essentially challenges the neuro-prostheses for dysphagia and they cannot currently be used to provide normal swallowing in daily life.

The introduction of micro-power UWB radars into biomedical research has opened a fascinating range of opportunities to monitor movements internal to the body completely non-invasive and with high precision. This research introduces the strong potential of micro-power UWB radar systems for designing the non-invasive bolus monitoring systems for patients with dysphagia.

OBJECTIVES
The system initially developed and tested in this study is through a series of finite difference time domain (FDTD) simulations. The system is aimed to monitor the transfer of the bolus inside the swallowing tract, detect bolus location information and pass it on as the input to the neuro-prosthesis. The neuro-prosthesis will use this information to artificially excite the required muscles to guide the bolus inside the tract and protect the airway. The design of this system aims to address the present gap in the otherwise non-functional design of neuro-prostheses for dysphagia.

METHODS
A simple two-dimensional FDTD model of human head is built using computerised tomography scans of human head and neck. The tissues of neck are comprised of bones, muscles, fatty tissues, skin layers, and we also consider a swallowed bolus. An array of 23 ultra-wideband electromagnetic (EM) radar antennas is implemented as a ring around the neck. A UWB micro-power pulse train is sent in the direction of the beam. This pulse is transmitted from five different directions and all the 23 antenna elements will receive the backscattered signals. The reflecting signal is used to generate a radar image. The final radar image is reconstructed using Delay and Sum (DAS) and modified-weighted-delay-and-sum (MWDAS) respectively to show the location of bolus.

RESULTS
The results, based on FDTD simulation, demonstrate the potential of using UWB microwave for monitoring bolus transit. The results also suggest that the design of the system has merit and it is feasible to use the ultra wideband radar system to image a bolus.

CONCLUSION
With proper design of UWB antennas, it is expected that a good performance of UWB microwave imaging can be achieved.

The Garnett Passe and Rodney Williams Memorial Foundation
PO Box 577
EAST MELBOURNE VIC 8002

P +61 3 9419 0280
F +61 3 9419 0282
E gprwmf@bigpond.net.au
W www.gprwmf.org.au