The Raine Study Annual Scientific Meeting 2021

Welcome Comments Speaker

William Aiken

William is a committed Gen2 (born into the study) Raine Study participant. William is father of one and is a Senior Manager of Compliance in the banking Industry. He has been a member of the Raine Study's Community Advisory Committee since 2019 and has served as the participant representative on the Raine Study's UJV Board since March 2021

Keynote Speaker

Prof Jeremy K. Nicholson
Director, Australian National Phenome Centre
Pro-Vice Chancellor for Health Sciences
Director of the Health Futures Institute, Murdoch University, Australia
Emeritus Professor of Biological Chemistry, Imperial College London

Prof Nicholson obtained his PhD in Biochemistry from St Thomas's Hospital Medical School (Kings College, London University) in 1980. After a series of academic appointments at Birkbeck College and University College, London University, he was made Full Professor of Biological Chemistry in 1992. He was appointed to be the University of London Established Chair in Biological Chemistry and Head of Biological Chemistry at Imperial College London in 1998. Subsequently appointed Head of the Department of Biomolecular Medicine in 1997, then Head of the Department of Surgery and Cancer in 2009. In 2012 he founded and became director of the world's first National Phenome Centre – the MRC-NIHR National Phenome Center at Imperial. He founded and chairs the International Phenome Centre Network (2016-to date). He left Imperial in late 2018 to become the Pro-Vice Chancellor for Health Sciences at Murdoch University and to direct the new Australian National Phenome Center in Perth, Western Australia which opened in October 2019.

Prof Nicholson has authored over 900 papers and articles on spectroscopy, informatics, metabolic biochemistry, and systems medicine. His major research focus is on the development of diagnostic and prognostic molecular phenotyping and computational technologies as applied to problems in personalised healthcare, microbiome-host metabolic signalling, metabolic diseases. For the last 18 months he has been leading an international team working on the metabolic sequelae of COVID-19. He is a Clarivate "Highly-Cited" Researcher in Pharmacology and Toxicology and Cross-Disciplinary Science (Clarivate H index = 135, Google H = 157). He has received various prizes for his work including: The Royal Society of Chemistry (RSC) Silver (1992) and Gold (1997) Medals for Analytical Chemistry; UK Chromatographic Society Jubilee Silver Medal (1994); Pfizer Prize for Chemical and Medicinal Technology (2002); RSC medal for Chemical Biology (2003); RSC International Interdisciplinary Prize (2008); Pfizer Global Research Prize for Chemistry (2006) and the Semelweiss-Budapest International Prize for Biomedicine (2010). Professor Nicholson holds multiple honorary and adjunct professorships including The Mayo Clinic, University of New South Wales, Nanyang Technological University, Shanghai Jiao Tong University, Zhejiang University, Fudan University, Clinical Professor, The University of Western Australia, Chinese Academy of Sciences, Wuhan and Dalian. He was elected, Fellow of The UK Royal Academy of Medical Sciences (2010); Honorary Lifetime Fellow of the International Metabolomics Society (2012); Honorary Lifetime Member of the US Society of Toxicology (2013); Albert Einstein Professor of the Chinese Academy of Sciences in Medical Biochemistry (2014); Elected Honorary Fellow of the Royal College of Physicians (2018); Honorary Doctor of Science, *Honoris Causa* (Hong Kong Baptist University), in 2019.

Systems Medicine in a Changing World: Molecular Phenomics in Personalised and Public Healthcare.

Changes in climate and population densities and distribution plus increasing socioeconomic stresses placed on healthcare systems pose a unique series of challenges in 21st Century medicine. A tension exists between the development of new investigative, diagnostic and prognostic technologies and the

ability of healthcare professionals to deliver effective translational solutions. The complex gene-environment interactions that create individual and population disease risks are also responsible for the expression of metabolic phenotypes in different body compartments and fluids. Thus, *metabolic phenotyping* offers an important window on human systemic activity and spectroscopic tools can be employed to help characterize personalised profiles, disease processes and responses to therapy. Existing epidemiological cohorts such as the Raine study have sample collections that help understand gene environment interactions that influence life outcomes and can also provide a baseline for studying the long-term impacts of emergent diseases. These approaches also provide a powerful adjunct to conventional procedures for disease assessment that are required for future developments in "*Precision Medicine*". Also, the *"Metabolome Wide Association Study*" concept provides powerful new tool to generate disease risk biomarkers, e.g., for cancers or cardiometabolic diseases, from epidemiological sample collections. Such population risk models can also link to individual patient healthcare models thus closing the personal and public healthcare modelling triangle. The ultimate challenge is to take complex validated data sets and models on human biology and to visualise these in engaging formats and forms that clinically actionable in an ever-changing background of human health. COVID-19 has emerged as a major human challenge to human health and healthcare systems and provides an exemplar for the application of molecular phenomics to understand and help mitigate long term effects of the disease.

The Raine Study Annual Scientific Meeting 2021

Session 1
Mid-Career Researcher Presentations

Chairs

Prof Romola Bucks
Director, The Raine Study

Romola Bucks is a professor in the School of Psychological Science at the University of Western Australia and former Deputy Dean of the Faculty of Science and Head of the School of Psychological Science at UWA. As Director of the Raine Study she provides leadership and direction for research activities, strategic direction, operations and partnerships.

Romola sits on the Board of Directors of the Australian Psychology Accreditation Council, and in 2018 was made a Fellow of the Association for Psychological Science for her contribution to the field. She is a passionate teacher and research supervisor, who is committed to mentoring young scientists.

A/Prof Rebecca Glauert
Scientific Director, The Raine Study

Rebecca Glauert joined the Raine Study in February 2021 as Scientific Director and works in partnership with the Director of the Raine Study to lead cohort research. She is also a principal research fellow at the School of Population and Global Health at UWA, leading research using linked administrative data to understand pathways and outcomes for vulnerable populations.

Speaker / Researcher

Dr Koya Ayonrinde, Gastroenterologist and Hepatologist, Fiona Stanley Hospital. oyekoya.ayonrinde@uwa.edu.au, @GutLiver

Researcher Bio

Dr Koya Ayonrinde is a Gastroenterologist and Hepatologist at Fiona Stanley Hospital. He has had a long relationship with the Raine Study from his PhD years. He continues to conduct research related to the liver and gastrointestinal tract in the Raine Study.

Title

Clustering of Rome IV-like irritable bowel syndrome, somatic pain and mental disorders in adolescents – a cross-sectional study

Background and aims: Irritable bowel syndrome (IBS) is a common lower gastrointestinal disorder featuring recurrent abdominal pain associated with diarrhoea and/ or constipation, and often abdominal bloating. Routine investigations do not diagnose IBS. IBS impacts on the wellbeing of individuals, as the symptoms often cause distress, interference with employment, education or recreation. Using data from the Raine Study, we aimed to examine associations between IBS and pain in different parts of the body, menstrual problems, and diet in adolescents, family socio-demographic characteristics, and mental health of the adolescents and their parents.

Methods: Seventeen-year-old Gen2 adolescents (n=1281) participating in the 17-year follow-up of the Raine Study, had a cross-sectional assessment, including questionnaires, physical assessments and blood tests. The questionnaires enquired about general health and wellbeing, medical history, gastrointestinal symptoms, pain in the abdomen and other parts of the body, menstrual problems, diet, mental health problems, health professional attendance, smoking, alcohol and medications use, family structure and family history. Adolescents self-rated their overall health status as “poor”, “fair”, “good”, “very good” or “excellent”, and also recorded how often they were bullied and how often they felt generally unhappy or sad. Additionally, the parents (Gen1) or primary care provider completed a questionnaire regarding their health and lifestyle and that of their Gen2 adolescent and documented a personal history of treatment for an emotional health problem and the family annual income. The data were used to establish a presumptive diagnosis of IBS using contemporary Rome IV-like criteria that requires recurrent abdominal pain at least 4 days per month associated with defecation or a change in the frequency or appearance of stool. We examined associations between IBS, gastrointestinal symptoms (abdominal pain, diarrhoea, constipation, nausea, vomiting), pain in other parts of the body (back, neck/ shoulder, arms/legs, headaches), diet, menstrual problems, eating disorders, self-reported rating of health status and happiness, family structure, and healthcare utilisation in the Gen2 adolescents, plus the relationship between IBS and diagnosed depression and anxiety in the Gen2 adolescents and their parents (Gen1) during the 17-year follow-up.

Results: The prevalence of Rome IV-like IBS symptoms was 6%. Adolescents with IBS had a higher prevalence of abdominal bloating, nausea, headaches, pain in the neck/shoulders, arms/legs, menstrual problems, eating disorders, anxiety and depression compared with those without IBS ($p<0.005$ for all). Those with IBS had lower family income, higher rates of general practitioner, emergency department and psychologist/ psychiatrist visits, analgesic, laxative and antidepressant medications use. Mothers of Gen2 adolescents with IBS had a higher prevalence of emotional disorders, while the fathers were more likely to spend less than one hour per day with the adolescent on weekdays and weekends ($p<0.05$). Using multivariable logistic regression analysis, abdominal bloating, recurrent headaches, neck/shoulder pain, anxiety and maternal history of emotional problems were independently associated with IBS ($p<0.05$), after adjusting for other covariates.

Conclusions: Adolescents with IBS experience a substantial burden of somatic pain, mental health disorders and reduced general wellbeing, compared with their peers. The impact of abdominal bloating, musculoskeletal pain and headaches, emotional health problems, family structure, and parent factors should be considered when managing adolescents with IBS.
Key words – Irritable bowel syndrome, IBS, adolescents, anxiety, depression, somatic pain, eating disorder, The Raine Study, emotional health, maternal, cross-sectional study.

Co-investigators

Frank M Sanfilippo[4,5] (frank.sanfilippo@uwa.edu.au)
Oyedeji A Ayonrinde[6,7] (oyedeji.ayonrinde@queensu.ca
Therese A O'Sullivan[8] (t.osullivan@ecu.edu.au)
Leon A Adams[2,9] (leon.adams@uwa.edu.au)
Leon Straker [3] (l.straker@curtin.edu.au)
John K Olynyk[1,8] (john.olynyk@health.wa.gov.au)

Affiliations:

1. Department of Gastroenterology and Hepatology Fiona Stanley Hospital, Murdoch, Australia.
2. Medical School, The University of Western Australia, Nedlands, Australia.
3. Faculty of Health Sciences, Curtin University, Bentley, Australia.
4. School of Population and Global Health, The University of Western Australia, Nedlands, Australia.
5. Department of Pharmacy, Royal Perth Hospital, Perth, Australia.
6. Department of Psychiatry, Queens University, Kingston, ON, Canada.
7. Providence Care Hospital, Kingston, ON, Canada.
8. School of Medical and Health Sciences, Edith Cowan University, Joondalup, Australia.
9. Department of Hepatology, Sir Charles Gairdner Hospital, Nedlands, Australia.

Speaker / Researcher

Dr Monique Robinson, NHMRC Early Career Fellow, Telethon Kids Institute,

Email: monique.robinson@telethonkids.org.au

Researcher Bio

Dr Monique Robinson completed PhD and MPsych (Clinical) degrees at The University of Western Australia. Monique is currently Senior Research Fellow at the Telethon Kids Institute with a primary research focus on how early life influences such as stress impact upon the later mental and physical health of the child.

Title

Increased risk for otitis media infection in offspring following maternal prenatal stress exposure

Abstract

Background: Amongst the most common of early childhood diseases, childhood otitis media (OM) is associated with an enormous social and economic burden. There is limited but compelling evidence that suggests prenatal factors, including maternal stress, may play a role in the aetiology of OM.

Aim: Using a longitudinal prospective pregnancy cohort, we aimed to determine the impact of multiple life stress events on the later reporting of OM infection and recurrent OM infection at ages three and five years.

Methods: Exposure data on stressful life events were collected from pregnant women (Gen1) in the Raine Study at 18 and 34 weeks' gestation. We used longitudinal regression models stratified by sex to examine associations between the number, type and timing of maternal prenatal stress events and the likelihood of any Gen2 OM infection in addition to recurrent OM infection at age three and age five, adjusting for numerous prenatal sociodemographic and environmental confounders.

Results: Each additional stressful life event experienced during pregnancy was associated with a significantly greater chance of reporting any OM infection at both ages three and five. These results were fortified when we examined recurrent OM infections as our outcome. While our analysis of the timing of stressful life events did not reveal significant differences between the first and second halves of pregnancy, we did observe that particular types of stress such as pregnancy problems, relationship problems and problems related to other children were individually linked to a higher likelihood for recurrent OM infection at age three and five years.

Conclusions: In both male and female children, a dose-response effect is evident in the maternal experience of additional stressful life events in pregnancy and the risk for offspring OM infection in the preschool years. This is particularly evident for children with recurrent OM infections. This is a novel finding with consequences for the developing understanding of the importance of the maternal stress experience on determining the later immune health of offspring.

Co-investigators

David Burgner [2,3,4]
Ashleigh Lin[1]
Peter Jacoby[1]
John Newnham[5]
Robert Eikelboom[6,7,8]
Shyan Vijayasekaran[9,10,11]
Christopher G. Brennan-Jones[1]

1. Telethon Kids Institute, The University of Western Australia
2. Murdoch Children's Research Institute, Parkville, Australia
3. Department of Paediatrics, University of Melbourne, Parkville, Australia
4. Department of Paediatrics, Monash University, Clayton, Australia
5. Division of Obstetrics and Gynaecology, The University of Western Australia
6. Ear Sciences Centre, Medical School, The University of Western Australia
7. Ear Science Institute Australia, Perth, Australia
8. Department of Speech-Language Pathology and Audiology, University of Pretoria, Pretoria, South Africa
9. Perth ENT Centre, Perth, Australia
10. Otolaryngology Head and Neck Surgery, Perth Children's Hospital, Perth, Australia
11. Medical School, The University of Western Australia

Speaker / Researcher

Dr Samantha Lee, Research Fellow, Lions Eye Institute, Email: samanthalee@lei.org.au

Researcher Bio

Dr Samantha Lee is a postdoctoral research fellow at the Lions Eye Institute. She has a special interest in the genetic and environmental factors of glaucoma, myopia, and their associated endophenotypes.

Title

Incidence of myopia and change in ocular biometry between 20 and 28 years old

Abstract

Background: Myopia (shortsightedness) is not simply a condition that requires wearing spectacles to see clearly. The increase in length of the eyeball (axial length) that occurs with myopia puts individuals with myopia at higher risk of visual impairment in their lifetimes. While myopia typically starts and progresses fastest during childhood, reports of university students becoming more myopic during their late-teens/early-20s suggest that the condition can develop or worsen during early adulthood. However, there has been limited exploration on the rates (incidence) and progression of myopia during early adulthood.

Aims: This study documented the 8-year myopia incidence and progression of myopia in a community-based sample of young adults from Gen2 of the Raine Study. Additionally, we determined if known risk factors of childhood myopia – having parents with myopia, reduce sun exposure, higher education – are also predictive of development or progression of myopia during young adulthood.

Methods: Gen2 participants of the Raine Study underwent measurements of their axial length and refraction at the 20- (baseline) and 28-year follow-ups. Participants without myopia or high myopia at baseline were included in the 8-year incidence analysis (n=526, 51% male and n=698, 50% males, respectively), while all participants who had complete data at both visits were included in the progression analysis (n=691, 49% male). Those with prior eye surgery that could affect their refraction were excluded. Information on education and parental myopia were collected using questionnaires. Sun exposure was quantified objectively using conjunctival ultraviolet autofluorescence (CUVAF) photography.

Results: The 8-year incidence of myopia and high myopia were 14.1% (95% confidence interval [CI]=11.5-17.4%; n=76) and 0.7% (95%CI=0.3-1.7%; n=5), and the overall myopia prevalence at the 28-year old cohort were 33.2% and 1.5%, respectively. There was a myopic shift (≥0.50D) in at least one eye in 38.1% of participants. Refraction and axial length changed by -0.03D/year and +0.02mm/year, respectively (both p>0.001). East Asian ethnicity (vs. Caucasians), parental myopia, and smaller CUVAF area (indicating less sun exposure) were significant risk factors for incident myopia, while female sex and parental myopia were associated with myopia progression and axial length increase (all p≤0.001). Education level was not associated with myopia incidence or progression.

Conclusions: Myopia progression and axial elongation continues during the third decade of life for more than one-third of adults. There is a protective effects of sun exposure against myopia in young adults, as observed previously in children.

Co-investigators
Dr Gareth Lingham, postdoctoral research fellow. Centre for Eye Research Ireland. Email: Gareth.Lingham@TUDublin.ie
Dr Paul Sanfilippo, research fellow, Centre for Eye Research Australia. Email: prseye@gmail.com
Dr Seyhan Yazar, postdoctoral research fellow, Garvan Institute of Medical Research. Email: seyhanyazar@gmail.com
Prof David Mackey, professor, Lions Eye Institute, Centre for Ophthalmology and Visual Science, the University of Western Australia david.mackey@utas.edu.au

Panel Presentation – Perspectives on new directions for the Raine Study

Facilitator: Prof Romola Bucks

Dr Alison Kerr

Alison is a committed Gen1 (a parent of those born into study) Raine Study participant having entered the study in 1991. Alison is a General Practitioner and Surgical Assistant and has been a member of the Raine Study Community Advisory Committee and representative on the Scientific Review committee since 2017.

Jessie Appleyard

Jessie is a committed Gen2 (born into the study) Raine Study participant. Jess is studying her art education masters and works in art gallery event management and optometry. Jess has been involved the Raine study participant engagement groups and workshops since her teens. Jess chaired the Raine Study Community Advisory Committee from 2017 to 2019 and is now as a collaborator on the Visual Consent project.

Charlotte Diaz

Charlotte is a committed Gen2 (born into the study) Raine Study participant. Charlotte is mother of one and a Superintendent of Community Engagement in the resource industry.

Charlotte has been engaged in workshops and forums since her teens and a member of the Raine Study Community Advisory Committee from 2017 and a representative on the Unincorporated Joint Venture board from 2017-2021.

A/Prof Ashleigh Lin

A/Prof Ashleigh Lin is a NHMRC Career Development Research Fellow and Program Head of Mental Health and Youth at the Telethon Kids Institute. Ashleigh's research is focused on early detection and intervention for mental health problems in adolescents and young adults.

Dr Koya Ayonrinde

Dr Koya Ayonrinde is a Gastroenterologist and Hepatologist at Fiona Stanley Hospital. Koya has had a long relationship with the Raine Study from his PhD years and continues to conduct research related to the liver and gastrointestinal tract in the Raine Study.

Dr Amy Reynolds

Dr Amy Reynolds is an Early-Mid Career Researcher in the field of sleep health, within the College of Medicine and Public Health at Flinders University. Amy’s research is focused on improving understanding of how sleep, sleep timing and health are related in population-level data and identify novel targets for intervention in members of the community impacted by poor sleep - from shift workers to patients living with chronic illness.

Visual Informed Consent for the Raine Study – A new initiative from the Comic Book Contracts team and Alternative Contracting

This presentation will highlight the innovative use of visual and comics in contracts and the benefits derived thereof. It will introduce a selection of the pioneering research of the Comic Book Contract project at UWA, as well as some of the projects carried out by collaborator, Alternative Contracting. We will share some insights into the what, why and how of these unusual contracts. The talk will then turn to the most recent collaboration, namely the visual informed consent form for the Raine Study, which is still in its early draft stages. We will show some (draft) images and concepts, and share some hints and tips relating to visual contract creation. The idea that law needs to change to become more effective and relational fits well with the concept of improving consent forms, and the project promises to be mutually beneficial. We will be joined by Raine Study participant Rachel Wilkinson, who will offer insight into the activities of the collaborative working group from a participant's perspective.

Prof Camilla Baasch Andersen

Camilla is a Professor at the School of Law at University of Western Australia. Throughout her career, she has served at numerous universities world-wide, including University of Leicester in the United Kingdom, Centre for Commercial Law Studies, University of London and University of Copenhagen in her native Denmark. She has lectured and examined externally for dozens of universities and institutions, and has worked with the CISG Advisory Council, as well as been appointed Trade Law Expert for UNCITRAL and worked with the UNCITRAL Australian Co-ordination Committee. Prof Andersen was the founding co-editor of The Journal of Comparative Law and has been the National Reporter for the United Kingdom for the International Academy of Comparative Law. She works closely with business, government and academia in pursuit of Commercial Law facilitating trade, and has written extensively on the CISG, international commerce, visual law and legal design, comparative method, dispute resolution, and pro-active approaches to law. She founded and leads the Comic Book Contract project at UWA (see www.comicbookcontracts.com). For more information, and an overview of her extensive publications, see: https://research-repository.uwa.edu.au/en/persons/camilla-andersen

Peter Alexander Corner

Peter is founding manager of Alternative Contracting, which consults and works with business on visualization of contracting. He works closely with the Comic Book Contracting project at UWA, which has allowed him to draw on his experience from various industries, and he holds degrees in History and a Master of Research from University of Leicester in the UK. He has also studied finance in his native

Denmark. He has lectured extensively on his work in legal contract design, including various universities and bar associations in Australia, Denmark, Netherlands, and the UK, the Lawyers Association Worldwide (LAW) and The International Association for Contract & Commercial Management/World Commerce and Contracting and numerous others. His work can be viewed at www.alternativecontracting.biz

With comments from Rachael Wilkinson

Rachael is a committed Gen2 (born into the study) Raine Study participant. Rachael lives and works in Melbourne as policy advisor on Industry Development with the Ai Group. Rachael was a member of the Raine Study Community Advisory Committee and the Raine Study Scientific Review Committee from 2017 to 2021 and is now a collaborator on the Visual Consent project.

The Raine Study Annual Scientific Meeting 2021

Session 2 Student Presentations

Chairs

Dr Michele Olaithe

Dr Michele Olaithe is a Research Fellow at the University of Western Australia and Psychologist for the Olive Branch Wellness Centre. Michele's research is focused on the relationship between sleep disruption and cognitive function across the lifespan.

Dr Amy Reynolds

Dr Amy Reynolds is an Early-Mid Career Researcher in the field of sleep health, within the College of Medicine and Public Health at Flinders University. Amy's research is focused on improving understanding of how sleep, sleep timing and health are related in population-level data, and identify novel targets for intervention in members of the community impacted by poor sleep - from shift workers to patients living with chronic illness.

Speaker / Researcher

Ms, Kelly Sansom, PhD student, the University of Western Australia,

Email: kelly.sansom@research.uwa.edu.au

Researcher Bio

Kelly Sansom is a PhD student at the Centre for Sleep Science at the University of Western Australia. Her research focuses on better understanding the relationship between sleep disorders and hypertension in both community and clinical populations.

Title

Estimating sleep duration: validation of open source actigraphy against in-laboratory polysomnography.

Abstract

Background: Wrist actigraphy is gaining popularity as a cheaper and more cost-effective objective measure of habitual sleep duration in large community populations. However, analysis is often limited by brand-specific software containing proprietary algorithms. Open source actigraphy analysis aims to overcome brand-specific analysis to improve reproducibility of actigraphy data across studies. It is currently unclear how open-source actigraphy compares to the gold standard in-laboratory polysomnography (PSG) assessment of sleep.

Aims: This study aimed to assess the validity of the open-source R-package GGIR for actigraphy sleep analysis compared to PSG in a community population.

Methods: 1098 middle aged individuals from the Raine Study Gen1-26-year follow-up were included in this analysis (F 58%; Age [SD] 56.7[5.7]). Participants completed one night of in laboratory PSG and contemporaneous actigraphy (GT3X+ ActiGraph LLC, Pensacola, FL) and sleep diary assessment at the Centre for Sleep Science, University of Western Australia (UWA). Participants with incomplete actigraphy, PSG and demographic data were excluded. The actigraphy PSG and actigraphy sleep duration were compared using Bland Altman (BA) Plots, Pearson's correlation coefficient(r) and intra-class correlation coefficient (ICC). Analysis was stratified by demographic and sleep characteristics.

Results: Of 1098 participants in this study 281 were excluded due to poor actigraphy data quality or not completing concurrent actigraphy and PSG sleep assessments and a further 108 were excluded for missing covariate information, leaving a final sample of 615 for analysis (F 58%; Age [SD] 56.9[5.6]). Same night sleep duration measured by PSG and Actigraphy were moderately correlated (r = 0.57, p <0.05) with a poor ICC (ICC = 0.4, 95% CI: 0.37-0.5). According to BA analysis, actigraphy over estimated PSG sleep duration by 0.52 hours, on average, with the lower and upper limits of agreement ranging from -1.10 hours to 2.14 hours. In stratified analysis higher agreement was found in individuals with less wake after sleep onset (WASO; r=0.7, p<0.005; ICC = 0.7, 95% CI: 0.6-0.7) and lower sleep onset latency (SOL; r= 0.7, p<0.005; ICC = 0.6, 95% CI: 0.5-0.7) relative to those with higher WASO and SOL.

Conclusion: The agreement between contemporaneous PSG and open source analysed actigraphy raw data is better in individuals with lower WASO and SOL.

Co-investigators

Professor Peter Eastwood, Director and Dean (Research) of Flinders Health and Medical Research Institute, College of Medicine and Public Health, peter.eastwood@flinders.edu.au
A/Professor Nigel McArdle, Respiratory and Sleep Physician at Sir Charles Gairdner Hospital - Pulmonary Physiology & Sleep Medicine and senior researcher at the Centre for Sleep Science School of Human Sciences UWA and the West Australian Sleep Disorders Research Institute, Nigel.McArdle@health.wa.gov.au
Dr Jennifer Walsh, Director of Centre for Sleep Science, School of Human Sciences UWA and research fellow at the West Australian Sleep Disorders Research Institute, jennifer.walsh@uwa.edu.au
Dr Kathleen Maddison, Research Officer & Lecturer at University of Western Australia - Centre for Sleep Science and research fellow at the West Australian Sleep Disorders Research Institute, Kath.Maddison@health.wa.gov.au
Clinical Professor Bhajan Singh, Head of Department at Sir Charles Gairdner Hospital - Pulmonary Physiology & Sleep Medicine and director of the West Australian Sleep Disorders Research Institute, bhajan.singh@health.wa.gov.au
Dr Amy Reynolds, Senior research fellow at Flinders Health and Medical Research Institute, College of Medicine and Public Health, amy.reynolds@flinders.edu.au
Assoc Prof Joanne McVeigh, Senior research fellow at Curtin School of Allied Health, Curtin University, Joanne.Mcveigh@curtin.edu.au
Dr Diego Mazzotti Assistant Prof, Division of Medical Informatics, Department of Internal Medicine, University of Kansas Medical Center, droblesmazzotti@kumc.edu

Speaker / Researcher

Bereket Duko, PhD Candidate, Curtin School of Population Health, Curtin University, WA.

Tel: 0488742278; Email: b.adema@postgrad.curtin.edu.au; twitter: https://twitter.com/BereketDuko

Researcher Bio

Bereket is at the final stage of his PhD study at Curtin School of Population Health, Curtin University and has a strong research experience. He has published over 50 research articles in international peer-reviewed reputable journals since 2015. He has won Curtin University International Postgraduate Research Scholarship in 2019 and the Raine Study PhD Top-up Scholarship in 2020.

Title

Prenatal Tobacco Smoking and the Risk of Conduct Disorder Symptoms in offspring: Evidence from the Raine Study

Abstract

Background: Although there is widespread consensus that maternal prenatal tobacco smoking may result in adverse behavioural and mental health problems in the offspring, a number of longitudinal studies have linked maternal prenatal tobacco smoking to offspring conduct disorder symptoms but with inconsistent findings. Further examination of maternal and paternal tobacco smoking during pregnancy may give vital clues to the etiological basis for conduct disorder symptoms. If maternal tobacco smoking during pregnancy, but not paternal tobacco smoking, is linked to an increased risk of conduct disorder symptoms in offspring, this observation may provide support for a prenatal causal pathway. However, if maternal and paternal tobacco smoking during pregnancy are both associated with an increased risk of this disorder, then this finding may implicate both *maternal prenatal tobacco smoking* and environmental tobacco smoke exposure, or the presence of unmeasured confounding.

Aim: To examine the association between maternal tobacco smoking during pregnancy and conduct disorder symptoms in Raine Study Gen2 adolescents at the age of 14 years using paternal tobacco smoking during the partner's pregnancy as a proxy for environmental tobacco smoke exposure.

Methods: We obtained data from the Raine Study; a multi-generational cohort study based in Perth, Western Australia. Data on maternal prenatal tobacco smoking was available for the first and third trimesters of pregnancy. The clinical Diagnostic and Statistical Manual-oriented scale of the Child Behaviour Checklist (CBCL) was used to measure conduct disorder (CD) symptoms in offspring. Negative binomial regression was used to estimate the risk as rate ratio (RR) of CD symptoms in offspring. To facilitate comparison with previous studies and to better investigate the role of potential confounders, risk factors were sequentially added as adjustment variables in separate models. We also computed the E-values to investigate the extent of unmeasured confounding. Paternal tobacco smoking during pregnancy was used as a proxy for environmental tobacco smoke exposure.

Results: Complete data were available for 1747 mother-child and 1711 father-child pairs. After adjusting for potential confounders, we found elevated risks of CD symptoms in adolescents born to mothers smoking tobacco during the first trimester [RR 1.52 (95% CI: 1.24-1.87)], third trimester [RR 1.36 (95% CI: 1.09-1.69)] and during both these trimesters of pregnancy [RR 1.50 (95% CI: 1.19-1.90)]. The rates of CD symptoms in adolescents increased with the level of exposure to maternal tobacco smoking during pregnancy. Based on the evidence from the E-values, moderate unmeasured confounders are needed to nullify the reported association between maternal prenatal tobacco smoking and CD symptoms in adolescents. However, we noted insufficient statistical evidence for an association between paternal smoking during pregnancy and CD symptoms in adolescents.

Conclusion: The associations we found for maternal but not paternal tobacco smoking during pregnancy may suggest a biological mechanism for intrauterine tobacco exposure leading to CD symptoms in adolescents. Early interventions assisting pregnant mothers to quit tobacco smoking, or avoid smoking initiation, have potential to contribute health benefits to both mothers and their children.

Co-investigators
1. Professor Gavin Pereira, Curtin School of Population Health, Curtin University, Kent Street, Bentley WA 6102, Australia. Email: Gavin.F.Pereira@curtin.edu.au 2. Dr. Robert Tait, National Drug Research Institute, Faculty of Health Sciences, Curtin University, 7 Parker Place Building 609, Level 2 Technology Park, Bentley WA 6102, Australia. Email: robert.tait@curtin.edu.au 3. Dr. Kim Betts, Curtin School of Population Health, Curtin University, Kent Street, Bentley WA 6102, Australia. Email: Kim.Betts@curtin.edu.au 4. Professor John Newnham, Head of Division of Obstetrics and Gynaecology, Faculty of Health and Medical Sciences, The University of Western Australia, 17 Monash Ave, Nedlands WA 6009, Australia. Email: john.newnham@uwa.edu.au 5. Professor Rosa Alati, Head of Curtin School of Population Health, Curtin University, Kent Street, Bentley WA 6102, Australia. Email: Rosa.Alati@curtin.edu.au

Speaker / Researcher

Mr Qiang Li, Medical Student, The University of Western Australia, Tel: 0435445824, qiangli@lei.org.au

Researcher Bio

Qiang is a final-year medical student at the University of Western Australia with an interest in ophthalmology.

Title

Evaluating the distribution of foveal avascular zone area in a healthy, young population

Abstract

Background: Optical coherence tomography angiography (OCTA) is a medical imaging technique for the blood vessels at the back of the eye (retina). OCTA offers unique advantages over traditional angiographic techniques in that it is non-invasive and allows extraction of quantifiable parameters. The foveal avascular zone (FAZ) is a zone in the centre of the retina with no overlying blood vessels for which the area (FAZA) can be quantified using OCTA. FAZA may have use in the diagnosis and monitoring of eye diseases, however, we must first understand its distribution in healthy individuals. Past studies have reported normative data for FAZA, however, largely did not account for variations in subjects' eye length (axial length). As axial length determines the scale of an OCTA image, neglecting to correct for axial length when extracting OCTA parameters leads to inaccuracies in the data obtained. Importantly, only 8% of the existing literature on FAZA corrects for variations in axial length. Other gaps in literature to be addressed are the lack of OCTA studies on young populations and on interocular agreement. Evaluating FAZA in a younger population is crucial to understanding its distribution in healthy individuals and evaluating interocular agreement is useful to define thresholds for pathological change and detect asymmetrical eye disease.

Aims:

1. To establish normative data for corrected FAZA in a healthy, young population
2. To evaluate the effect of correction for axial length on FAZA
3. To evaluate interocular agreement in FAZA

Results: The present study retrospectively analysed OCTA scans from 504 healthy, young individuals who underwent a comprehensive eye examination as part of the Raine Study Gen2-28 year follow-up. The mean (SD, range) corrected FAZA was 0.222 mm^2 (0.099, 0.027 to 0.416). The mean difference between uncorrected and corrected FAZA was -0.005 mm^2 and the relative change in FAZA post-correction was greater than 5% in 56% of eyes. The mean interocular difference in corrected FAZA was +0.006 mm^2 (95% confidence interval: -0.055 to +0.066mm^2).

Conclusion: We are, to the best of our knowledge, the largest study to evaluate FAZA in healthy eyes, with correction for axial length. The normative data provided in the current study can serve as control data in the emerging OCTA research field. We conclude that routine correction for axial length is important when evaluating FAZA in healthy eyes. Lastly, there is high interocular symmetry in FAZA. The limits of agreement reported may have use in the detection of asymmetrical eye disease.

Co-investigators

- Dr Jason Charng, Postdoctoral Fellow, Lions Eye Institute, jasoncharng@lei.org.au
- Professor David Mackey, Head of Genetics and Epidemiology, Lions Eye Institute, david.mackey@uwa.edu.au
- Associate Professor Fred Chen, Head of Ocular Tissue Laboratory, Lions Eye Institute, fredchen@lei.org.au
- Dr Peijun Gong, Early Career Researcher, UWA, peijun.gong@uwa.edu.au
- Mr Hao Ho, Engineering Student, UWA, haoho@lei.org.au

Speaker / Researcher

Ms Phoebe Ng, PhD Candidate; The University of Queensland, Laboratory for Motor Control and Pain Research, School of Biomedical Sciences, QLD, Australia and KK Women's and Children's Hospital, Physiotherapy Department, Singapore; phoebe.ng@uqconnect.edu.au

Researcher Bio

Phoebe Ng graduated with a Bachelor in Physiotherapy with Honours at the University of Queensland in 2011. Since 2016, a focus of her clinical practice in Singapore has been in the conservative treatment for people with Adolescent Idiopathic Scoliosis (AIS). She commenced her PhD in 2019 and is pleased to present on the Raine Study component of her project, exploring the profile of people likely to have AIS in the cohort.

Title

What is the prevalence of idiopathic scoliosis, and do BMI, body image or back pain differ in those with idiopathic scoliosis?

Abstract

Background: Idiopathic scoliosis (IS) is a three-dimensional spinal deformity of unknown origin, that is commonly detected in adolescence. It is diagnosed by a Cobb angle ≥10° on a standing radiograph in combinations with unilateral rib prominence present in forward bend position.

Cross-sectional and retrospective studies have suggested poor body image, eating disorders and lower bone mineral density (BMD) may be more common in adolescents with progressive scoliotic deformity than those without. Greater reports of back pain have been associated with IS. In longitudinal cohort studies, lower body mass index (BMI) has also been associated with the development of IS. Most studies examining factors related to IS have used biased clinical samples.

Dual energy x-ray absorptiometry (DEXA) scans from the Raine Study Gen2 at age 20, present a contemporary opportunity to screen for participants with likely IS in an unbiased community sample. This also enables comparison of psychological and physical factors between people with IS and those without.

Aim:

The aims of this study were to:

1. Identify likely IS in an Australian cohort using DEXA scans at age 20,

2. Compare the prevalence of psychological and physical factors, at ages 8, 10, 14, 17 and 20 between those with likely IS and those without.

Methods: To identify likely IS, a concordance of agreement was sought between (i) modified Ferguson angle ≥10° on DEXA, (ii) self-reported diagnosis of idiopathic scoliosis/kyphoscoliosis, and (iii) qualitative examination of DEXA curve presentation by an expert in scoliosis imaging. Descriptive statistical comparisons were calculated for BMI, BMD, the weight and eating disorder questionnaire, and self-reported diagnosis of back pain were made between those with likely IS and those without. To compare medians of continuous variables of those with likely IS and without, the Mann-Whitney U test was applied. To compare the relationship of categorical variables with likely IS, the chi-square test was applied.

Results: Out of 1238 Gen2 participants who completed DEXA scans, 26 participants were identified with likely IS. The prevalence was 2.1%, with a female:male ratio of 1.4:1. The mean±SD modified Ferguson angle was 14.0±3.5°. Thirty-three participants (2.7%) had little or no scoliotic curve but reported a diagnosis of IS. Eleven participants (0.9%) had a ≥10° DEXA scan curve but did not report any scoliosis. 1139 had no indication of scoliosis.

Between those with likely IS and those without, there were no statistically significant difference ($p>0.05$) with BMI ($median_8$: 16.54kg/m^2 vs 16.17kg/m^2; $median_{10}$: 17.52kg/m^2 vs 17.70kg/m^2; $median_{14}$ 19.21kg/m^2 vs 20.32kg/m^2, $median_{17}$: 20.77kg/m^2 vs 21.94kg/m^2; $median_{20}$: 22.02kg/m^2 vs 23.3kg/m^2).

In the weight and eating disorder questionnaire, there was no difference ($p>0.05$) in unhappiness in body shape (IS_{14}: ~19.0% vs non-IS_{14}: ~10.0%, $p=0.14$), and reports of any form of eating disorder (IS_{14}: ~9.5% vs non-IS_{14}: ~8.3%; IS_{17}: ~19% vs non-IS_{17}: ~12%, IS_{20}: 25% vs non-IS_{20}: ~16%).

Those with likely IS had a lower BMD ($median_{20}$: 1.00 g/cm^2 vs 1.07 g/cm^2, $p=0.03$), and more reports of back pain diagnosis ($IS_{14\text{-}20}$: ~23-45% vs non-$IS_{14\text{-}20}$: ~5-14%, $p<0.05$) than those without.

Conclusions:

Where DEXA scans are captured to screen for other health measures, they may also present an opportunity to estimate prevalence and assist screening for IS. Comparisons of psychological and physical factors demonstrate lower BMD and greater reports of back pain diagnosis in those with likely IS. The contributors to lower BMD in those with likely IS have not been identified yet, though it is unlikely to be BMI, given that it did not vary between groups. Similarly, it is not known if presence of scoliosis contributed to the reported back pain.

Co-investigators

1. Assoc Prof Kylie Tucker

The University of Queensland, Laboratory for Motor Control and Pain Research, School of Biomedical Sciences, QLD, Australia, k.tucker1@uq.edu.au

2. Ms Maree Izatt

Queensland University of Technology at the Centre for Children's Health Research, Biomechanics and Spine Research Group, QLD, Australia, m.izatt@qut.edu.au

3. Prof Leon Straker

Curtin University, School of Allied Health, WA, Australia, l.straker@curtin.edu.au

4. Dr Jennepher Downs

Curtin University, School of Allied Health, WA, Australia

Telethon Kids Institute, WA, Australia, j.downs@exchange.curtin.edu.au

5. Dr Andrew Claus

The University of Queensland, School of Health & Rehabilitation Sciences, QLD, Australia

Royal Brisbane Children's and Women's Hospital, Tess Cramond Pain and Research Centre, QLD Australia, a.claus1@uq.edu.au

Speaker / Researcher

Mr. David Balfour, student completing the Bachelor of Psychology (Honours) at Flinders University, 0413157032, balf0020@flinders.edu.au

Researcher Bio

David Balfour is completing the Bachelor of Psychology (Honours) at Flinders University this year. This abstract was based on his honours thesis.

Title

Developmental Sleep Trajectories and Adolescent Epigenetic Age Acceleration: A Prospective Cohort Study

Abstract

Approximately 600 words, structured as follows: Background, Aim(s), Results, Conclusion

Background: Research on the molecular consequences of poor sleep in childhood and adolescence may help to understand the relationship between sleep and health in this important developmental period. Epigenetic age acceleration (EAA) is a molecular measure of the extent to which biological age deviates from calendar age; it has been associated with increased risk of chronic disease and all-cause mortality. Biological ageing is a gradual, lifelong loss of physiological integrity, resulting in functional decline, morbidity, and mortality. Poor sleep has been associated with higher EAA in adults, suggesting it may speed up biological ageing, which may in turn lead to poorer health. Sleep problems are common in childhood and adolescence, but it is not yet known if these are associated with EAA.

Aims: This study aimed to investigate if sleep in childhood and adolescence is associated with EAA in late adolescence. To this end, caregiver-reported sleep trajectories from age 5 to 17 and current self-reported sleep problems at age 17 were examined in relation to EAA at age 17 in a representative sample of 1,192 young Australians from Gen2 of the Raine Study. Trajectories represented persistent, moderate but declining, and consistently minimal sleep problems. The trajectories were previously identified using latent class growth analysis on caregiver-reported sleep problem scores from the Child Behaviour Checklist at ages 5, 8, 10, 14, and 17. Scores used for the trajectories were based on the following items: “nightmares,” “overtired without good reason,” “sleeps less than most kids,” “sleeps more than most kids during day and/or night,” “talks or walks in sleep”, and “trouble sleeping”. Current self-reported sleep problem scores were calculated from nominally equivalent items on the Youth Self Report at age 17. Three measures of EAA were calculated from peripheral blood DNA methylation at age 17, representing different aspects of biological age: AgeAccelGrim, Extrinsic EAA (Hannum), and Intrinsic EAA (Horvath). It was expected that persistent sleep problems and higher current sleep problem scores would be associated with higher EAA.

Results: There was no evidence for a difference in any measure of EAA at age 17 between caregiver-reported sleep trajectories, representing sleep problems from age 5 to 17. There was also no evidence for an association between current self-reported sleep problem score at age 17 and any measure of EAA at the same age, after controlling for body mass index, ethnicity, family income, sex, and smoking. Supplementary analyses revealed that participants and their caregivers agreed on the presence or absence of individual sleep problems at age 17 67% of the time, representing a 33% error rate. Caregiver-reported sleep problem scores at age 17 were roughly one third of nominally equivalent self-reported scores at the same age, indicating a need to follow up findings with alternative, objective measures of sleep.

Conclusions: To our knowledge, this was the first study to investigate if patterns of sleep over a period of years are associated with EAA. There was no evidence for an association between trajectories of sleep in childhood and adolescence and EAA in late adolescence. There was also no evidence for an association between current sleep and EAA in late adolescence, or for an association between sleep and biological age more generally. Future research should use alternative, ideally objective measures of sleep.

Co-investigators *Title, name, position, institution, email*
Dr. Phillip E. Melton, University of Tasmania, phillip.melton@uwa.edu.au
Associate Professor Joanne A. McVeigh, Curtin University, joanne.mcveigh@curtin.edu.au
Associate Professor Rae-Chi Huang, Telethon Kids Institute, rae-chi.huang@telethonkids.org.au
Professor Peter Eastwood, Flinders Health and Medical Research Institute, Flinders University, peter.eastwood@flinders.edu.au
Ms. Sian Wanstall, Bachelor of Psychology (Honours) student at Flinders University, sian.wanstall@flinders.edu.au
Dr. Amy C. Reynolds, Flinders Health and Medical Research Institute, Flinders University, amy.reynolds@flinders.edu.au
Associate Professor Sarah Cohen-Woods, Flinders University, sarah.cohenwoods@flinders.edu.au

Speaker / Researcher

Natasha Wood, PhD Candidate College of Education, Psychology, and Social Work. Flinders University. Email: natasha.wood@flinders.edu.au; @natashamwood15

Researcher Bio

Natasha is a Psychologist and a Clinical Psychology PhD student in the College of Education, Psychology and Social Work, Flinders University. Her PhD research uses epigenetics (biological mechanisms that modify gene expression without modifying the genetic code) to explore how kinds of childhood stress affect mental health. She specifically investigates whether socioeconomic position and young adult mental health outcomes are linked by changes known as DNA methylation, which work like tags on our DNA to tell a gene whether it should be expressed or not. Natasha was also successful in securing a Fulbright Future Scholarship (2021-2022) to work with the Psychiatric and Neurodevelopmental Genetics Unit at the Massachusetts General Hospital.

Title

Scars of Socioeconomic Stress: Social Epigenetics

Abstract

Background: Childhood socioeconomic position (SEP) has previously been associated with epigenetic alterations, including epigenetic age in early adulthood. Epigenetic age is an estimate of biological age based on DNA methylation levels of selected CpG sites and can be calculated in a variety of ways from different epigenetic clocks. Some evidence suggests that SEP might be associated with differences in epigenetic change, however the current evidence demonstrates findings to be inconsistent between cohorts, and epigenetic clocks. SEP can be measured in a variety of ways, and current research has focussed on area-level or cross-sectional SEP predictors in association with epigenetic age. This is a limitation, and it may be that individual level predictors may be more informative for individual level outcomes such as epigenetic age. Cross-sectional measures provide only a snapshot of the effect of SEP whereas trajectory measures include information about SEP over time, which may be more indicative of cumulative, or chronicity, of SEP patterns on outcomes.

Aim: The aim of this study was to establish a link between individual level childhood SEP trajectories, and epigenetic age in early adulthood in an Australian cohort.

Methods: The Raine Study (WA, Australia) is a longitudinal prospective cohort, with information gathered across pregnancy, childhood, adolescence, and adulthood. DNA methylation was taken from whole blood and measured Illumina HumanMethylation450K BeadChip from 1128 participants (male=606, female= 584) who attended the Gen2-17 year follow-up of the Raine Study. Epigenetic age was then calculated using a variety of epigenetic age calculators. Individual level SEP trajectories and classes were developed by latent class growth analysis. These were constructed based off domain information available at seven timepoints (year 1, 2, 3, 5, 8, 10, 14). The domains were family structure, finance and occupational prestige. Individuals missing information from three or more timepoints were excluded from the analyses. Regressions were used to examine the relationship between individual level childhood socioeconomic position and epigenetic age. These models were adjusted for sex, racial ancestry, BMI, and smoking status.

Results: Four SEP classes were identified (high, mid-consistent, mid-decreasing, and low). There was a relationship between SEP class and epigenetic age acceleration. Specifically, there were higher epigenetic age acceleration in the lower SEP classes compared to the higher SEP classes. This effect remained for the high vs low class after adjusting for covariates.

Conclusion: These findings are new in an Australian cohort. The impact of SEP trajectories on epigenetic age will be discussed. Individual level SEP measures are better suited to describe individual level outcomes and effects, such as epigenetic age. In the future, these individual level variables may be of further use in explaining the association between individual level childhood SEP, epigenetic changes, and mental and physical health outcomes.

Co-investigators
Dr Alexander O'Donnell Flinders University alexander.odonnell@flinders.edu.au Dr Phillip Melton University of Western Australia phillip.melton@uwa.edu.au Dr Richard Woodman Flinders Centre for Epidemiology and Biostatistics richard.woodman@flinders.edu.au Associate Professor Rae-Chi Huang UWA Centre for Child Health Research Rae-Chi.Huang@telethonkids.org.au Associate Professor Sarah Cohen-Woods Flinders University sarah.cohenwoods@flinders.edu.au

Speaker / Researcher

Dr Ashish Yadav PhD Candidate, The University of western Australia Medical School, Tel: +61-468734363, Email: ashish.yadav@research.uwa.edu.au Twitter: @AshishYadavMD

Researcher Bio

Ashish is a public health physician & clinical researcher. He did his residency training in Preventive Medicine from India and master's in public health from Johns Hopkins Bloomberg School of Public Health, Baltimore, USA. Ashish is in his final year of PhD from The University of Western Australia, Perth and has been working with the cardiometabolic group of The Raine Study under the supervision of Emeritus Prof Lawrie Beilin, Prof Trevor Mori & A/Prof Rae-Chi Huang.

Title

Fetal Growth Trajectories and their association with Adiposity & Inflammation in Young Adulthood

Abstract

Background

Obesity has become a major health problem, with approximately half of the adults worldwide either overweight or obese in 2016. Early life determinants of the cardio-metabolic risk and adiposity may have an important role in programming metabolic control mechanisms which may subsequently contribute to obesity and inflammation in the offspring. Previous studies have examined the association between birth weight and adiposity and found an inverse relationship. However, there is limited literature providing insight into the association of antenatal measures of fetal growth and subsequent adiposity.

Aim: This study aimed to investigate the relationship between intrauterine growth trajectories determined by serial ultrasound and markers of adiposity and inflammation in the adult offspring.

Methods

Ultrasound fetal biometric measurements including abdominal circumference (AC), femur length (FL) and head circumference (HC) from 1333 mother-fetal pairs (Gen1-Gen2) in the Raine Study were used to develop fetal growth trajectories using group-based trajectory modeling. Linear mixed modeling investigated the relationship between body mass index (BMI), waist circumference (WC) and high-sensitivity C-reactive protein (hsCRP) of Gen2 at 20 (n=485), 22 (n=421) and 27 (n=437) years and the fetal growth trajectory groups, adjusting for age, sex, adult lifestyle factors and maternal factors during pregnancy.

Results: Approximately 90% of participants had two Caucasian parents. Males and females had a similar BMI at all three ages. However, males were more likely to be overweight (BMI >25 and <30 kg/m2) and have a greater waist circumference, and more females were obese (BMI >30 kg/m2) at each age. Median hs-CRP values tended to be higher in females compared to males at each follow up. In relation to maternal (Gen1) characteristics, 7% reported preterm deliveries, 3.3% gestational diabetes, 26.4% Uncomplicated-HTN and 4.7% complicated-HTN. More than 16% of Gen1 mothers smoked and >56% consumed alcohol during pregnancy.

Seven AC, five FL and five HC growth trajectory groups were identified (Figure 2A, 2B and 2C). Compared to the average-stable (reference) group, a lower adult BMI was observed in falling AC trajectories: trajectory group-4 (β= -1.45 kg/m^2, 95%CI: -2.43 to -0.46, P=0.004) and trajectory group-6 (β= -1.01 kg/m^2, 95%CI: -1.96 to -0.54, P=0.038). Trajectory group-4 participants also showed a lower WC (β= -3.10cm, 95%CI= -5.48, -0.72, P=0.011), compared to the reference group. In addition, higher adult BMI (2.58 kg/m^2, 95%CI: 0.98 to 4.18, P=0.002) and hsCRP (34%, 95%CI: 10–62%, P=0.004) were observed in a rising FL trajectory group-2 compared to the reference group. A high-stable HC trajectory group-5 associated with 21% lower adult hsCRP (95%CI: 6–33%, P=0.009) when compared to the reference group.

Conclusion: Growth patterns established *in utero* may persist to adult life and influence adult anthropometry and inflammation, related to the risk of future cardiovascular disease.

This study highlights the long-term health legacy of growth during gestation and emphasizes the importance of understanding factors influencing the maternal pregnancy environment.

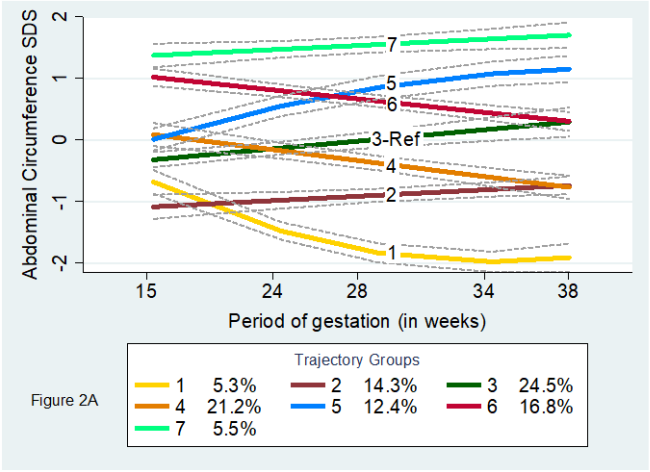


Figure 2A

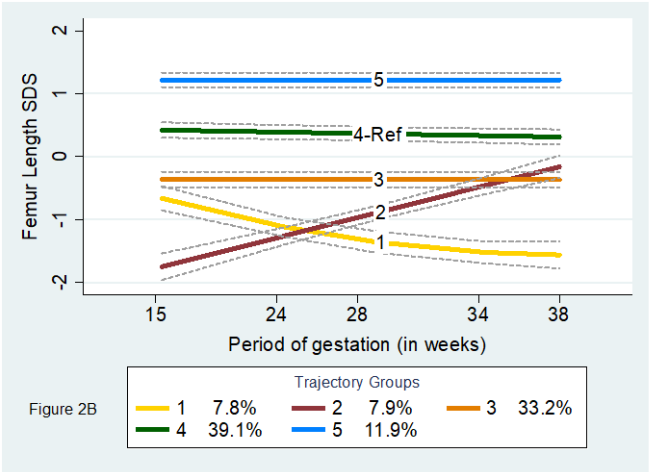


Figure 2B

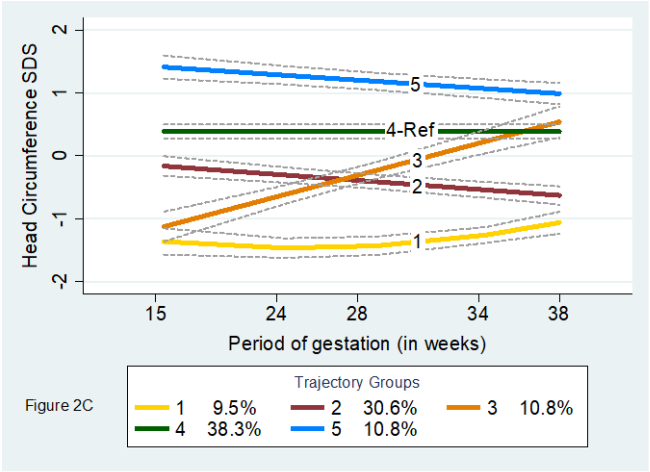


Figure 2C

Trajectories based on 1333 mother-fetal pairs; SDS – standard deviation scores, Dotted lines represent 95% confidence intervals, Percentages represent individual group membership

Co-investigators

Emeritus Prof Lawrie Beilin

Senior Honorary Research Fellow, Faculty of Health & Medical Sciences, Internal Medicine, University of Western Australia (UWA) Email: lawrie.beilin@uwa.edu.au

Prof Trevor Mori

Senior Principal Research Fellow, Faculty of Health and Medical Sciences, Internal Medicine, University of Western Australia (UWA) Email: trevor.mori@uwa.edu.au

A/Prof Rae-Chi Huang

Research Associate Professor, Faculty of Health and Medical Sciences, Centre for Child Health Research, University of Western Australia (UWA) Email: rae-chi.huang@uwa.edu.au

Mr. Philip Vlaskovsky

Research Associate, Faculty of Health and Medical Sciences, Internal Medicine, University of Western Australia (UWA) Email: philip.vlaskovsky@uwa.edu.au

Prof John Newnham

Professor, Faculty of Health and Medical Sciences, Obstetrics and Gynaecology, University of Western Australia (UWA) Email: john.newnham@uwa.edu.au

Dr Scott White

Associate Professor, Faculty of Health and Medical Sciences, Surgery, University of Western Australia (UWA) Email: scott.white@uwa.edu.au

Speaker / Researcher

Miss Carrie-Anne Ng, PhD Candidate; Institution: Department of Medicine, School of Clinical Sciences at Monash Health, Monash University; Tel: (+65) 83861003; Email: carrie.ng@monash.edu

Researcher Bio

Carrie-Anne is a 3rd year PhD candidate in the School of Clinical Sciences at Monash Health (Monash University). Her doctoral research investigates the effects of impact osteogenic exercise on skeletal health over the lifespan, with an added focus on reducing falls and fracture risk later in life. She is also interested in the utilisation of tools used to assess the mechanical loading of everyday physical activity and their association with bone health.

Title

Physical Activity and Healthy Bones in Young Adults

Abstract

Background: Physical activity is important for bone health, but the most important aspect may be the ground impacts that occur during running and jumping. Unfortunately, physical activity questionnaires used in research usually only estimate the amount of energy required to carry out the physical activities reported ("energy expenditure"). We do not know how much energy expenditure, nor how much ground impacts of these reported physical activities relate to bone health. Additionally, little is known about the effects of physical activity in young adults (around 20 years old) whose bones have fully matured.

Aims: This study investigated a new way of measuring ground impacts while using a traditional physical activity questionnaire. We explored how estimates of physical activity of higher and faster impact, measured at ages 17 and 20 years, from this questionnaire compared with the standard energy expenditure estimates. We also compared the newly developed physical activity impact score relative to the energy expenditure score to evaluate how they relate to bone health at age 20 years.

Results: 826 young adults from the Raine Study Gen2 self-reported their usual physical activity over the past week using a physical activity questionnaire at ages 17 and 20 years. From this questionnaire, we calculated energy expenditure scores following the standard procedures. We also created new impact scores based on our understanding of the general range of high and fast ground impacts achieved during different types of physical activities. A whole-body dual-energy x-ray absorptiometry (DXA) scan at age 20 years measured bone health status. We looked at whether there was agreement between the energy expenditure scores and impact scores. Despite being calculated from the same questionnaire, we found these two scores were very different. Next, we examined the relationship of the energy expenditure scores and impact scores with bone health measurements from the DXA scan. This investigation controlled for differences we might see with sex, body size, smoking status, alcohol consumption, calcium from diets and vitamin D status. We found that higher impact scores, but not energy expenditure scores, at ages 17 and 20 years were related to better bone health at age 20 years.

Conclusion: This study showed that impact scores and energy expenditure scores measure very different aspects of physical activity, suggesting that measurement of energy expenditure only cannot be relied upon to provide insight into the ground impacts obtained from physical activity. Our new way of measuring ground impacts from a traditional physical activity questionnaire was also related to better bone health measures, confirming that the ground impacts, rather than the intensity, of physical activity are the main contributor to building stronger bones. Given many studies in young and older people have previously measured physical activity using traditional questionnaires, there may be opportunities to further our understanding of the relationships between physical activity and bone health across different age groups by calculating impact score measurements from existing datasets in Australia and overseas.

Co-investigators

Dr David Scott
- Associate Professor; Research Fellow
- Institute for Physical Activity and Nutrition, School of Exercise and Nutrition Sciences, Deakin University
- d.scott@deakin.edu.au

Dr Marc Sim
- Adjunct Research Fellow
- Institute for Nutrition Research, Edith Cowan University
- marc.sim@ecu.edu.au

Dr Kun Zhu
- Adjunct Associate Professor
- Department of Endocrinology and Diabetes, Sir Charles Gairdner Hospital
- Discipline of Internal Medicine, Medical School, The University of Western Australia
- kun.zhu@uwa.edu.au

Dr Aris Siafarikas
- Clinical Professor
- Department of Endocrinology and Diabetes, Perth Children's Hospital
- aris.siafarikas@health.wa.gov.au

Dr Nicolas H Hart
- Senior Research Fellow
- Caring Futures Institute, College of Nursing and Health Science, Flinders University.
- School of Medical and Health Sciences, Edith Cowan University.
- Institute for Health Research, The University of Notre Dame Australia
- n.hart@ecu.edu.au

Ms Jocelyn Tan
- PhD Candidate
- School of Health Sciences, the University of Notre Dame Australia
- jocelyn.tan@my.nd.edu.au

Dr Paola Chivers
- Adjunct Senior Research Fellow
- Institute for Health Research, The University of Notre Dame Australia
- School of Medical and Health Sciences, Edith Cowan University
- paola.chivers@nd.edu.au

Keynote Speaker

Prof Fiona Wood
Director, Burns Service of Western Australia (BSWA)
Consultant Plastic Surgeon, Fiona Stanley Hospital and Perth Children's Hospital
Co-founder of the first skin cell laboratory in WA
Winthrop Professor, School of Surgery, The University of Western Australia
Co-founder of the Fiona Wood Foundation (formerly The McComb Foundation)

Winthrop Professor Fiona Wood University of Western Australia is a Plastic & Reconstructive Surgeon specialising in the field of burn care, trauma and scar reconstruction.

As Director of the WA Burns Service of Western Australia since 1991 she is consultant surgeon at both the South Metropolitan Heath Service, Fiona Stanley Hospital and the Child and Adolescent Health Service, Perth Children's Hospital.

As director of burns research, she leads an interdisciplinary team with broad collaboration focused on translation to improve clinical outcomes.

The story of n=1

A young patient who survived an 80% total body surface area burn injury died due to a hepatocellular carcinoma 4 years later. It could be rationalised as a coincidence or simply bad luck. The question to was, did the burn injury or therapeutic interventions contribute to this outcome? Data linkage gives us the opportunity to explore such questions and to drive the development of hypothesis. The data linkage program and the subsequent exploration of mechanism will be presented in the context of the linkage and the role of cohort studies.

The Raine Study Annual Scientific Meeting 2021

Session 3 Early-Career Researcher Presentations

Chairs

Prof Martha Hickey

Prof Martha Hickey is Professor of Obstetrics and Gynaecology at the University of Melbourne and Adjunct Professor of Obstetrics, Gynaecology and Reproductive Sciences at Yale University, CT. Martha is the Chair of Obstetrics & Gynaecology at the Royal Women's Hospital/Mercy. She is in active clinical practice with a research expertise in menstrual disorders and menopause. Martha is also a co-leader of the Raine Study Hormonal and Reproduction Special Interest Group.

Prof Donna Geddes

Prof Donna Geddes is a Professor in the School of Molecular Sciences at the University of Western Australia. Donna is the director of the Geddes Hartmann Human Lactation Research Group. Donna originates from a medical imaging background with an emphasis in ultrasound imaging. She has integrated this modality into many of the group’s studies providing a ‘window’ to different physiological processes during lactation. Her findings have attracted much international attention and she is often requested to speak at both International and National Scientific Meetings. She is a member of the Nutrition Society of Australia and Secretary for the International Society for Research in Human Milk and Lactation.

Speaker / Researcher

Dr. Anupama Bharadwaj, Research Fellow, Centre for Transformative Work Design, Future of Work Institute, Curtin University, +61414783460, anu.bharadwaj@curtin.edu.au

Researcher Bio

Anu Bharadwaj is a Research Fellow at the Centre for Transformative Work Design at Curtin University. Her current work focuses on developing work design interventions to prevent psychological injury for employees in the care sector. Anu graduated with a PhD and Master of Industrial and Organisational Psychology from UWA in July 2021; while completing her studies, Anu was involved in conducting the Raine Study's Personality, Work & Wellbeing surveys.

Title

Flexible work fosters a flexible future work-self: the interplay of job autonomy and self-efficacy in the development of future work-self flexibility.

Abstract

Background: An individual's future work self is a psychological representation of themselves in the future that reflects their hopes and aspirations in relation to work (Strauss et al., 2012). One's future work self is an important motivator for proactive behaviour that aims to help one achieve a fulfilling career (e.g., networking, seeking career advice). However, maintaining a flexible outlook on one's future work self (i.e., future work self-flexibility) is also likely to have significant benefits for coping with uncertainty about one's career trajectory. Individuals with flexible future work selves have a fluid view of the type of career or jobs they end up in, and are less likely to be self-critical if the end up on a career path that they had not clearly imagined. With the constantly evolving nature of work and the COVID-19 pandemic significantly disrupting individuals' work lives and opportunities to proactively meet career goals (Akkermans et al., 2020), being flexible about one's future work aspirations has never been more critical.

Little is known about the determinants of future work-self flexibility but research suggests that flexible work-related mindsets are influenced by prior work experiences (e.g., work design) and personality (e.g., self-efficacy) (Ibarra,1999). Here, we investigate how a key aspect of good work design, job autonomy, interacts with self-efficacy in navigating new experiences to foster future work self-flexibility.

Work design refers to the content and organisation of the tasks, activities, relationships and responsibilities within one's job or role (Parker, 2014). In particular, work design characterised by high levels of job autonomy has been shown to promote flexible thinking (Parker et al., 2021). Job autonomy is one of the classic and most important characteristics of good work design, and is the extent to which one has the discretion to decide how, when, and where they perform their work tasks. Evidence to date suggests that autonomy fosters exploration behaviours, learning, idea generation, and the use of problem-solving strategies, because autonomy stimulates one's desire to learn or engage in learning-oriented behaviours. Therefore, experiencing higher job autonomy early in one's career may foster a long-term willingness to learn and adapt to new situations (e.g., working a job that one had not previously considered or thought to be useful for meeting career goals). This sense of willingness to learn and adapt in the future may further be strengthened in individuals who perceive they are capable of completing tasks and navigating new situations well (i.e., have high self-efficacy).

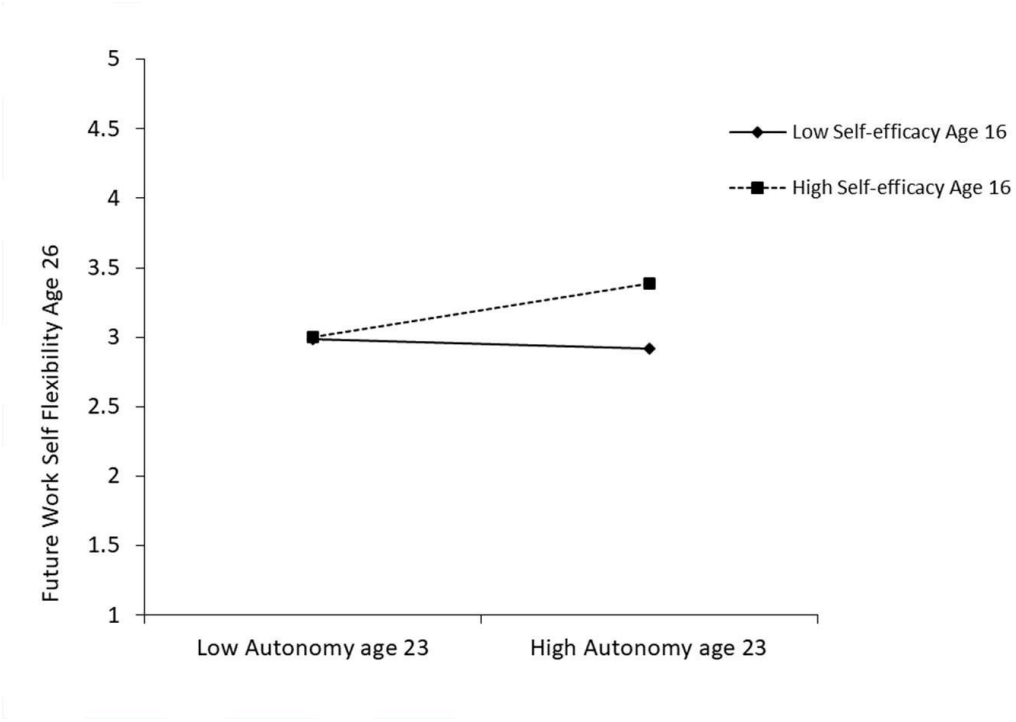
Aim(s): The aim of this study was to examine how one's work job autonomy in early adulthood and self-efficacy for navigating new experiences interact to influence future work self-flexibility. The Raine Study data presents a unique opportunity to examine these important, yet little understood, relationships.

We analysed data across three Raine Study follow-ups (total N=275): Gen2-17 (self-efficacy), Gen2-22 (job autonomy), and Gen2 25-27 Personality, Work & Wellbeing Sub-study (future work-self flexibility). Scores for self-efficacy and work adjustability were mean-centred and a moderated regression analysis was conducted using IBM SPSS Statistics 27.

Results: The interaction between job autonomy and self-efficacy for predicting future work-self flexibility was significant F (2, 272) = 4.71, p=.003, R2 =.02. Specifically, individuals with higher job autonomy were more likely to have a flexible outlook towards their future work self and this effect was stronger for participants with higher self-efficacy (see Figure 1).

Conclusion: This study suggests that high self-efficacy and job autonomy in young adulthood are important facilitators of future work self-flexibility. That is, feeling confident in navigating new situations in adolescence and being able to make decisions about one's work in young adulthood likely helps individuals maintain flexibility about their future jobs. Young adults should be encouraged to maintain an open mind towards new experiences, especially as pre-imagined career pathways may not be viable either due to the changing nature of work or the COVID-19 pandemic.

Figure 1. Moderating Effect of Self-efficacy on the Relationship Between Job Autonomy and Future Work Self Flexibility



Co-investigators

John Curtin Distinguished Professor Sharon Parker, Centre for Transformative Work Design, Future of Work Institute, Curtin University, s.parker@curtin.edu.au

Associate Professor Patrick Dunlop, Future of Work Institute, Curtin University, patrick.dunlop@curtin.edu.au

Speaker / Researcher

Name: Dr Katie Dyer, Research Associate; Lions Eye Institute; Tel: 0418 108 342

Email: kathleendyer@lei.org.au

Researcher Bio

Katie completed a Doctor of Medicine at the University of Western Australia last year and is currently working as a medical intern at Fiona Stanley Hospital. She has also previously achieved a Bachelor of Philosophy (Honours) with majors in Mathematics and Physics. Katie has been undertaking research within the genetics and epidemiology research group at the Lions Eye Institute for the past four years, with a particular focus on early life programming of eye development.

Title

The relationship between fetal growth and retinal nerve fibre layer thickness in a cohort of young adults

Abstract

Background: Retinal nerve fibre layer (RNFL) thinning is associated with a number of optic and retinal neuropathies. In particular, it is one of the earliest diagnostic markers of glaucoma, a disease that is often asymptomatic in its early-to-moderate stages, meaning that significant damage to the optic disc may occur prior to its diagnosis. Identifying individuals at risk of changes in optic disc morphology such as RNFL thinning would aid in early diagnosis of conditions such as glaucoma and timely intervention to slow progression to severe disease.

The optic nerve develops during fetal life and during early childhood. Several recent studies have demonstrated that deviations in birth parameters such as low birth weight and small head circumference, that may reflect adverse early life conditions and fetal growth restriction, are associated with changes in optic disc morphology including decreased RNFL thickness, with these relationships persisting into adulthood. However, these studies have largely relied on cross-sectional birth parameter measures as surrogates of fetal growth and wellbeing, with no existing research having analysed for associations with fetal growth as characterised by trajectories based on longitudinal measurements performed during gestation.

Aim: The aim of our study was to explore relationships between patterns of fetal anthropometric growth, as reflective of early life influences on fetal wellbeing, and global RNFL thickness measured in young adulthood.

Methods: A subset of singleton Caucasian Gen2 participants (n = 481) from the Raine Study were included in the analysis. Participant mothers underwent serial ultrasound scans at 18, 24, 28, 34 and 38 weeks' gestation, with Gen2 fetal biometry measured at each scan. An eye examination including measurement of RNFL thickness via spectral-domain optical coherence tomography imaging was undertaken at the Gen2-20 year follow-up. Growth trajectories based on measurements of fetal head circumference (FHC), abdominal circumference (FAC), femur length (FFL) and estimated fetal weight (EFW) were constructed via group-based trajectory modelling. Generalised estimating equations were used to evaluate differences between groups of participants with similar growth trajectories with respect to global RNFL thickness.

Results: The median RNFL thickness across the study population was 101µm (interquartile range [IQR] = 94 to 107) in the right eye and 101µm (IQR = 95 to 107) in the left eye. Participants with consistently large FHCs throughout gestation had significantly thicker RNFLs than those with consistently small, consistently moderate or accelerated FHC growth (p = 0.023). This association remained significant even after adjusting for the potential confounders of fetal sex, maternal smoking during pregnancy, gestational age at birth, intraocular pressure, and axial length (p = 0.037). Based on model fit statistics, FHC growth trajectory was a better predictor of RNFL thickness than birth weight or head circumference at birth. There were no significant differences in RNFL thickness between trajectory groups in the FAC, FFL or EFW models, although similar trends to those in the FHC model were demonstrated.

Conclusions: FHC growth is associated with RNFL thickness in young adulthood and is moreover a better predictor than either birth weight or head circumference at birth. These findings support the hypothesis that long-term optic nerve health is influenced by factors that concurrently affect fetal growth, including environmental conditions or underlying genetics. There may be implications for the long-term risk of conditions linked to RNFL thinning, such as glaucoma, which the Raine Study provides a unique opportunity to explore as the Gen2 participants continue to be followed through adult life.

Co-investigators

Name: Dr Paul Sanfilippo
Position/Institution: Research Fellow, Centre for Eye Research Australia
Email: prseye@gmail.com
Name: Dr Seyhan Yazar
Position/Institution: Senior Research Officer, Garvan Institute of Medical Research
Email: seyhanyazar@lei.org.au
Name: Professor Jamie Craig
Position/Institution: Chair of Department of Ophthalmology, Flinders University
Email: jamie.craig@flinders.edu.au
Name: Professor Alex Hewitt
Position/Institution: Professor of Ophthalmology, Menzies Institute for Medical Research
Email: alex.hewitt@utas.edu.au
Name: Professor John Newnham
Position/Institution: Professor of Obstetrics, University of Western Australia
Email: john.newnham@uwa.edu.au
Name: Professor David Mackey
Position/Institution: Professor of Ophthalmology, Lions Eye Institute
Email: davidmackey@lei.org.au
Name: Dr Samantha Lee
Position/Institution: Postdoctoral Research Fellow, Lions Eye Institute
Email: samanthalee@lei.org.au

Speaker / Researcher

Dr Syed Zulqarnain Gilani, Research Fellow, Centre for Artificial Intelligence and Machine Learning, School of Science Edith Cowan University Tel: (08) 6304 3946, s.gilani@ecu.edu.au

Researcher Bio

Dr Gilani received his PhD in Computer Science from the University of Western Australia. His research interests include 3D face analysis, medical imaging, machine learning, statistical modelling, and vision and language. He is currently a Research Fellow at the Edith Cowan University and also holds the position of "Editor" of the Australian Pattern Recognition Society.

Title

3D craniofacial analysis: applications in health.

Abstract

Introduction: The human face is an important biometric which conveys a wealth of information about biologicalsex, age, and ethnic background. The developmental disorders which affect the human brain also affectthe facial morphology, and therefore, facial morphometrics can be used to investigate the cause, origin orpresence of the disorder. Our research focuses on performing morphometric analysis of 3D faces using computer vision tools to achieve the latter goals and makes significant contributions to interdisciplinary scientific research. We present a set of two studies using 3D craniofacial analysis on Raine Study data.

STUDY-1

Background: Aside from questionnaires, which are subjective and inaccurate, there exists no capacity to rapidly identify the presence or severity of obstructive sleep apnoea (OSA). The current gold standard test is overnight polysomnography (PSG), which is expensive and time consuming.

Aim: The aim of this study was to see if 3D craniofacial data could predict OSA severity.

Methods: Fifty participants from the Raine Study Gen1-26 year follow-up and 350 patients from Sir Charles Gardiner Hospital underwent diagnostic PSG and facial photography. OSA severity (apnoea hypopnoea index; AHI) was determined from PSG. A classification algorithm was employed to distinguish between OSA (AHI≥5 events/hr, n=300) and non-OSA (AHI<5 events/hr, n=100) groups. Twenty-Four landmarks were annotated on the 3D faces of the subjects to extract 26 3D linear and geodesic distances. These distances were subjected to non-linear classification technique using Support Vector Machines (SVM).

Results: A combination of linear and geodesic distances was able to separate the OSA from non-OSA group withan accuracy of 90% with 0.92 Area Under the Curve. Using Turkey-Kramer method with Bonferroni correction, geodesic upper face depth, lower face depth and total face height were able to separate thegroups of non-OSA, mild, moderate and severe OSA ($p<<0.0001$).

Conclusion: 3D facial measurements, unique to 3D photography, predict OSA severity better than two dimensional photographs. Geodesic measurements may be more representative of the underlying skeletal and soft tissue facial structures that contribute to the pathogenesis of OSA than Euclidean facial measurements.

STUDY-2

Background: Atypical facial morphology, particularly increased facial asymmetry, has been identified in some individuals with Autism Spectrum Conditions (ASC). Many cognitive, behavioural, and biological features associated with ASC also occur on a continuum in the general population. Recent studies have shown that children on the Autism Spectrum as well as biological parents of autistic individuals show greater facial asymmetry as compared to typically developing children or the general adult population.

Aim: The aimof this study was to examine subthreshold levels of autistic traits and facial morphology in non-autistic individuals.

Methods: Facial asymmetry was measured using three-dimensional facial photogrammetry, and the Autism-spectrum Quotient (AQ) was used to measure autistic-like traits in a community-ascertained sample of young adults (n = 289) who were part of the Raine Study Gen 2. The participants had completed theAQ at the 20-year follow-up (mean age = 19.95 years; SD = 0.42 years) and had their facial photographs taken at the 22-year follow-up (mean age = 22.06 years; SD = 0.52 years).

Results: After accounting for covariates, there were no significant associations observed between autistic-like traits and facial asymmetry.

Conclusion: The results suggest that any potential facial morphology differences linked to ASC may be limited to the clinical condition.

Co-investigators

Peter Eastwood
Nigel McArdle
David Hillman
Jennifer Walsh
Kathleen Maddison
Mithran Goonewardene
Ajmal Mian
Maryam Boutrus
Murray T. Maybery
Gail A. Alvares
Diana Weiting Tan
Andrew J. O. Whitehouse

Speaker / Researcher

Dr Jeffrey Junhua Lee, Intern at Fiona Stanley Hospital; Tel: 0416806168

Email: Jeffrey.lee@health.wa.gov.au

Researcher Bio

Jeffrey Lee is an intern at Fiona Stanley Hospital and a University of Western Australia and University of Sydney graduate. He began his research career as part of his Master of Public Health (Specialising in Research Methods) degree and has interests in Gastroenterology and Hepatology. His current research focuses on using the data collected in the Raine Study to gain greater understanding about the developmental origins of nonalcoholic fatty liver disease.

Title

The relationship between foetal head circumference growth trajectories and nonalcoholic fatty liver disease in adolescents

Abstract

Background: Intrauterine and childhood factors are associated with nonalcoholic fatty liver disease (NAFLD) in adolescents and adults. Previous studies have associated intrauterine growth restriction (IUGR), small for gestational age (SGA) and intrauterine exposures such as smoking in pregnancy, and excessive gestational weight gain, with NAFLD in offspring. Various maternal factors and intrauterine influences determine foetal growth patterns and birth weight. As a result, serially measured foetal head circumference (HC) provides a useful measure of foetal growth patterns and IUGR.

Aim: We aim to examine associations between foetal HC growth trajectories and subsequent NAFLD during adolescence.

Methods: Repeated antenatal ultrasound with foetal morphometry was measured in 1440 pregnant women (Gen1) in the Raine Study, between 16 weeks gestation and delivery. Using standard deviation scores or z-scores for the HC measurements, five foetal head circumference trajectories were developed. Offspring (Gen2) birth weight was recorded and IUGR, SGA and large for gestational age (LGA) were determined for the live-born neonates. The duration of breastfeeding was recorded. As part of the 17-year follow up of the Gen2 cohort, health and lifestyle questionnaires, anthropometry, fasting blood tests and liver ultrasound, were performed. A subset of 576 adolescents had both liver ultrasound and foetal ultrasound HC trajectories data.

Results: NAFLD was diagnosed in 92 of 576 (16%) adolescents (52% male). Adolescents with NAFLD had higher body mass index (BMI), waist circumference, supra-iliac skinfold thickness, serum alanine aminotransferase (ALT), gamma glutamyl transpeptidase, triglycerides, total and low density lipoprotein cholesterol, leptin, C-reactive protein and Homeostasis Model Assessment for Insulin Resistance (HOMA-IR), but lower high density lipoprotein cholesterol and adiponectin levels compared with those without NAFLD ($p<0.05$ for all). Birth weight, gestational age, IUGR, SGA and LGA were not associated with NAFLD. Using multivariable logistic regression analysis, low-stable HC trajectory group 1 (OR, 3.54; 95% CI, 1.21-10.35, $p=0.02$), suprailiac skinfold thickness (OR 1.09, 95% CI 1.05-1.13, $p<0.001$), serum ALT (OR 1.03, 95% CI 1.01-1.06, $p=0.02$) and serum leptin (OR 1.03, 95% 1.02-1.05, $p=0.001$) were associated with NAFLD.

Conclusion: The HC trajectory associated with a persisting small HC, but not birth characteristics, was associated with increased risk of subsequent NAFLD in adolescents. The association of a low foetal HC trajectory with NAFLD in adolescence supports the Developmental Origins of Health and Disease (DOHaD) hypothesis linking early life events with subsequent disease.

Co-investigators

1. Dr Ashish Yadav – Public health physician and epidemiologist at the University of Western Australia: ashish.yadav@research.uwa.edu.au
2. Professor Trevor Mori – Senior Principal Research Fellow at the University of Western Australia Medical School: trevor.mori@uwa.edu.au
3. Associate Professor Rae-Chi Huang – Paediatric physician and clinical researcher at the Telethon Kids Institute and the University of Western Australia: rae-chi.huang@uwa.edu.au
4. Associate Professor Leon A Adams – Consultant Hepatologist and Gastroenterologist at Sir Charles Gairdner Hospital: leon.adams@uwa.edu.au
5. Emeritus Professor Lawrence J Beilin – Senior Honorary Research Fellow at the University of Western Australia Medical School: Lawrie.beilin@uwa.edu.au
6. Dr Elizabeth McKinnon – Biostatistician at Murdoch University Institute for Immunology and Infectious Diseases and Telethon Kids Institute: bethy.mckinnon@telethonkids.org.au
7. Professor John Olynyk – Consultant Hepatologist and Gastroenterologist at Fiona Stanley Hospital: john.olynyk@health.wa.gov.au
8. Professor Craig Pennell – Chair of Obstetrics and Gynaecology at the University of Newcastle School of Medicine and Public Health: craig.pennell@newcastle.edu.au
9. Clinical Senior Lecturer Dr Oyekoya T Ayonrinde – Consultant Hepatologist and Gastroenterologist at Fiona Stanley Hospital: oyekoya.ayonrinde@uwa.edu.au

Speaker / Researcher

Dr. Eleanor Carey, Royal College of Surgeons in Ireland, +353879773682, eleanorcarey1@rcsi.ie.

Researcher Bio

Dr. Eleanor Carey completed her PhD in the Department of Psychiatry in the Royal College of Surgeons in Ireland and currently works for Jigsaw, the National Centre for Youth Mental Health in Ireland.

Title

Evidence that Infant and Early Childhood Developmental Impairments are associated with Hallucinatory Experiences: Results from a Large, Population-Based Cohort Study

Abstract

Background: Psychotic experiences (PE), the subclinical expressions of psychotic symptoms, occur in the absence of a psychotic disorder and mainly concern auditory (both verbal and non-verbal) and, less commonly, visual hallucinatory experiences (HE) (Kelleher, Harley, Murtagh, & Cannon, 2011). Psychotic experiences are most prevalent during late childhood, with 17% of 9-12 year olds within the general population reporting these phenomena (Kelleher, Connor, et al., 2012), and a further 12% of children and adolescents reporting auditory hallucinations specifically (Maijer, Begemann, Palmen, Leucht, & Sommer, 2018). Cognitive and motor dysfunction are hallmark features of the psychosis continuum, and have been detected during late childhood and adolescence in youth who report PE. However, previous investigations have not explored infancy and early childhood development. It remains unclear whether such deficits emerge much earlier in life, and whether they are associated with psychotic, specifically hallucinatory, experiences (HE).

Aims: The present study had the following aims: 1. To determine if early childhood development in separate or multiple domains of development in the first three years of life is associated with HE in childhood and adolescence. 2. To compare these associations with those of early childhood development and anxiety/depression in childhood and adolescence. 3. To investigate whether the presence of early childhood developmental delays is associated with the recurrence of HE in adolescence, which is a marker for poorer outcomes. In order to address these aims, this study included data from Gen1 and Gen2 participants of the Raine Study (n=1,101). Five areas of childhood development comprising: communication; fine motor; gross motor; adaptive (problem-solving); and personal-social skills, were assessed serially at ages 1, 2 and 3 years. Information on HE, depression and anxiety at ages 10, 14 and 17 years was obtained. HE were further subdivided into those with transient or recurrent experiences. Random effects logistic regression models and cumulative risk analyses based on multiple developmental domain delays were performed.

Results: Early poorer development in multiple areas was noted from ages 1, 2 and 3 years among youth who reported HE. Early developmental delays significantly increased the risk for later HE. This association was particularly marked in the recurrent HE group, with over 40% having early developmental delays in multiple domains, and an almost 8-fold increased risk (OR: 7.68, CI: 2.73-21.58, $p < .001$). There was no significant association between early childhood development and later anxiety/depression apart from lower gross motor scores at age 3.

Conclusion: The findings suggest that early pan-developmental deficits are associated with later HE, with the effect strongest for young people who report recurrent HE throughout childhood and adolescence.

Co-investigators
Dr. Colm Healy Ph.D, Dept. of Psychiatry, Royal College of Surgeons in Ireland, Dublin, Ireland. colmhealy@rcsi.ie
Dr. Yael Perry Ph.D, Telethon Kids Institute, The University of Western Australia, Perth, WA, Australia. yael.perry@telethonkids.org.au
Dr. Diane Gillan D.Clin.Psy, Dept. of Psychology, Beaumont Hospital, Dublin, Ireland. dianegillan@beaumont.ie
Dr. Andrew J.O. Whitehouse Ph.D, Telethon Kids Institute, The University of Western Australia, Perth, WA, Australia. andrew.whitehouse@telethonkids.org.au
Prof. Mary Cannon M.D., Ph.D, Dept. of Psychiatry, Royal College of Surgeons in Ireland, Dublin, Ireland and Dept. of Psychiatry, Beaumont Hospital, Dublin, Ireland. marycannon@rcsi.ie

Flinders University – Institutional Partner of the Raine Study

A/Prof Sarah Cohen-Woods

A/Prof Sarah Cohen-Woods is the Head of the Behavioural Genetic and Environmental Mechanisms (Behavioural GEMs) Lab at Flinders University. Sarah's research focuses on incorporating environmental factors, such as life-stress, with genetic variation in depression, psychosis (bipolar disorder and schizophrenia), and cognition. Sarah is the Raine Study's representative at Flinders University.

Presentation of the Raine Medical Research Foundation prizes

Dr Amanda Cleaver

Executive Director, Raine Medical Research Foundation

Dr Amanda Cleaver has a background in cancer biology and a 20-year career in research and research management. As the Executive Director of the Raine Medical Research Foundation, Amanda is responsible for the foundation's operational and partnership management, as well as overseeing its strategic priorities. She has recently been awarded the 2021 Aspire Award.

The Raine Medical Research Foundation is an outstanding example of what can be achieved when a generous act of philanthropy is directed toward improving the lives of others. This was Mary Raine's wish when in 1957 she made the decision to leave her wealth to The University of Western Australia for the establishment of a medical research foundation.

Mary Raine's story is inspirational. Her humble beginnings were an unlikely launching pad for the success and wealth she came to achieve in her lifetime. Through hard work and the application of business acumen rarely seen in a woman in the early years of the 20th century, Mary Raine went on to build a large real estate empire.

She was a visionary and saw the establishment of the Raine Foundation as a unique opportunity for her life's work to live on in perpetuity – to grow and develop into something more important and more valuable than the business success and wealth that she had personally achieved. She did this by giving scientists and clinicians the means and opportunity to embark on medical research and to seek answers to questions that were not known in her lifetime.

The Raine Medical Research Foundation has a sixty-year history of supporting health and medical research in WA through competitive grants, fellowships and awards programs.

The Raine Medical Research Foundation has generously donated two $750 prizes for the Best ECR Presentation and Best Student Presentation at the Raine Study 2021 Annual Scientific Meeting.

The Raine Study Annual Scientific Meeting 2021

Our UJV partners