ANATOMICAL SOCIETY

SUMMER MEETING

14th–16th July 2025

St John's College, University of Oxford
Oxford, OX1 3JP

Human Cerebral Cortex Development III

Dear Colleagues,

We were thrilled to be appointed the organizers and co-chairs of Summer Meeting 14-16th July 2025 at St John's College, Oxford by the Council of the Anatomical Society. We have planned a symposium "Human Cerebral Cortex Development". The symposium will be main focus of the meeting, allocated almost two complete days, alongside the usual sessions on imaging and education. We are delighted that we can have a conference at this level on human cortical development.

The symposium will explore various aspects of human cortical development, including cellular and molecular mechanisms regulating cell number and diversity, migration and circuit assembly from the beginning of cortical plate formation until birth. We have selected speakers to invite from around the world who will describe how advances in developmental neurobiology, organoids, transcriptomics and imaging are offering new insights into the mechanisms controlling the development of the human cerebral cortex, as well as the developmental abnormalities and clinical advances.

This symposium is a follow up to two highly successful meetings in 2010 and in 2018 together with the acclaimed issues of the Journal of Anatomy http://onlinelibrary.wiley.com/doi/10.1111/joa.2010.217.issue-4/issuetoc and https://onlinelibrary.wiley.com/toc/14697580/2019/235/3. We hope you will consider contributing an article; original research or review or opinion piece, long or short, to a new 2025 symposium issue. Please see this as an opportunity to promote younger members of your laboratory or to collaborate with other participants at the symposium in order to present a fresh view.

With very best wishes,

Zoltán Molnár MD DPhil
University of Oxford, UK

and Gavin Clowry DPhil
Newcastle University, UK

Please do share your thoughts across social media.

X: @anat_soc BlueSky: @anatsoc.bsky.social hashtag: #AnatSocSummer25 #AnatSocOxford

Thanks to the Team

Lyndsay Murray- Meetings Officer
Hannah Webb- Anatomical Society Meetings Administrator
anatomicalsocietymeetings@gmail.com

The Auditorium, Garden Quadrangle, St John's College, St Giles, Oxford OX1 3JP, UK

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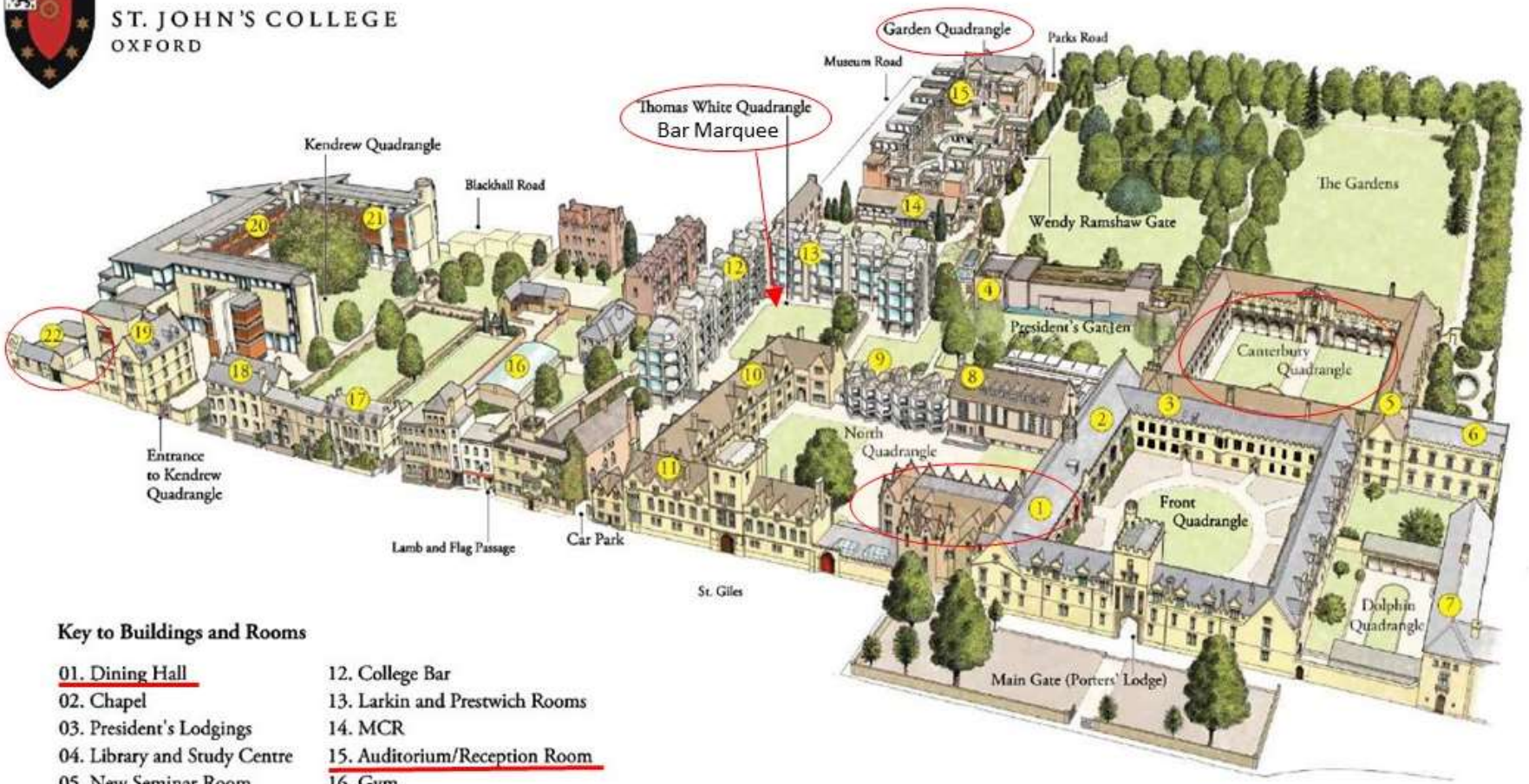

Key to Buildings and Rooms

01. Dining Hall
02. Chapel
03. President's Lodgings
04. Library and Study Centre
05. New Seminar Room
06. Holmes Building
07. Dolphin Lecture Room
08. SCR
09. Beehive
10. Bursary
11. North Lecture Room
12. College Bar
13. Larkin and Prestwich Rooms
14. MCR
15. Auditorium/Reception Room
16. Gym
17. St Giles House
18. Alumni Office and Guest Rooms
19. 21 St Giles
20. Kendrew Café/Gym/Events Room
21. Law Library
22. The Barn/Artist's Studio

Early career pre conference workshop

Date and Time: 14th July, 10 am to 12 pm. *Venue: Medical Science Teaching Centre (13 mins walk from St John's College)*

In recent years, The Department of Physiology, Anatomy and Genetics (DPAG) and the Medical Science Division (MSD) of Oxford University have embraced innovative teaching methods along with conventional teaching and learning for pre-clinical and biomedical students. At the pre-conference event, attendees will witness this remarkable transformation, discovering how the department uses creativity and innovation to inspire and educate our students. If you are eager to explore our facility and resources, please register, as spaces are limited. To know more about our recent work visit here.

Journal of Anatomy Early Career Research Workshop

Date and Time: 14th July 12pm-1pm. *Venue: The Auditorium, The Garden Quadrangle*

This is an interactive workshop chaired by the Journal of Anatomy Editors and Early Career Researcher Editorial Board. The goal of the session is to inform authors of the requirements for publication, reviewing and editing and avoid common pitfalls that are frequently a barrier to acceptance in a journal. The workshop aims to demystify the editorial and reviewing processes. Note: if you wish to attend the workshop please ensure that you join the earlier lunch sitting for this day.

Oral Presentation

Please bring your PowerPoint presentation in a form that we can easily upload to the AV computer, and find our helpers to hand over your slides for your presentation before your session begins. Presentations will be in the Auditorium of the Garden Quadrangle.

Poster Presentations

- Poster session 1: Monday 14th July 6-7pm in the Bar marquee, Thomas White Quadrangle
- Poster session 2: Tuesday 15th July 12:30-1:30pm in the Bar marquee, Thomas White Quadrangle

Presenters in Poster session 1 will be allowed to display their poster between midday on Monday 14th and midday on Tuesday. Those assigned Poster session 2 can display their poster between midday on Tuesday 15th until the end of the meeting.

Anatomical Society Cave Young Investigator best poster prize

Awarded for the best poster presentation by an attendee, normally of relatively junior status at the AS summer meeting. The work presented shall have been carried out while the first author was an undergraduate or postgraduate student and presented within 1 year of the award of the Doctorate. Young Investigators will be judged during the poster sessions.

Sophie Miller Prize Presentation

Date and Time: Tuesday 15th July 2:25pm

Orla Mitchell- Early life adversity and brain structure: A longitudinal structure human MRI study.

Dr Sophie Miller was an Anatomical Society funded PhD student from 2011-2014 at the University of Cambridge. She investigated olfactory ensheathing cells (OECs) and their potential for transplant-mediated repair of the central nervous system. During this time, she presented at many Anatomical Society meetings, with one of the publications from her PhD work appearing in the September 2016 issue of the Journal of Anatomy. Sophie was particularly supportive to her other early career researchers and colleagues in scientific and career development. She passed away in December 2016. In her memory, her family have generously provided support for young and aspiring anatomical researchers through the Anatomical Society.

Tea and coffee breaks

Refreshments will be held in the bar marquee in the Thomas White Quadrangle.

WiFi

The Cloud Wifi is free to use across St John's college.

Buffet Lunch

The buffet lunch will be held on Monday and Tuesday 12-2pm in The Hall at St John's College and will be in two sittings. If you are registered to attend the Journal of Anatomy workshop please attend the first sitting on Monday.

Drinks receptions

Date and Time: Monday 6pm *Venue: The Bar Marquee* **Sponsored by Anatomage**
Date and Time: Tuesday 6:45 *Venue: in the Canterbury Quadrangle*

Early Career and Student Social

Date and Time: Monday 14th July 7pm. *Venue: TBC*

There is an early career and student social following on the first evening of the conference, hosted by the early career team at Anatomical Society at the Bar Marquee, from 7pm. Casual drinks and a few fun social activities to help you get to know others in a similar position in their careers. Everyone is welcome! If you have any questions contact Samuel Snowdon- samueljsnowdon@gmail.com

Photography exhibition and drinks

Date and Time: Monday 14th July 6:30pm. *Venue: The Barn Gallery*

A drinks reception along with a chance to see the black and white photography exhibition by Caroline Seymour: Beyond Fear. Surgery, Hands, Healing. With a speech by Anatomical Society president Tracey Wilkinson.

Gala dinner details:

Date and Time: Tuesday 15th July 7:30pm

The gala dinner is to be held in the 16th Century Hall at St John's College. This will include an after dinner speech by the college President Professor Sue Black, Lady Black of Strome. Tickets have been sold separately.

A private viewing of this exhibiton by Caroline Seymour will be held on Monday, 14th July from 6:30 in the Barn gallery.

The exhibition shall be opened by the President of the Anatomical Society Professor Tracey Wilkinson

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BEYOND FEAR

Surgery, Hands, Healing

Beyond Fear is an exhibition of black and white photographs by Caroline Seymour, documenting patient journeys through cancer.

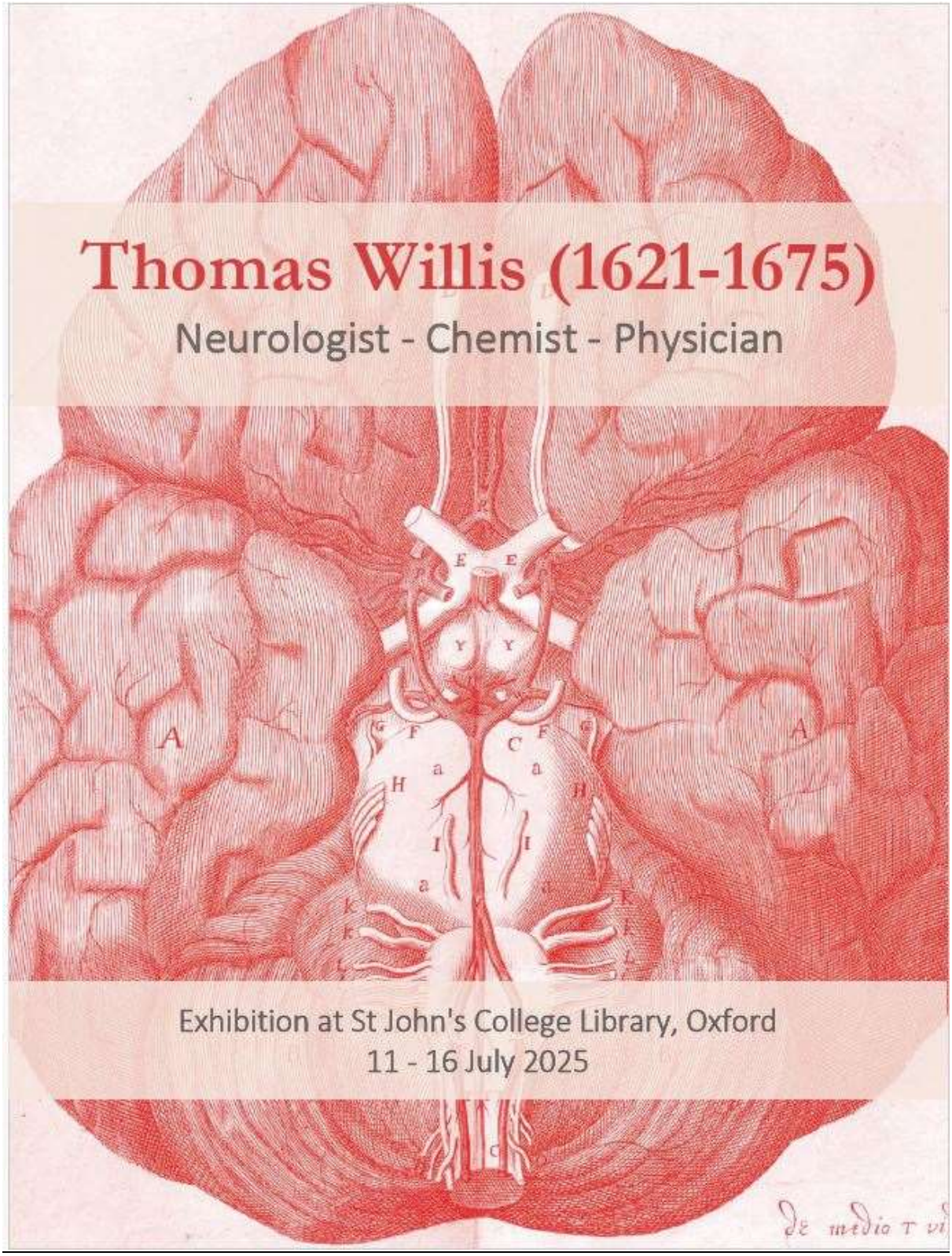
Over the last five years Caroline has photographed several patients, before, during and after surgery. She worked in close collaboration with surgeons and their teams at the John Radcliffe Hospital and Nuffield Orthopaedic Centre in Oxford, and with the patients and their families.

This exhibition will combine two series of challenging images. The first, taken in 2019 and 2020, was of patients with breast cancer, and was first shown during Photo Oxford 2021. The second, of patients with bone sarcomas, was shown at The Royal College of Surgeons of Dublin, Glasgow and London, in 2024. Images from both series were also juxtaposed with her photographs of details of old master paintings and sculpture from national collections in a book, *Beyond Fear*, Dewi Lewis Publishing, 2024.

In addition to this, by kind permission of the owner, we are privileged to be able to show two of Barbara Hepworth's surgical drawings, made in the late 1940s.

The exhibition runs from July 10th to 25th in The Barn Gallery, St John's College, Oxford
Opening hours: 11 am to 6 pm

Exhibition celebrating the founder of neurology, Thomas Willis (1621-1675)
- Neurologist - Chemist - Physician -
St John's College Library & Study Centre 11-16 July, the entrance is located in the Canterbury quadrangle



Anatomical Society Oxford Meeting 2025 Schedule

10 and 25 min talks.

Day 1	Auditorium	Other locations
9.30 onwards		Registration: Porters' lodge then from 12 at the Garden quad. auditorium foyer
10:00-12:00		**Pre-meeting workshop**: Anatomy Suite, Oxford University Medical Sciences Teaching Centre
12:00-2:00		Buffet lunch in the hall
1:00-2:00	**Workshop**: How to get published in the Journal of Anatomy	
2.00-2.10	Opening remarks: Tracey Wilkinson, Zoltan Molnar, Gavin Clowry	
2.10-3.55	**Symposium session 1. Chair-** Flora Vaccarino	
2.10-2.35	**Madeline Lancaster**- Exploring mechanisms controlling human brain evolution using organoids	
2.35-3.00	**Katie Long**- How the extracellular matrix shapes the developing human cortex.	
3.00-3.25	**Eva Anton**- Primary Cilia: A Novel Signaling Gateway to Cortical Neural Circuits	
3.25-3.35	**Thomas Theil**- Modelling the role of the primary cilia gene CEP41 in autism spectrum disorder using human cortical organoids	
3.35-3.45	**Sinaoife Andrews: Elsevier Presentation-** Complete Anatomy New Neuroanatomy Model	
3.45-4.15		Refreshments in the Marquee
4.15-5.50	**Symposium session 2: Chair-** Masahiro Tsuji	
4.15-4.40	**Rebeccah Slater**- The painful brain: developing pain perception in early infancy	
4.40-5.05	**Jetro Tuulari-** Prenatal exposures and early life neuroimaging – the importance of looking beyond the first weeks of life	
5.05-5.30	**Ana Namburete-** Mapping Fetal Brain Anatomy with Ultrasound and AI.	
5.30-5.40	**Michael O'Connor**- Mapping Early Psychosis: Hippocampus and Amygdala output differences in Adolescents with Psychotic Experiences	
5.40-5.50	**Aaron Barron**- Peripheral immune proteins predict reduced cortical thickness in 5-year-old human children	
6:00-7:00		**Poster session 1** and drinks reception sponsored by **Anatomage** in the Marquee
6.30-8:00		Art exhibition, drinks in The Barn- speech by Anatomical Society President Tracey Wilkinson

7:00 onward		Student Social event location to be confirmed
Day 2	**Auditorium**	**Other locations**
8.25-10.40	**Symposium session 3: Chair-**Gavin Clowry	
8.25-8.35	**Aarushi Vaidya**-Can early forebrain patterning/ holoprosencephaly (HPE) be modelled *in vitro* using 2D and/or 3D human induced pluripotent stem cell models?	
8.35-8.45	**Daniel Berg**- Mapping and modelling neural stem cell dynamics in the developing human dentate gyrus	
8.45-8.55	**Muhammad Assir**- IL-17A Alters Human Cortical Development in a 3D Ex Vivo Model of Maternal Immune Activation	
8.55-9.05	**Andrew Copp-** Chiari II brain malformation is secondary to open spina bifida: evidence from a new mouse genetic model	
9.05-9.15	**Nicoletta Kessaris**- Molecular multitaskers: the pleiotropic power of transcriptional co-factors in mouse cortical development	
9.15-9.40	**Chiaki Ohtaka-Maruyama**- Molecular Basis of Subplate Layer Expansion in Human Fetal Brain Development	
9.40-10.05	**Arnold Kreigstein** - Genomic insights into human brain development and disease	
10.05-10.30	**Maxwell systems presentation: Anastasiia Tourbier-** Next-Generation Electrophysiology for Functional Characterization of Human Neural Organoids and Assembloids.	
10.30-11.00		Refreshments in the Marquee
11.00-12:00	**Symposium session 4: Chair-** Alain Chedotal	
11.00-11.25	**Nenad Sestan**- Origins of the Prefrontal Cortex and Cognitive-Emotional Networks: What Makes Us Human	
11.25-11.50	**Zeljka Krsnik-** Initial regional patterning and laminar dynamics in the developing human prefrontal cortex.	
11.50-12.00	**Mohammed Abuelem**- Cortical Layer 6 Drd1a-Cre+ neurons mediate dopaminergic-driven activation of the murine medial prefrontal cortex	
12:00-2:00		Buffet lunch in Hall
12:30-1:30		**Poster Session 2** in Marquee
2.25-3.40	**Symposium session 5: Chair-** Zoltán Molnár	
	Sophie Miller prize talk: Orla Mitchell- Early Life Adversity & Brain Structure: A Longitudinal Structural Human MRI study.	
2.25-2.50	**Masahiro Tsuji**- Pathophysiology of neurodevelopmental disorders associated with low birthweight.	
2.50-3.15	**David Price**- Variation in human brain development. **Sponsored by Primal Pictures**	
3.15-3.40	**Helen Stolp**- Short- and long-term effects of acute early-life activation of the $GABA_A$ receptor on neuronal development.	
3.40-4.10		Refreshments in the Marquee
4.10-5.50	**Symposium session 6:** Chair- Zeljka Krsnik	

4.10-4.35	**Alain Chedotal**- tridimensional analysis of human nervous system development	
4.35-5.00	**Anton Tonchev**- An insight into human cortical development from adult neurogenesis	
5.00-5.25	**Tim Zolnik**- Orexin-activated neurons of the human cortex	
5.25-5.50	**Sara Bandiera**- Extrinsic modulation of cortical development by early thalamic innervation in the human foetal brain	
6:00-6.30	History of neuroscience lecture on Thomas Willis (1621-1675): **Zoltan Molnar. Introduced by the Anatomical Society president Tracey Wilkinson.**	
6.45 for 7.30		Drinks reception at the Canterbury Quadrangle, followed by the **Gala dinner** in The Hall

Day 3	Auditorium	Other locations
8.30-10.30	**Symposium Session 7. General Anatomy and Education:** Chair- Cecilia Brassett	
8.30-8.40	**Jason Sparks**- Pituitary adenylate cyclase-activating polypeptide (PACAP) mediates bacterial endotoxin-induced fever via an effect on cyclooxygenase-2 and inflammatory cytokines in mice.	
8.40-8.50	**Natalia Penar**- Mechanisms of epithelial symmetry-breaking during mammalian morphogenesis	
8.50-9.00	**Eavan Pakenham**- Selenium and Magnesium Functionalised Scaffolds for Dual Bone Regeneration and Anti-Cancer Therapy	
9.00-9.10	**Louise Hosty**- Development of a Pro-Angiogenic Hyaluronic Acid Hydrogel Decorated with Vascular Cell-Derived ECM	
9.10-9.20	**Meric Goker**- Advanced Synovial Microneedle Technology for Drug Delivery to Prevent Post Traumatic Osteoarthritis	
9.20-9.30	**Sophie Mok**- Evaluating osteoblast-fibroblast co-culture in a multiphasic calcaneofibular bone-ligament scaffold	
9.30-9.40	**Anne O'Callaghan** - Developing an Injectable Hyaluronic Acid-based Hydrogel Containing Non-viral P2X7R Silencing RNA Nanoparticles For The Treatment Of Post-Traumatic Temporal Lobe Epilepsy	
9.40-9.50	**Ryan Smith**- A simplified clinically applicable classification of Circle of Willis variants.	
9.50-10.00	**Honey Zahra**- Exploring Anatomy Education: A Comparative Analysis of Cadaver Dissection and 3D Anatomical Study Tool	
10.00-10.10	**Leandros Rapteas**- Equipping future clinicians: Inclusive anatomy teaching amid legal and social challenges to gender equity	
10.10-10.20	**Andras Nagy**- exploring the teaching traditions of Central European anatomists through the Erasmus+ LEANbody collaborative project	

10.20-10.30	**Anatomage presentation: Daniela Cacciabue-** Anatomy at Sheffield- From Scalpel to Virtual Dissection and Beyond	
10.30-11.20	**Symposium session 8:** Chair- Nenad Sestan	
10.30-10.55	**Tom Nowakowski-** Uncovering the strategies of human radial glia using high throughput genomics	
10.55-11.20	**Becky Carlyle-** Advances in human brain proteomics; Increased-throughput, sub-cellular discovery, and post-translational modifications	
11.20-11.50		Refreshments in the Marquee
11.50- 1.10	**Symposium session 9:** Chair-David Price	
11.50-12.15	**Flora Vaccarino-** Organoid models of human brain development and developmental disorders	
12.15-12.40	**Faye McLeod-** Modelling monogenic epilepsy in human foetal brain slice cultures	
12.40-1.05	**Luana Campos Soares-** 3D printing cortical progenitors to study human brain development	
1.05-1.20	**Closing remarks and prizes.**	

With thanks to our sponsors…

and Enatom

You can find the sponsors in the Bar Marquee in the Thomas White Quadrangle.

Name	Poster Session	Poster Number	Young Investigator
Hitomi Achiwa	2	7	Young investigator
Maznah Abdullah Alhesain	1	3	Young investigator
Alaa Alshwayyat	2	9	Young investigator
Diyya Ameen	1	22	Young investigator
Laura Andreae	1	5	
William Antcliff	2	15	Young investigator
Lauren Barrett	2	10	Young investigator
Denis Barry	1	6	
Ashley Benge	1	17	Young investigator
Thewarid Berkban	1	24	
Sourav Bhattacharjee	1	1	
Mihaela Bobic-Rasonja	2	4	
Patrick Cavanagh	2	13	Young Investigator
Arada Chaiyamoon	1	20	
Advait Dinesh	2	21	Young Investigator
Peter Dockery	1	9	
Anuch Durongphan	1	19	
Sid Xiuyan Gao	2	18	Young investigator
DoHyeon Gim	1	12	
Asmita Goswami	2	28	
Pedro Hecht-López	1	27	
Ernie Ho	1	8	Young investigator
Lara Jane Ismair	1	13	Young investigator
Daniel Johnston	2	25	
Aragorn Jones	2	1	
Karuna Katti	2	31	
Saima Khan	2	26	
Radik Khayrullin	1	21	
Janja Kopic	2	8	
Georgia Koudigkeli	2	19	Young investigator
Lelika Lazarus	1	15	
Mariah Lelos	2	11	
Viktoria Levkanicova	1	11	Young investigator
ChunKim Lim	1	4	Young investigator
Rashmi Malhotra	2	22	Young investigator
Irene Manjaly	2	27	Young investigator
Lana Manjouneh	1	10	Young investigator
Zdravko Petanjek	2	6	
Yasmine Popa	2	24	Young investigator
Sharmila Saran Rajendran	1	26	
Leandros Rapteas	1	25	
Jessica Roles	2	23	Young investigator
Femina Sam	2	20	
Rarinthorn Samrid	1	18	Young investigator
Shreya Sankar	1	7	Young investigator
Montserrat Rayman Silva	2	29	
Rumyana Smilevska	1	28	

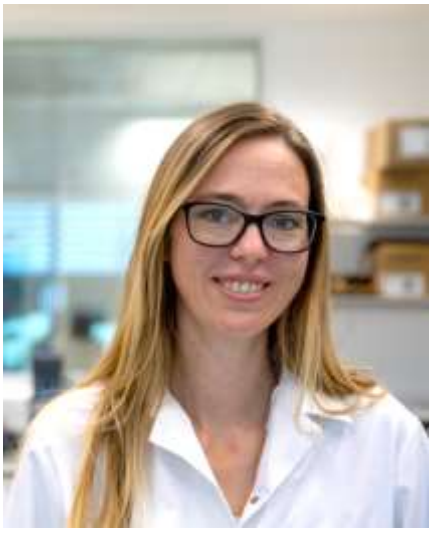
Pavan Sohal	2	17	Young investigator
Jason Sparks	1	29	Young investigator
Imani Stanard	1	23	Young investigator
Dimo Stoyanov	1	2	
Daiki Sugita	1	31	Young investigator
Jagraj Thandi	2	12	
Seyedeh Torabi	2	30	
Sara Valkila	2	5	Young investigator
Thomas Van-Parys	1	16	Young investigator
John Varghese	1	30	Young investigator
Zak Vincent	1	14	Young investigator
Natalie Wucherer	2	2	Young investigator
Emily Malini Young	2	16	Young investigator
Lusi Zhao	2	3	Young investigator

INVITED SPEAKER

Exploring mechanisms controlling human brain evolution using organoids

Madeline Lancaster
MRC lab of Molecular Biology, Francis Crick Avenue, Cambridge
@mad_lancaster

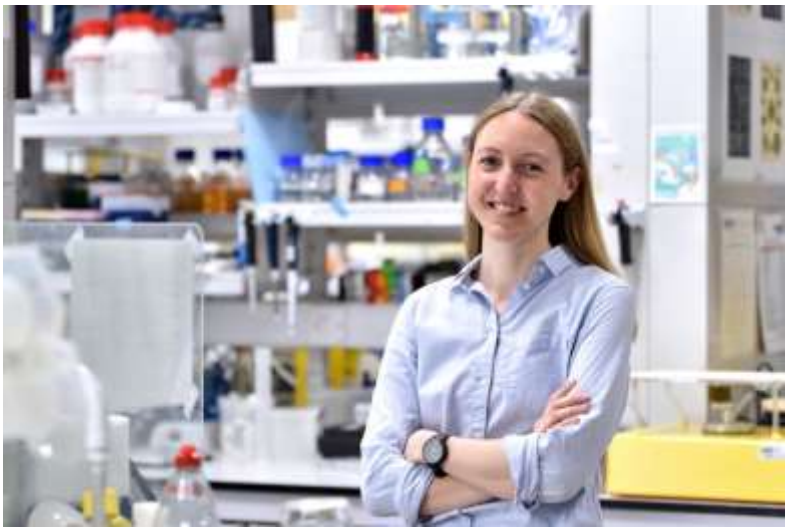
The human brain is greatly enlarged and complex, even when compared with our closest living great ape relatives. How this evolutionary elaboration has come about is still unclear, but neural organoids are enabling comparative studies to uncover the underlying mechanisms. Our recent findings highlight delayed developmental transitions underlying this increased size and complexity. In particular, we have uncovered a delay in neuroepithelial transition that enables increased progenitor expansion and tissue growth. Turning to later stages of development, namely the development of long-range projections, we have discovered a similar human delay, in this case a slower transition at the end of axon growth. These studies are revealing crucial differences in timing of the duration of cell states, thus enabling increased tissue growth and neuronal complexity during brain development. Ethics statement: This research has been approved by the ERC and the UK Stem Cell Board for the use of human embryonic stem cells, and animal cell lines have been approved by AWERB and the ERC.



INVITED SPEAKER

How the extracellular matrix shapes the developing human cortex

Katie Long
King' College London, London, UK



INVITED SPEAKER

Primary Cilia: A Novel signalling gateway to cortical neural circuits.

Eva Anton
University of North Carolina at Chapel Hill

Modelling the role of the primary cilia gene CEP41 in autism spectrum disorder using human cortical organoids

Kerstin Hasenpusch-Theil, Alexandra Lesayova, Alexandra Jänis, Zrinko Kosic, Owen Dando, Thomas Theil

University of Edinburgh, Edinburgh, UK

Primary cilia – small protrusions from the cell surface – act as the cell's antennae and control cell-cell signalling. Ciliary dysfunction can cause severe neurological symptoms, most commonly intellectual disability (ID) and autism spectrum disorder (ASD). Conversely, several candidate genes for ASD, schizophrenia, and ID affect primary cilia function. Despite these findings and their critical function as signaling hubs, roles of primary cilia in the ASD pathomechanism remain largely unexplored. Here, we analysed the function of CEP41 in human corticogenesis. It encodes a centrosomal protein located at the basal body and the ciliary axoneme and is mutated in ASD patients and in Joubert syndrome, a ciliopathy with high incidence of ASD. To gain insights into its role in ASD aetiology, we characterised human cortical organoids carrying the CEP41 R242H point mutations found in ASD patients. This mutation did not interfere with CEP41's ciliary localisation but cilia were shorter and had lower levels of tubulin polyglutamylation indicative of altered cilia stability and signalling. Moreover, scRNAseq analyses revealed that in interneurons and their progenitors the altered expression of several transcription factors with critical roles in interneuron development coincided with changes in interneuron differentiation. The CEP41 mutation also caused decreased cortical progenitor proliferation and an augmented formation of upper layer cortical neurons. In addition, we are investigating the effects of the R242H mutation on the morphology of projection neurons and on neuronal network activity. Taken together, these findings indicate that CEP41 controls excitatory and inhibitory neuron differentiation, alterations in which might lead to an excitation/inhibition imbalance that is widely recognized as a convergent mechanism underlying neurodevelopmental disorders. No ethical approval is required.

Complete Anatomy New Neuroanatomy Model

Sinaoife Andrews
Medical Digital Content Specialist, Elsevier

Over the last couple years, the team at Complete Anatomy have been updating all parts of the gross anatomy model within in the app. The brain is one of the last areas that needs updating as it currently does not match the high level of detail and accuracy as the rest of the model. Thus, extensive work is underway to develop a new neuroanatomy model for Complete Anatomy. From our research, we have found that there are many pain points when it comes to learning neuroanatomy, and one of those is access to reliable cross-sections of the brain. That is why we decided to base our new brain model off MRI data, provided with consent by Dr. Jonathan Wisco of Boston University. This method of modelling will ensure medical accuracy and reliability, allowing us to create precise cross-sections of the brain. In addition to having detailed structure, our model will also be functional for students and educators alike. In doing so, we hope to improve the learning experience of students, ultimately combatting neurophobia. In designing this model, we are also ensuring it is relevant for educators by fully covering learning outcomes. All of this work has meant that we are building the most accurate and functional brain model on the market.

INVITED SPEAKER

The painful brain: developing pain perception in early infancy.

Rebeccah Slater

Department of Paediatrics, University of Oxford, Oxford, UK

INVITED SPEAKER

Prenatal exposures and early life neuroimaging- the importance of looking beyond the first weeks of life

Jetro Tuulari

Neurocenter Finland, Turku, Finland

INVITED SPEAKER

Mapping fetal brain anatomy with ultrasound and AI.

Ana Namburete

Department of Computer Science, University of Oxford, Oxford, UK

Mapping Early Psychosis: Hippocampus and Amygdala output differences in Adolescents with Psychotic Experiences

Michael O'Connor, Lucy-Anne O'Sullivan, Claire O'Doherty, George-Paul O'Bryne, Ryan Lukin, Judith Linares Gomez, Darren Roddy.

Michael O'Connor Royal College of Surgeons, Dublin, Ireland, Lucy-Anne O'Sullivan Royal College of Surgeons, Dublin, Ireland, Claire O'Doherty Royal College of Surgeons, Dublin, Ireland, George-Paul O'Byrne University of Limerick, Limerick. Ireland, Ryan Lukin Royal College of Surgeons, Dublin, Ireland, Judith Linares Gomez Royal College of Surgeons, Dublin, Ireland, Darren Roddy Royal College of Surgeons, Dublin, Ireland.

Psychotic experiences (PEs) in adolescence have been linked to structural changes in brain regions such as the hippocampus and amygdala, yet there is limited research on the output tracts of these regions. This study focuses on the fornix and stria terminalis (ST), two major tracts that connect the hippocampus and amygdala to the basal forebrain and hypothalamus. These tracts are divided into anterior (precommissural) and posterior (postcommissural) fibres by the anterior commissure. The aim of this study was to investigate the structural integrity of these tracts in young adolescents with PEs compared to healthy controls across two timepoints. 51 adolescents with PEs (37 female) and 43 healthy controls (25 female) underwent high angular diffusion imaging at TP1, with 39 PEs and 29 controls returning for a follow-up at TP2. Diffusion tensor imaging (DTI), which measures water diffusion along axonal fibres to map brain tissue structure, was employed to analyse these tracts. The fornix and ST were isolated and their precommissural and postcommissural fibres were examined. Covariance analysis was conducted with adjustments for age, sex, and intracranial volume, comparing the two groups using diffusion metrics: fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (AD), and radial diffusivity (RD). At TP1, adolescents with PEs exhibited significant alterations in the right pericommissural fornical fibres, specifically increased MD ($p=0.035$) and RD ($p=0.009$), and decreased FA ($p=0.045$). These changes were further amplified at TP2, with significant increases in MD ($p=0.004$), RD ($p=0.005$), and AD ($p=0.042$). After Bonferroni correction, only the increases in MD and RD at TP2 remained significant ($p<0.0083$). No significant differences were found in the ST fibres after correction. These findings suggest that in adolescents with psychotic experiences (PEs), the right fornix, linking the hippocampus to the basal forebrain, is selectively altered, while other pathways remain intact. This right-sided change aligns with previous findings in psychosis and suggests a key role for the right basal forebrain in early disease stages. The findings enhance our understanding of psychosis-related brain changes and may help identify future biomarkers. Ethics approval was granted by the RCSI Human Research Ethics Committee

Peripheral immune proteins predict reduced cortical thickness in 5-year-old human children

Aaron Barron[1], Elmo Pulli[1], Ekaterina Saukko[2], Minna Lukkarinen[1], Alex Dickens[1], Tuulia Hyötylainen[3], Matej Orešič[1,3], Linnea Karlsson[1], Hasse Karlsson[1], Jetro Tuulari[1]
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This study utilised immune proteomics and multimodal magnetic resonance images (MRIs) analysis, studying hundreds of immune proteins and multiple whole-brain structural parameters simultaneously to characterise the role of inflammation in brain structure in children. Participants were 5-year-old children from the FinnBrain Birth Cohort Study (N=126). Blood was collected and serum immune proteomics analysed using Olink Explore Inflammation 384, comprising 356 immune proteins which were summarised into 6 clusters by Gaussian mixture modelling. Children underwent T1- and diffusion-weighted MRI, and the resulting images were pre-processed to create maps of grey matter volume, white matter fractional anisotropy and mean diffusivity, and cortical thickness and surface area. Voxel- and vertex-level data were combined by linked independent component analysis to produce 10 independent components summarizing the maximum structural variance across all modalities. Partial correlation analysis identified a strong negative association between one immune cluster and IC4, which is weighed almost entirely by whole-brain cortical thickness. This cluster comprises 49 proteins, representing 13% of the measured immune proteome, and it is characterised by pro-inflammatory type I cytokines such as TNFα, IFNγ, IL-6, IL-17A, and IL-18. Each protein in this cluster was regressed against IC4, adjusting for age, sex, and BMI. 14 proteins were nominally significant ($p < 0.05$), while 3 proteins, IL-17A ($R2 = 0.18$), CXCL10 ($R2 = 0.10$), and SIRPB1 ($R2 = 0.09$), were significant after false discovery rate adjustment. These three proteins were added to vertex-wise models to determine if they predict regional cortical thickness by linear regression adjusted for age, sex, and BMI. IL-17A, CXCL10, and SIRPB1 each predicted reduced cortical thickness of one cluster in the left fusiform gyrus, right postcentral/posterior parietal cortex, and left superior temporal gyrus, respectively ($pFDR < 0.025$, threshold adjusted for testing each hemisphere separately). Combining immune proteomics with multimodal neuroimaging analysis identified a cluster of immune proteins associated with reduced cortical thickness, three of which - IL17A, CXCL10, and SIRPB1 - have strong, negative associations with global and regional cortical thickness. Given that these are typically-developing children, the findings are relevant to the general population, implicating peripheral inflammation in human cortical development. Ethics statement: All participants have have given full, informed consent. The study was approved by the Ethics Committee of the Hospital District of Southwest Finland (VARHA/18203/13·02·02/2023).

YOUNG INVESTIGATOR

Can early forebrain patterning/holoprosencephaly (HPE) be modelled in vitro using 2D and/or 3D human induced pluripotent stem cell models?

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Holoprosencephaly (HPE) occurs due to failed or dysregulated midline cleavage of the developing brain, and the most severe form, alobar, often results in foetal termination. Mutations in nine genes, many of which are linked to the SHH signalling pathway, are implicated in the pathogenesis of HPE. This project investigates whether forebrain patterning/HPE can be modelled in vitro using 2D monolayer (neural induction) and 3D (forebrain organoid) human induced pluripotent stem cells (hiPSCs) models. Existing animal models fail to recapitulate the complexity of human HPE and therefore lack clinical translation. The hypothesis is that early forebrain patterning, including HPE gene expression, can be recapitulated in hiPSCs cultured in vitro using a neural induction approach. Different combinations of three small molecules (SB431542, XAV939 and LDN-193189) resulted in different morphologies of the uniform field of Pax6 expression. Notably, the monolayers fed with neural induction media (NIM) only (no small molecules) and XAV939 only formed Pax6/Sox2 positive 3D eye spots, suggesting anterior neural character. Preliminary findings from hiPSC monolayers (fed with NIM only) generated a uniform field of Six3 expression with Pax6/Sox2 positive spots that may be forebrain progenitors. After 5 days of NIM only or XAV939 treatment in the hiPSC monolayers, WNT signalling was activated or inhibited for 5 days, using XAV939 or CHIR99021, respectively. Immunolabelling of day 10 hiPSC monolayers confirmed the expression of Foxg1 and Pax6, suggesting forebrain identity. Higher expression of anterior forebrain markers like Foxg1 and Six3 are predicted in qPCR gene expression profiles of monolayers treated with XAV939 for 10 days. 3D spheroids were generated using NIM with or without small molecules. Preliminary findings suggest similarities in the uniform morphology of the spheroids and the uniform field of Pax6 expression in cells treated with NIM and small molecules. Future directions include optimising early forebrain patterning by controlling SHH signalling and generating knock-in reporter hiPSC lines for Six3 or Pax6 to study live gene expression. No animals or human subjects were used. No ethical approval was required; local guidelines for use of hiPSCs were followed. AICS-0075-085 and AICS-0054-091 hiPSC lines were obtained from the Allen Cell collection.

Mapping and modelling neural stem cell dynamics in the developing human dentate gyrus

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The dentate gyrus (DG), a subregion of the archicortex within the human cerebral cortex, is unique for its capacity to support neurogenesis well beyond birth, potentially continuing into adulthood. Adult-born neurons in the DG contribute to learning, memory formation, and emotional regulation, and disruptions to this process have been implicated in several neurological and psychiatric disorders. However, the developmental origins of this long-lived neurogenic niche remain poorly understood, particularly regarding the timing, migratory behaviour, and regulation of neural stem cells (NSCs) during early human DG formation. We analysed postmortem human fetal brain tissue between gestational weeks 12 and 18 using immunohistochemistry with markers for NSCs (SOX2), immature neurons (DCX), and dentate granule cells (PROX1), allowing us to map the spatiotemporal distribution of progenitor populations and trace their migration from the dentate neuroepithelium through the dentate migratory stream into the dentate primordium. Division plane analysis using phospho-vimentin (P-VIM) revealed region-specific variation in NSC mitotic behaviour. In parallel, we generated iPSC-derived hippocampal organoids using region-specific patterning cues, and transcriptomic analysis confirmed hippocampal identity. These organoids produced PROX1-positive dentate granule-like neurons with functional properties validated through calcium imaging and electrophysiology. Quiescence is a hallmark of postnatal dentate gyrus NSCs, and in older organoids, we identified a population of quiescent NSCs lacking proliferation markers and EdU incorporation. This combined approach using human tissue and 3D organoid modelling provides new insight into the cellular architecture and temporal dynamics that establish the neurogenic niche in the developing human dentate gyrus, forming a foundation for future studies into its regulation and relevance to neurodevelopmental disorders. Human fetal tissue used in this study was obtained through the Scottish Advanced Fetal Research (SAFeR) study (NCT04613583), approved by the North of Scotland Research Ethics Committee (REC reference: 15/NS/0123), with written informed consent from participants.

YOUNG INVESTIGATOR

IL-17A Alters Human Cortical Development in a 3D Ex Vivo Model of Maternal Immune Activation

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Maternal immune activation (MIA) during pregnancy is strongly associated with an increased risk of neurodevelopmental disorders (NDDs) in offspring. However, the mechanisms by which inflammatory conditions disrupt human cortical development in utero, contributing to NDD pathology, remain largely elusive. To elucidate these mechanisms, a novel high-throughput 3D ex vivo model of human fetal brain tissue, termed cerebroids, was developed. These cerebroids preserve the cytoarchitectural organization and cellular complexity characteristic of in vivo brain development. Exposure of cerebroids to Interleukin 17A (IL-17A)—a key cytokine implicated in both MIA and NDDs—elicited premature cortical folding, increased cortical thickness, and expanded neuronal populations, thereby recapitulating cortical phenotypes observed in NDDs like autism spectrum disorder (ASD). Additionally, MIA conditions accelerated neuronal subtype specification and drove precocious maturation of excitatory cortical neurons. Mechanistically, these changes were underpinned by enhanced neurogenesis in neural stem cells (NSCs), accompanied by sustained NSC pools through increased cell cycle re-entry. Transcriptomic analysis identified activation of key inflammatory pathways as well as changes in epigenetic regulators and genes associated with extracellular matrix (ECM) remodelling in response to IL-17A. Complementary proteomic analyses confirmed extensive ECM remodelling, including upregulation of the chondroitin sulfate proteoglycans Brevican (BCAN) and Versican (VCAN). These molecular alterations were orchestrated by nuclear factor kappa B (NF-κB) signalling and histone deacetylase complex 1 (HDAC1). Notably, pharmacological inhibition of NF-κB and HDAC1 with Parthenolide reversed IL-17A-induced changes, restoring cortical structure, neuronal populations, and BCAN expression. This work unveils the profound impact of MIA on cortical development and delineates its cellular and molecular underpinnings through an innovative 3D model of the human fetal brain. These findings offer critical insights into how inflammatory insults during pregnancy may contribute to the pathogenesis of NDDs. Ethics statement: Fetal tissues from elective terminations of normally progressing pregnancies were obtained as part of the Scottish Advanced Fetal Research (SAFeR) study (NCT04613583) at the University of Aberdeen, UK. The collection process was conducted under a protocol approved by the North of Scotland Research Ethics Committee (REC reference: 15/NS/0123) and adhered to the ethical guidelines of the Declaration of Helsinki.

Chiari II brain malformation is secondary to open spina bifida: evidence from a new mouse genetic model

Maryam Clark[1], Timothy J. Edwards[1], Dawn Savery[1], Gabriel L. Galea[1], Nagaraj Samy[1], Erwin Pauws[1], Nicoletta Kessaris[2], Nicholas D.E. Greene[1], Andrew J. Copp[1]

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The Chiari II brain malformation affects 90% of children with open spina bifida. The hindbrain herniates through the foramen magnum into the vertebral canal leading to frequent hydrocephalus and occasional respiratory emergency. Chiari II is not confined to the back of the brain, but is a global brain syndrome, with supratentorial defects that are associated with learning disability, affecting 20-25% of children with open spina bifida. The reason for the association between Chiari II and open spina bifida has long been debated. Separate effects on the brain and spinal cord of causative genetic or non-genetic factor(s) are possible. Conversely, Chiari II may be secondary to open spina bifida, and a prominent hypothesis cites chronic leakage of cerebrospinal fluid through the open spinal lesion as causative. To resolve the issue of causation, we developed a novel mouse model, in which females homozygous for a floxed allele of Pax3 were mated with males of genotype Cdx2cre; Pax3fl/+. This deleted Pax3 gene function solely in the lower body, whereas the head remained wild-type. Open spina bifida was seen in all Cdx2cre/+; Pax3fl/fl embryos and fetuses, together with many of the features of Chiari II in the wild-type brain of the mice. These included: hindbrain and cerebellar herniation, cortical thinning, hypogenesis of the corpus callosum and hippocampus, heterotopic neurons in the cerebral cortex and habenula and thickening of the proliferative zone. Posterior skull defects were also observed, as in humans with Chiari II. We conclude that the brain defects of Chiari II occur secondary to open spina bifida, with the implication that these may arise early in human gestation through disturbed neurogenesis. The Cdx2cre/+; Pax3fl/fl mouse provides a model for improved understanding of Chiari II pathogenesis. Mouse research in this study was conducted under auspices of the UK Animals (Scientific Procedures) Act 1986 Amendment Regulations (SI 2012/3039).

Molecular multitaskers: the pleiotropic power of transcriptional co-factors in mouse cortical development

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The cerebral cortex is responsible for higher-order cognitive functions like memory, learning and thought. These functions rely on a complex network composed of an array of excitatory and inhibitory neurons. Understanding how this neuronal diversity is established offers insights into the construction of neural networks and how genetic mutations and neuronal deficiencies can impact behaviour. The acquisition of cell identity is governed by genetic programs and driven by transcription factors which either bind directly to DNA or act as co-factors recruiting protein assemblies. We recently discovered that the transcriptional co-factor RUNX1T1 plays a crucial role in the specification of cortical inhibitory neuron identity during embryogenesis. This aligns with evolutionarily conserved roles for RUNX1T1 in flies and other species, where mutations in this gene lead to changes in cell fates. The importance of RUNX1T1 is underscored by human studies linking it to intellectual disability, mental retardation and autism spectrum disorder. In addition to the cortical inhibitory interneuron deficits, mouse embryos lacking RUNX1T1 show abnormalities in excitatory neuron numbers and their projections, indicating deficiencies in the neuronal composition of the cortex and its ability to transmit information. Utilizing a robust method for identifying endogenous protein complexes in tissues, we discovered several putative interacting partners of RUNX1T1 in the embryonic brain, including DNA-binding proteins and other co-factors. Notably, a large fraction of these potential partners are candidate genes for neurodevelopmental disorders in humans. Our findings indicate that RUNX1T1 may serve as a critical co-regulator of disease-associated genes, potentially exerting pleiotropic effects on cortical development. Mouse colonies were maintained at the Wolfson Institute for Biomedical Research, University College London, in accordance with United Kingdom legislation (ASPA 1986), and at the BSRC "Al. Fleming", according to the European Union ethical standards outlined in the Council Directive 2010/63EU of the European Parliament on the protection of animals used for scientific purposes.

INVITED SPEAKER

Molecular Basis of Sub-plate Layer Expansion in Human Fetal Brain Development.

Chiaki Ohtaka-Maruyama

Tokyo Metropolitan Institute of Medical Science, Tokyo, Japan

The cerebral cortex, responsible for complex brain functions in mammals, exhibits a precise six-layered structure, formed through a highly coordinated process of neurogenesis, migration, layer formation, and circuit development during fetal growth, with remarkable reproducibility. Subplate neurons (SpNs), among the earliest neurons to emerge, reside in the deepest cortical layer and play pivotal roles in early brain development. They relay signals from the thalamus to the cortex and guide migrating neurons to their correct positions. In primates, particularly humans, the subplate (SP) layer undergoes significant expansion during mid-gestation, unlike in mice, suggesting a critical role in the evolution of advanced cortical structures. This study explores genes highly expressed in primate SpNs, hypothesizing their involvement in SpN generation and SP layer expansion. We identified ST18, a gene absent in the embryonic mouse brain but prominently expressed in primate SpNs, as a key candidate. Using in utero electroporation, transient ST18 overexpression in mouse SpNs induced cell clustering and increased SpN populations, indicating enhanced SpN production. To further investigate, we generated transgenic mice overexpressing ST18 in dorsal cortical progenitor cells. These mice exhibited a dramatically expanded SP layer and increased thalamic axon projections, mirroring features of primate brain architecture. Spatial transcriptomic analysis with Visium confirmed robust ST18 expression in the SP layer of marmoset and human fetal brain sections, reinforcing its role in primate-specific cortical development. Additionally, we examined CYP26A1, a retinoic acid-metabolizing enzyme highly expressed in parts of the marmoset fetal SP layer. Our findings suggest that retinoic acid concentration gradients modulate thalamic-cortical axon projections, fine-tuning connectivity in the primate cortex. Together, these results highlight the SP layer's crucial role in shaping primate brain complexity and connectivity. This study provides insights into the molecular mechanisms underlying cortical evolution and development. Conducted with approval from the Ethics Committee for Human Research and the Animal Experimentation Ethics Committee at the Tokyo Metropolitan Institute of Medical Science, our findings pave the way for understanding primate-specific brain development.

INVITED SPEAKER

Genomic insights into human brain development and disease.

Arnold Kriegstein
Kriegstein Lab, UCSF, San Francisco

Next-Generation Electrophysiology for Functional Characterization of Human Neural Organoids and Assembloids

Anastasiia Tourbier, Laura D'Ignazio, Elvira Guella, Zhuoliang Li, Silvia Oldani, Praveena Manogaran, Marie Engelene Obien
MaxWell Biosystems AG, Zurich, Switzerland

Human induced pluripotent stem cell (hiPSC)-derived neural models have emerged as invaluable tools for studying neurological disorders, such as epilepsy, Alzheimer's, and Parkinson's disease. Real-time, label-free measurement of electrical activity in self-organizing in vitro cellular models provides critical insight into the complexity of their neuronal networks. High-density microelectrode arrays (HD-MEAs) enable non-invasive electrophysiological recordings from various electrogenic samples, including iPSC-derived neurons, retinal explants, brain slices, and neural organoids.In this study, we used MaxOne and MaxTwo high-density MEA platforms (MaxWell Biosystems AG, Switzerland), with 26,400 electrodes per well to record extracellular action potentials in neural organoids at different scales, ranging from cell population networks to single-cell resolution and subcellular levels. We showcased the flexible selection of electrodes for recording neural activity, increasing the reproducibility and statistical power of the data collected. Key metrics such as firing rate, spike amplitude, and network burst profile were extrapolated in a parallelized manner to capture even the smallest neuronal signals. Furthermore, we characterized axonal function and structure using the AxonTracking Assay, which allows measurement of action potential conduction velocity, latency, axonal length, and branching. This automated assay facilitates high-throughput characterization of disease models targeting axon initial segments, axonal branching, development, and conduction. MaxWell Biosystems' HD-MEA platforms, along with automatically generated plots and extracted metrics, provide a unique, user-friendly approach to identifying and isolating functionally active regions in 3D cultures. These powerful platforms enable long-term in vitro disease modeling and compound testing in acute recordings and/or longitudinal studies.

INVITED SPEAKER

Origins of the Prefrontal Cortex and Cognitive Emotional Networks: What Makes Us Human.

Nenad Sestan
Yale school of Medicine, New Haven, USA

INVITED SPEAKER

Initial regional patterning and laminar dynamics in the developing human prefrontal cortex and cingulate cortex.

Željka Krsnik
School of Medicine, University of Zagreb, Croatian Institute for Brain Research, Zagreb

Understanding how the human cerebral cortex develops from a relatively uniform prenatal structure into a highly organized adult structure with distinct Brodmann areas has been the subject of decades of research. From classical studies to the present, it is known that the development of structurally and functionally distinct cortical areas results from both intrinsic genetic programming and extrinsic inputs, such as thalamic projections. In this talk, I will present recent findings on early regional patterning and laminar dynamics in the developing prefrontal and cingulate cortex, with a focus on the early fetal and early midfetal periods. Using a combination of classical histology, molecular markers for deep-layer projection neurons (DPN), and spatial transcriptomics, we identify early cytoarchitectonic features and molecular signatures that precede the final arealization of the cortex. We show that the subplate (SP)—a transient yet prominent cortical compartment—displays region-specific expansion patterns, i.e. cortical plate (CP) neurons spread-down, particularly in association areas of the frontal cortex, driven by early axonal ingrowth. Additionally, our findings in the cingulate cortex reveal a clear distinction in laminar organization between dorsal (isocortical) and ventral (mesocortical) portion of the cingulate cortex as early as 8 postconceptional weeks (PCW), providing novel insights into the timing and mechanisms of cortical type differentiation. In conclusion, initial **r**egional differences in cortical compartments are evident as early as the second month of gestation, even though cortical arealization is a gradual process, heavily influenced by thalamic input and continuing into postnatal life. These data highlight the significance of laminar organization and SP dynamics in early cortical regionalization, offering new frameworks for understanding human-specific neurodevelopmental processes. IRB Statement: The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Ethics Committee of School of Medicine University of Zagreb (protocol number Ur. Broj: 251-59-10106-23-111/158, Klasa: 641-01/23-02/01).

Cortical Layer 6 Drd1a-Cre+ neurons mediate dopaminergic-driven activation of the murine medial prefrontal cortex

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Cortical layer 6 (L6) neurons play an important role in driving cortical arousal via the higher-order corticothalamic system. Many of these L6 neurons are remnants of the transient developmental subplate, which contains some of the earliest generated cortical neurons involved in the establishment of thalamocortical circuits. Altered distribution and transcriptomic profile of these deep layer neurons are implicated in neurodevelopmental disorders such as autism and schizophrenia. In the murine somatosensory cortex and medial prefrontal cortex (mPFC), a subpopulation of L6 neurons expressing the dopamine D1 receptor (L6-*Drd1a*) selectively project to higher-order thalamic nuclei and are highly sensitive to the wake-promoting neuropeptide orexin, playing an important role in gating cortical arousal and anxiety behavior. However, the modulatory mechanism through which these L6-*Drd1a* neurons mediate dopaminergic-driven mPFC activation remains poorly understood. Thus, we investigated the effects of 'silencing' L6-*Drd1a* neurons using a *Snap25* conditional knockout mouse model (*Drd1a-Cre*$^{+/-}$*;Snap25*$^{fl/fl}$*;tdTomato*$^{STOPfl/fl}$) on the dopaminergic modulation of network activity in mPFC acute slices using high-density planar multielectrode arrays and whole-cell patch clamp recordings. We found that D1 receptor agonist SKF-81297 significantly increased broadband local field potential activity in the infralimbic mPFC, which was eliminated upon chronic 'silencing' of L6-*Drd1a* neurons. On the other hand, D2 receptor agonist quinpirole only increased infralimbic network activity in L6-*Drd1a* 'silenced' slices. Subsequent whole-cell electrophysiological characterization of L6 neurons in the mPFC revealed that D1 receptor activation selectively increased L6-*Drd1a* intrinsic excitability and spontaneous synaptic potential amplitude, while D2 receptor activation non-selectively excited L6 neurons. Taken together, these results suggest a postsynaptic mechanism of D1 receptor activation that increases L6-*Drd1a* excitability to drive mPFC network arousal, along with a compensatory mechanism of D2 receptor activation in the functional absence of these L6-*Drd1a* neurons. Our findings provide novel insight into the dopaminergic modulation of L6-*Drd1a* neurons in the mPFC that likely contributes to their orexinergic gating of cortical arousal, with relevant therapeutic implications for anxiety and stress-related disorders. All animal experiments were approved by a local ethical review committee and conducted in accordance with personal and project licenses under the UK Animals (Scientific Procedures) Act 1986.

SOPHIE MILLER PRIZE TALK

Early Life Adversity & Brain Structure: A Longitudinal Structural Human MRI study.

Orla Mitchell, Michael Connaughton, Darren Roddy.
Royal College of Surgeons in Ireland, Dublin, Ireland

Exposure to early life adversity is strongly linked to poor physical health outcomes and increased risk of developing psychopathology. However, the underlying mechanisms driving these outcomes remain unclear. The IMAGEN project is a European multicentre research initiative focusing on how genetic, environmental, and social factors influence brain development and mental health in adolescents. This investigation took longitudinal structural MRI data from the IMAGEN consortium, collected at 14, 19 and 22 years of age, to investigate the impact of exposure to adverse experiences in early life on structural brain development. Exposure to adverse events was measured through a self-report questionnaire, the Life Events Questionnaire. A stressful life event frequency score was calculated to quantify cumulative exposure to adversity. To analyse the effects of early life adversity on brain development over time, a top-down mixed-effects model selection procedure was implemented. This approach systematically refines mixed effects models to identify the optimal fit for each brain region examined. This is particularly important for longitudinal structural brain investigations as different brain regions have different developmental trajectories. The findings of this investigation indicate significant associations between early life adversity and altered brain development. High stressful life event scores were significantly associated with both increases and decreases in volumes in cortical and subcortical regions across the brain. These findings reinforce the understanding that exposure to early life adversity is associated with altered brain development. Some of the associated structural changes were identified in regions with functions related to limbic and executive control, which may posit a neurobiological framework to explain the risk of later life psychopathology. The next phase of this research will examine whether these volumetric changes mediate the relationship between early life adversity and increased psychopathology risk, as well as whether resilience factors, such as caregiver attachment, play a protective role. By improving the understanding of how adversity shapes the developing brain, this work aims to identify potential intervention targets, ultimately contributing to better outcomes for those affected by early adversity. Ethical approval was obtained by the IMAGEN consortium from local research ethics committees at each recruitment site, and written informed consent was provided by all participants in accordance with the Declaration of Helsinki.

INVITED SPEAKER

Pathophysiology of neurodevelopmental disorders associated with low birthweight: insights from a rat model.

Masahiro Tsuji
Kyoto's Women's University, Kyoto, Japan

One in seven babies worldwide is born with low birthweight (<2,500 g) due to preterm birth and/or fetal growth restriction. These individuals are at increased risk for neurodevelopmental disorders, such as attention-deficit/hyperactivity disorder (ADHD) and autism spectrum disorder (ASD). The major causes of low birthweight include infection/inflammation and placental insufficiency/hypoperfusion. However, the mechanisms by which such adverse intrauterine environments lead to neurodevelopmental disorders remain unclear. We developed a rat model of mild intrauterine hypoperfusion, which results in low birthweight, hyperactivity, and reduced sociability, without overt anatomical or histological changes in the brain. This model, therefore, partially reproduces conditions observed in children with neurodevelopmental disorders associated with low birthweight. Compared to sham-control animals, our rat model shows increased levels of inflammatory cytokines in the placenta, while cytokine levels in the serum and cerebrospinal fluid of the offspring show only marginal increases. The number of microglia in the offspring's brain does not increase. However, the corpus callosum in low birthweight rats is thinner than that in sham-control rats. No significant changes are observed in brain vasculature. Although histological analyses do not show significant changes, single-cell RNA sequencing reveals alterations in the composition of brain cell types in low birthweight pups. Imaging mass spectrometry reveals a significant decrease in serotonin levels in the cortex, with trends toward decreased serotonin in the brainstem and decreased norepinephrine in the locus coeruleus. Single-cell RNA sequencing shows changes in specific cell clusters. These results suggest that reduced levels of neurotransmitters in specific brain regions may contribute to the pathophysiology of neurodevelopmental disorders associated with low birthweight. Our findings align with hypotheses proposed in the literature, suggesting that maternal immune activation and altered neurotransmitter levels may contribute to the pathophysiology of these disorders. All animal experiments were approved by the institutional ethical committee for animal experiments and conducted in accordance with the Guidelines for Proper Conduct of Animal Experiments (Science Council of Japan).

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INVITED SPEAKER

Variation in human brain development.

David Price, John Mason and Wai Kit Chan
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The heritability of a phenotype or trait is a measure of how much of the inter-individual variation in that trait is due to genetic variation. The amount of phenotypic variation that is not accounted for by genetic variation could be due to external environmental variation. However, many studies have shown that genetic and external environmental variation are not sufficient to explain all of the observed phenotypic variation in many traits. A third source of variation is likely to be the ever-changing internal environment during development and the inevitable random person-to-person variability that occurs in the massively complex biochemical events that unfold as we grow (in other words, noise in the system). It is likely that many genes function primarily to limit the impact of this internal variability and random fluctuations, thereby ensuring reproducible outcomes within limits compatible with evolutionary survival. I will illustrate this with two examples of the effects of removing the function of either a single gene (*PAX6*) or a polygenic region (16p11.2) on brain cells developing in organoids. In both cases, the major effect of removal was an increase in the range of phenotypic outcomes. Our findings highlight the fact that increased variability in a phenotype rather than a change in the average might be the main outcome of deleting some genes. This might help explain why some human genetic variants have highly variable effects on individuals.

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INVITED SPEAKER

Short- and long- term effects of acute early-life activation of the GABAa receptor on neuronal development in mouse.

Ane Goikolea-Vives[1], Michael Thomas[2], Claire Thornton[1], Cathy Fernandes[3], Helen Stolp[1]

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Neurodevelopmental disorders affect up to 5% of the population, contribute to life-long disability, and arise from a mixture of genetic and environmental events. Excitatory-inhibitory (EI) imbalance in the brain has been identified as part of the pathophysiology of neurodevelopmental disorders, though there is variation in how this imbalance manifests between conditions and sub-groups of affected individuals. To test the hypothesis that early-life EI-imbalance may alter the developmental trajectory of the brain, in a manner that is age- and sex-dependant, we used the $GABA_A$ receptor agonist muscimol to produce an acute EI imbalance at three developmental stages in the postnatal mouse. Primary neurons were cultured from E14 mouse cortex and treated with 0, 1 and 5µM Muscimol at DIV3 or DIV6, prior to assessment at DIV7. Treatment with 1µM and 5µM of Muscimol on DIV3 reduced neural branching complexity, average neurite length and neurite number. When cells were treated with 1µM and 5µM of Muscimol on DIV6, reduced neural branching complexity and average neurite length, but not neurite number, were observed. Calcium imaging revealed alteration in network activity on DIV7. Postnatal mice, C57Bl/6 background, received daily i.p. injections of 5µl saline or muscimol (Sigma, 0.5mg/kg) at postnatal day (P)3-5, P7-9, or P14-16. Tissue was collected at multiple time points from 4h to adulthood. Animal experiments were performed with ethical approval from the Royal Veterinary College AWERB and under home office licence number PDAD9E285. Muscimol treatment resulted in acutely elevated cytokines (interferon and IL-10) in the developing brain, as well as small age-dependent changes in cortical layering. Long-term behavioural differences were identified in mice treated at P3-5. In particular, female mice treated with muscimol showed reduced social behaviour. Together these data support the hypothesis that early-life EI-imbalance can alter the developmental trajectory of the brain, in a manner that is age- and sex-dependant. Breeding and experimental procedures were carried out in accordance with the UK Home Office (Scientific procedure) Act (1986) and project approval from the Royal Veterinary College Animal Welfare and Ethical Review board.

INVITED SPEAKER

Tridimensional analysis of human nervous system development.

Alain Chedotal
Institut de la Vision, Paris

INVITED SPEAKER

An insight into human cortical development from adult neurogenesis.

Anton Tonchev
Department of Stem Cell Biology, Research Institute, Medical University of Varna , Bulgaria

Brain progenitor cells reside along the subventricular zone (SVZ) along the lateral ventricle of the adult mammalian brain. These cells decrease with age and are scarce in the primate SVZ. In order to enhance their proliferation in primates, we applied a model of brief global cerebral ischemia to adult macaque monkeys, microdissected the SVZ and studied the differentially expressed genes following bulk RNA-Sequencing. Among the up-regulated genes that by Gene Ontology exhibited functional features of “cell proliferation” and “Nervous system development” we identified a group that was not associated with brain progenitors in the adult mammalian brain. A top-expressed gene of those was the apelin receptor (APLNR) that transduces to cells signals from the small peptide apelin. In addition to the adult brain SVZ niche, we found APLNR expression in the developing human cerebral cortex: in progenitor cell of the ventricular zone and in the outer SVZ. Electroporation of APLNR an its ligand apelin in human cortical organoids lead to increased proliferation (Ki67+ cells) and generation of FAM107A-positive apical radial progenitors and TBR2-positive non-apical progenitors. This lead to increased numbers of CTIP2+ and SATB2+ neurons in the organoids. These data suggest that the apelin-APLNR system might act in the cortical organoid stem cell niche to affect the neuronal output.

Orexin-activated neurons of the human cortex

Tim Zolnik
Charité Universitätsmedizin, Berlin

Extrinsic modulation of cortical development by early thalamic innervation in the human foetal brain.

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The cerebral cortex underlies the cognitive abilities that make humans unique. During prenatal development, cortical areas are patterned through a complex interplay between intrinsic genetic programs and extrinsic signals, primarily conveyed by early thalamocortical afferents (TCAs). Yet how these early thalamic inputs shape cortical development in humans remains poorly understood. To address this, we traced TCAs in mid-fetal human brains. As expected, TCAs innervated the subplate (SP), their earliest cortical target. Unexpectedly, we also found TCA collaterals reaching the expanded outer subventricular zone (OSVZ), as well as establishing physical contact with primate-enriched outer radial glia (oRGCs). This previously unrecognized interaction suggests that the thalamus may directly influence human cortical neurogenesis through multiple mechanisms. Both SP neurons and OSVZ progenitors were positioned to respond to secreted thalamic signals. We identified VGF as a promising candidate. While in rodents VGF expression is specifically restricted to sensorial thalamic nuclei, and the protein serves as a modulator for patterning of sensorial cortices, we demonstrate that in the human brain its thalamic expression has evolved to extend into the associative nuclei, including the mediodorsal nucleus (MD). Interestingly, the main target of TCA projecting from this nucleus is the prefrontal cortex (PFC), the cortical area underwent the most remarkable expansion over evolution culminating in human, and crucially responsible for our unique cognitive functions. Finally, we tested the effect of VGF secretion on the cortical cell populations target by the early TCA, and we showed that this molecule significantly enhances both proliferation of OSVZ progenitors and spontaneous activity of SPN in organotypic cortical slices in vitro, thus promoting the progression of cortical neurogenesis in a dual fashion. Overall, our study demonstrates that illustrate how evolutionarily conserved

neural connections and molecular pathways can converge with novel features to orchestrate the development of the human cortex. ***Ethical Statement:*** The study described was conducted using human fetal brain samples provided by the joint MRC/Wellcome Trust-funded Human Developmental Biology Resource (https://www.hdbr.org; HDBR) at Newcastle University (Projects 200538 and 200428). All tissue was collected with appropriate maternal consent and approval from the Newcastle and North Tyneside NHS Health Authority Joint Ethics Committee (REC reference: 23/NE/0135). Specimens were shipped according to a Material Transfer Agreement (MTA NU-008095) between Newcastle University and the University of Oxford. One human fetal sample used for transcriptomics was obtained with approval from the institutional ethics committees of Osaka National Hospital （approval no. 123）, Kyoto Prefectural University of Medicine (approval no. RBMR-C-638-3), and Tokyo Metropolitan Institute of Medical Science (approval no. 22-22). Cynomolgus monkey (*Macaca fascicularis*) facility and all experimental protocols were approved by the Animal Care and Use Committee CELYNE (C2EA#42). Common marmosets (Callithrix jacchus) were derived from a breeding colony at the Tokyo Metropolitan Institute of Medical Science (TMIMS). Animal experiments were approved by Institutional Animal Care and Use Committee of the TMIMS.

YOUNG INVESTIGATOR

Pituitary adenylate cyclase-activating polypeptide (PACAP) mediates bacterial endotoxin-induced fever via an effect on cyclooxygenase-2 and inflammatory cytokines in mice.

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Pituitary adenylate cyclase-activating polypeptide (PACAP) signalling is involved in various inflammatory processes. A common manifestation of systemic inflammation is fever, which is typically induced in animal models with the administration of bacterial lipopolysaccharide (LPS). It was suggested that there could be a role for PACAP signalling in LPS-induced fever, but the underlying mechanisms of how PACAP contributes to the febrile response have not yet been clarified. In this study, LPS (120 µg/kg) was administered intraperitoneally to mice with the Pacap gene, i.e., the gene encoding the PACAP protein, either present (Pacap+/+) (n=15) or absent (Pacap−/−) (n=14). Their thermoregulatory responses, serum cytokine levels, and tissue cyclooxygenase-2 (COX-2) expression were measured. The LPS-induced febrile response was found to be attenuated in Pacap−/− mice compared to their Pacap+/+ littermates starting from ~120 min postinfusion. Administration of LPS resulted in amplification of COX-2 mRNA expression in the lungs, liver, and brain of the mice in both genotypes at 210 min post-infusion. Serum concentration of the pyrogenic cytokines (pg/ml) interleukin (IL)-1α and β were significantly increased in Pacap+/+ mice in response to LPS compared with saline (IL-1α: WT-LPS: 52.5±13.5, WT-saline: 3.9±2.2; IL-1β: WT-LPS:26.5±8.3; WT-saline: 0.4±0.1; $p<0.001$), whereas the change was not significant between the treatment groups in Pacap−/− mice. For IL-1α and β, the intergenotype difference between the LPS-treated groups was also significant (IL-1α KO-LPS: 28.6±4.0, WT-LPS: 52.6±13.5; IL-1β: KO-LPS: 10.7±2.7, WT-LPS: 26.5±8.3; $p<0.05$). The serum concentrations of IL-6, IL-10, and TNFα were higher in LPS-treated than in saline-treated mice of both genotypes. However, the rise in IL-10 was significantly attenuated in Pacap−/− compared to Pacap+/+ mice in the LPS-treated group (KO-LPS: 29.3±5.2, WT-LPS: 45.7±7.1; $p<0.05$). PACAP signallingis known to be necessary for normal fever maintenance. Our results suggest that PACAP contributes to the later phases of LPS-induced fever by modulation of COX-2 protein expression in the periphery and the brain, as well as by augmentation of pyrogenic cytokine levels in the circulation. By advancing the understanding of the crosstalk between PACAP signaling and the “cytokine-COX-2” axis in systemic inflammation, these findings can create opportunities for new therapeutic approaches. Ethical approval: BA02/2000-6/2018 Grants and support:ÚNKP-23-3-II-PTE-1781

YOUNG INVESTIGATOR

Mechanisms of epithelial symmetry-breaking during mammalian morphogenesis

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Morphogenesis, the process through which cells organise to form tissues and organs, is fundamental to the development of branched structures in organs such as lungs and kidneys. Tissue branching significantly increases surface area to volume ratio, facilitating an efficient exchange of nutrients and waste products. The development of branches usually begins when some cells advance and their neighbouring cells do not, even though they are of the same cell type. The mechanism behind branching onset is not completely understood. The aim of this project is to understand what causes the system to break its symmetry – essentially, what makes identical cells behave differently, with some growing forward and others remaining behind. In this project, we investigate the factors that trigger the initiation of branching by examining the role of cytoskeletal changes in individual cells. Previous research has demonstrated that kidney epithelial cells at convex 2D culture borders exhibit increased protrusive activity compared to cells at concave borders, and that this process is independent of a diffusible autocrine inhibitor of motility. We hypothesise that tension-mediated motility may be responsible for making some cells protrude more than others, subsequently driving branch formation. To test this hypothesis, we test whether directly inducing cytoskeletal alterations to promote cell protrusion in a 3D culture system is sufficient to make the cells become branch tip leaders. We use Madin-Darby Canine Kidney (MDCK) cells, which form 3D cysts when cultured in collagen hydrogels, acting as a model of renal development. We have created mixed cysts comprising both wild-type and genetically modified cells. The modified cells express OptoShroom3, an optogenetic construct designed by Miki Ebisuya's group. OptoShroom3 induces apical constriction in cells upon blue light exposure. By selectively altering the shape of single cells within the cysts, we assess whether such cytoskeletal change increases the cell's propensity to become a branch tip leader. Our findings will contribute to a better understanding of the cellular mechanisms that underlie the initiation of branching morphogenesis. No ethical approval required.

YOUNG INVESTIGATOR

Selenium and Magnesium Functionalised Scaffolds for Dual Bone Regeneration and Anti-Cancer Therapy

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Bone-related cancer defects are challenging to treat due to disrupted bone formation and resorption, inhibiting bone regeneration and poses a risk of recurrence from residual cancer cells. Incorporating bioactive ions into biomaterials has gained significant attention. Magnesium (Mg) can modulate bone resorption and formation, while Selenium (Se) has shown positive results as a cancer therapeutic, exhibiting oxidative and apoptosis-inducing effects against cancer cell lines. Nano-hydroxyapatite nanoparticles (nHA) are excellent candidates for ion delivery as their crystal structure can accommodate ionic substitution. This project aims to develop and characterise novel Se and Mg functionalised nHA to enhance the therapeutic effects of these ions followed by incorporation into a collagen-nHA scaffold to create a multifunctional bone regenerative and anti-cancerous scaffold for treating bone cancer defects. Se, Mg, and Se/Mg functionalised nHA particles and scaffolds (0–50 mM) were synthesised and characterised using FTIR, DLS, and ELS analysis. FTIR confirmed successful ion incorporation, with characteristic nHA peaks at 560, 602, and 1019 cm^{-1}, while size and charge remained unchanged. Scaffold compressive modulus was unaffected, though degradation rates increased at higher ion concentrations. Osteoclasts (RAW-264.7), mesenchymal stem cells (MSCs), and prostate cancer (LNCaP) cells were cultured with functionalised nHA nanoparticles and scaffolds to assess cytotoxic limits using quantitative assays such as Alamar Blue™ and Pico Green™. At 50 mM, across all groups, osteoclast, MSC, and LNCaP proliferation was significantly reduced. 1–10 mM, Se and Mg-nHA enhanced proliferation. When combined, Se and Mg exhibited a synergistic effect, significantly enhancing MSC proliferation while halting osteoclast proliferation. LNCaP proliferation on ion-loaded scaffolds (1, 5, 10mM) was also assessed. Se-nHA scaffolds (10 mM) completely inhibited LNCaP proliferation, while Mg had no significant impact on proliferation. Se/Mg-nHA scaffolds (10mM) exhibited an inhibitory effect compared to Se alone, with LNCaP proliferation remaining significantly reduced. By creating a multifunctional scaffold, it will allow for multi-targeting therapeutic that not only enhances bone formation but inhibits cancer cell proliferation, advancing the gold standard and future treatment options. This research is funded by the Anatomical Society. No ethics is required for this project due to commercial cell lines being used.

YOUNG INVESTIGATOR

Development of a Pro-Angiogenic Hyaluronic Acid Hydrogel Decorated with Vascular Cell-Derived ECM

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Chronic wounds present a significant global healthcare burden, due to their non-healing nature. Diabetic foot ulcers are particularly debilitating and life-threatening, affecting 19-34% diabetic patients. In vitro-generated ECM-derived biomaterials constitute an innovative approach to wound healing, as cell-derived ECM has the biological complexity required to control cell behaviour. Owing to their origin, we hypothesise that human induced pluripotent stem cell (hiPSC)-derived vascular cells will deposit ECM which enhances pro-angiogenic processes in vitro. As a source of pro-angiogenic ECM, hiPSCs were differentiated towards a vascular lineage through mesoderm induction by addition of CHIR-99021 while vascular specification was stimulated by addition of VEGF. Cells were separated by CD31 expression using magnetic-activated cell sorting, leading to two distinct cell populations: CD31-positive endothelial cells (iEC) and CD31-negative stromal cells (iSC). iSCs were subsequently characterised by PDGFR-α, SM-22, and vimentin immunostaining. ECM deposition by iSCs was stimulated by ascorbic acid (AA) and carrageenan (C), a macromolecular crowder. Following 21 days, decellularisation of iSC-deposited ECM was achieved by freeze-thaw, triton X-100, ammonium hydroxide, water, and DNase, and confirmed by DNA quantification and DAPI staining. Initial ECM characterisation was done by immunostaining. Scratch and tube formation assays determined the capacity of solubilised ECM to support angiogenic processes. Vascular differentiation of hiPSCs and separation into iECs and iSCs was confirmed by immunostaining and flow cytometry, while iSCs were characterised by positive PDGFR-α, SM-22, and vimentin immunostaining. Treatment of iSCs with AA and C increased ECM deposition over 21 days, without compromising cell viability. Decellularisation was confirmed by reduced DNA concentration and negative DAPI staining. Immunostaining of ECM components confirmed deposition of fibronectin, which was retained after decellularisation. Supplementation with ECM enhanced iEC migration and the formation of tube-like networks. Our results show that iSCs deposit an ECM that when decellularised, enhances iEC migration and tube formation in 2D culture, suggesting its capacity to support angiogenesis. Next steps will focus on histological and proteomic analysis of the ECM, and probing the pro-angiogenic potential of the ECM when incorporated within an AcHyA hydrogel. Ultimately the pro-angiogenic and reparative potential of this ECM-AcHyA hydrogel will be assessed in a pre-clinical model.

YOUNG INVESTIGATOR

Advanced Synovial Microneedle Technology for Drug Delivery to Prevent Post Traumatic Osteoarthritis

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Post-traumatic osteoarthritis (PTOA) is a subtype of osteoarthritis (OA) that commonly develops after acute joint injuries, such as anterior cruciate ligament (ACL) rupture. OA is a leading cause of mobility-related disability, and the rising incidence of PTOA places a growing burden on healthcare systems. While current surgical approaches to knee injury focus on mechanical stabilization, they do not address the underlying inflammatory processes that contribute to PTOA development. Moreover, conventional biologic treatments are limited by rapid clearance from the joint space via vascular or lymphatic drainage. To overcome these challenges, a novel microneedle array patch (MAP) system was designed for intra-synovial insertion during arthroscopic surgery. This system enables the controlled, localized release of bioactive molecules to modulate post-injury inflammatory responses. MAPs were fabricated using polycaprolactone (PCL) loaded with MCC950, a selective NLRP3 inflammasome inhibitor. The polymer-drug mixture was cast into micromoulds and thermally processed at 80°C under vacuum. Mechanical testing confirmed that the MAPs had adequate strength for tissue insertion, and scanning electron microscopy revealed well-formed needle structures. A validated high-performance liquid chromatography (HPLC) method was developed in line with the International Council for Harmonisation of Technical Requirements of Pharmaceuticals for Human Use (ICH) guidelines to assess MCC950 release and polymer degradation over a 45-day hydrolytic incubation. Thermal stability of the formulation was confirmed via differential scanning calorimetry and thermogravimetric analysis. In vitro assays using LPS-primed THP-1 monocytes demonstrated that MCC950 significantly reduced IL-1β secretion, confirming its bioactivity. This platform holds promise as a prophylactic treatment strategy for PTOA by combining mechanical delivery with controlled release of an anti-inflammatory therapeutic. Ongoing studies are developing a 3D in vitro synovial tissue model to further evaluate the therapeutic potential of the MAP system.

YOUNG INVESTIGATOR

Evaluating osteoblast-fibroblast co-culture in a multiphasic calcaneofibular bone-ligament scaffold

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The calcaneofibular ligament (CFL) of the lateral ankle ligament complex is frequently injured and contributes to the onset of chronic ankle instability. Injuries commonly occur at the ligament's attachment to bone, the enthesis, where complex mechanical and structural properties result in poor healing outcomes. These limitations have driven the exploration of tissue engineering approaches for ligament repair. In earlier stages of this study, a bone-ligament scaffold model was developed to replicate the macro and micro-anatomical features of the native CFL, guided by detailed morphological analysis. The current work builds upon this foundation by assessing the biological performance of the engineered scaffold. Therefore, the aim of this study is to (1) assess cell adhesion and proliferation on the individual scaffold components and (2) develop a co-culture system that supports the integration of both cell types to replicate the full structure of the CFL, including its enthesis. Cell adhesion and proliferation were assessed on both scaffold components: brushite cement blocks and poly-lactic acid (PLA) electrospun fibres. Proliferation was monitored over 7 days to evaluate cell growth. For co-culture setup, differentiated rat osteoblasts (dROBs) were seeded onto bone blocks and cultured for 3 days prior to adding rat tendon fibroblasts (RTFs) to the ligament portion. Once cell proliferation was completed, three bone-ligament model variants were tested: (1) CFL model with electrospun fibres, (2) CFL model with electrospun fibres and fibrin gel, and (3) CFL model with fibrin gel alone. CFL constructs were cultured for 14 days. Tissue growth and enthesis development were examined histologically. Mechanical strength was evaluated through tensile testing of all CFL model variants. The scaffolds supported cell viability, with no signs of cytotoxicity or adhesion issues and allowed for anatomically accurate cell organisation. Imaging demonstrated even cell distribution across the scaffold, including infiltration into porous regions, while quantitative analysis indicated sustained cell proliferation over time. This model provides a foundation for developing anatomically accurate, tissue-engineered CFL replacements, potentially improving treatment outcomes for ligament injuries and surgical repair strategies.

YOUNG INVESTIGATOR

Developing An Injectable Hyaluronic Acid-based Hydrogel Containing Non-viral P2X7R Silencing RNA Nanoparticles For The Treatment Of Post-Traumatic Temporal Lobe Epilepsy

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Temporal lobe epilepsy (TLE) is the most prevalent acquired seizure disorder, often caused by brain injury. Anti-seizure drugs are ineffective in 33% of patients, classed as having drug-refractory TLE. These systemic treatments additionally fail to tackle the underlying disease pathophysiology and are associated with cognitive side effects. The purinergic receptor P2X7R, highly expressed on microglia within injured brain regions, contributes to chronic inflammation. Notably, systemic P2X7R inhibition has shown disease-modifying effects in murine TLE models. However, as P2X7R is widely expressed throughout the body, focal delivery is crucial for future P2X7R-targeting therapies. Therefore, the key aim of this study was to develop a brain-compatible injectable hyaluronic acid (HA) hydrogel carrying encapsulated P2X7R-targeting silencing RNA (siRNA) for non-viral delivery to the brain for the treatment of TLE. A photo-crosslinkable hydrogel was produced by reacting HA with methacrylic anhydride. The degree of methacrylation was measured by NMR spectroscopy and material gel properties were characterised. P2X7R-targeting siRNA was delivered to murine microglial cells using a non-viral vector, and P2X7R knockdown and cell phenotype were validated by PCR. Pro-inflammatory cytokine release was quantified by ELISA. Crosslinked MeHA exhibited mechanical properties compatible with neural cells, a mesh size suitable for retaining encapsulated siRNA, and a robust degradation profile. Using reporter siRNA, an optimal nanoparticle concentration of 50nM was found to achieve high microglial cell internalisation with minimal cytotoxicity. Following non-viral P2X7R siRNA transfection, P2X7R knockdown was successfully demonstrated in reactive microglial cells as well as significant downstream reductions in IL-1β release. Injectable hydrogels can act as tuneable drug delivery vehicles for neural applications that overcome several limitations associated with systemic drugs. Here we tuned the properties of a MeHA hydrogel to mimic native brain tissue, optimising it for cortical delivery of P2X7R-targeting siRNA. In vitro experiments indicate that siRNA transfection promotes microglial P2X7R knockdown which reduces neurotoxic cytokine release, and future work will involve confirming the disease-modifying effects of this system in vivo using a murine TLE model. In summary, this gene-activated hydrogel demonstrates potential to act as a novel disease-modifying treatment strategy for drug-refractory TLE patients. Funded by Research Ireland. No ethical approval required.

YOUNG INVESTIGATOR

A simplified clinically applicable classification of Circle of Willis variants.

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The Circle of Willis (CoW) displays considerable variability that must affect the nature and haemodynamics of the collateral blood supply with potential consequences in cerebrovascular disease. Mechanical thrombectomy following computed tomography angiography (CTA) has become a routine treatment for ischaemic stroke, and CTA has facilitated assessment of CoW variation in many more individuals compared to previous work based on cadaveric dissection. This study reviews the role of CoW variants in cerebrovascular disease, focusing on aplastic (not visible on CTA) and hypoplastic (<1mm) elements. A Pubmed search identified five systematic reviews and meta-analyses evaluating the roles of CoW variants in cerebrovascular conditions, encompassing over 50 primary studies. The incidence of ischaemic stroke (OR = 1.38), intracranial aneurysm (OR = 7.97), and leukoaraiosis (OR = 1.66) was found to be associated with absent CoW components. A pooled analysis for intracranial aneurysm revealed that aplastic/hypoplastic CoW components were associated with aneurysm rupture (OR = 1.87). The influence of CoW variants on functional outcome in stroke was less clear. Current descriptions of all CoW variants are unwieldy and not clinically relevant. Therefore, we propose a simple clinically applicable system based on aplastic/hypoplastic vessels and laterality that could guide radiological intervention and patient management. This suggested coding identifies the vessel (e.g., AC for anterior communicating; P for posterior cerebral), laterality (left-L, right-R, or bilateral-B), and aplasia/hypoplasia (A or H). Some of the most common variants are hypoplastic posterior communicating arteries (PC), coded as PC(L-H) unilaterally, or PC(B-H) bilaterally. This simplified coding provides a quick method of reporting clinically significant variation. Current literature largely reports aplasia/hypoplasia of the AC and PC where variations are common and have predominantly poor prognostic consequences in ischaemic stroke and aneurysm rupture. However, variants have different effects, e.g., a fetal-type posterior communicating artery has been reported to be associated with improved functional outcome following brainstem occlusive disease, suggesting that some variants may even be protective. Use of the proposed system in neuroradiological reports will aid future research into the association of variants with pathology by identifying them before data collection and facilitate improvement in patient management.

Exploring Anatomy Education: A Comparative Analysis of Cadaver Dissection and 3D Anatomical Study Tool

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Anatomy being a foundational subject in medical education offers crucial insights into the structure and function of the human body. For eons, cadaveric dissection has been the standard method of teaching anatomy. However, over the past few decades, advancements in teaching tools and methods have been explored due to change in the students approach to learning. Also, regulatory bodies have emphasized the inclusion of imaging and 3D anatomy. The incorporation of modern technologies and teaching methods has the potential to enhance both student engagement and resolve the issue. Worldwide use of Technology and AI is at its peak, thus it is necessary to assess the effectiveness of 3D animation tools in the field of anatomy. To introduce 3D imaging tool for teaching human anatomy. To evaluate the acceptability, feasibility and effectiveness of using anatomy by 3D Imaging tool teaching. A prospective crossover randomized controlled study was conducted with 160 Phase I medical students who had no prior knowledge of the gross Anatomy topic being studied. The students were randomly divided into three groups, each taught the same topics using different methods: Group 1 learned through 3D animation on the Sectra tool, Group 2 taught on cadaver displayed through camera and LCD screens and Group 3 studied with cadaveric specimens. Pre- and post-tests were administered to assess knowledge gains, and online feedback surveys were collected from the students to evaluate their experiences.An Informed consent was taken from each student. The initial compilation of results shows a very impressive increase in knowledge with the use of Sectra and teaching on cadaver displayed through camera and LCD screens. The feedback from the students for these methods also show a greater satisfaction. The detailed analysis of the scores and feedback is under progress. While cadaveric learning remains the most widely used method for teaching anatomy, recent technologies like 3D software and camera with LCD are also seen as valuable educational tools. However, more research is needed before these can be confidently integrated into a multimodal curriculum, as the findings from this study are limited to the gross anatomy of limited topics.

Equipping future clinicians: Inclusive anatomy teaching amid legal and social challenges to gender equity

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Anatomy education has historically underrepresented cisgender female, transgender female, intersex, ethnically diverse, and sexually diverse identities. This lack of representation reinforces narrow clinical norms and contributes to social and health inequalities. This project aimed to apply an original equality, diversity, and inclusion (EDI) framework to identify and address bias within the undergraduate medical anatomy curriculum. The framework focuses on three key areas: promoting positive representation of diversity, deconstructing assumed "norms," and integrating social responsibility. It was used to evaluate and create inclusive anatomy worksheets, case studies, and illustrations, and to design four small-scale, student-led, mixed-methods studies exploring bias and perceptions in anatomy and clinical education. Medical students and anatomy teaching staff at the University of Birmingham participated in surveys and educational sessions. One study focused on reproductive anatomy and found that students believed female external genitalia were taught in less detail than male genitalia ($p < 0.05$) and reported feeling less prepared to address female health concerns ($p < 0.05$). Staff reported lower confidence in teaching female and intersex anatomy ($p < 0.05$), citing cultural sensitivities and a lack of training. Other studies explored student observations of gender and ethnicity bias in pain management. Students noted that female patients often had to advocate more strongly for pain relief and that psychological causes were more frequently attributed to women. However, many struggled to recognise the intersection of gender and ethnicity bias. To address underrepresentation, inclusive hybrid 3D-printed wax models representing diverse genital anatomy were developed. These were integrated into a self-directed session for students and staff, resulting in shifts in confidence and perceptions. The EDI framework also informed public engagement activities that aimed to challenge societal perceptions of bodies and pain. This project shows how an EDI framework can be used to improve representation and awareness in medicine and society. This need is amplified by the 2025 UK Supreme Court ruling, which upheld a legal definition of "woman" based solely on biological sex, excluding transgender and intersex individuals. Ethical approval was granted by the Department of Biomedical Science Ethics Committee, University of Birmingham, under reference numbers BMSRP_2025_EDU014, BMSRP_EDU015, BMSRP_2025_EDU17, and BMSRP_2025_PGR001.

Exploring the teaching traditions of Central European anatomists through the Erasmus+ LEANbody collaborative project

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Central European anatomists from Brno (Czechia), Pécs (Hungary), and Zagreb (Croatia) investigated whether the quality of their traditional anatomy courses can be further developed with the support of anatomists from the University of Cambridge and educational developers from the Karolinska Institute in the LEANbody ERASMUS+ project from 2021-2024. While course organisers from these medical schools have adapted some features of their teaching styles to the multicultural and multilingual contexts of their profitable international programmes, the attrition rate remains high. Out of 69 Central European anatomists surveyed, over 70% admitted to having limited knowledge of the following: international quality standards of medical education, student-centered pedagogy, professional development of the attitudes of both medical students and teaching faculty, and mental health management in the workplace. 69% of Hungarian, 50% of Czech, and 10% of Croatian anatomists reported high failure rates in anatomy examinations. As high as 63% of students failed in their first attempt, and among those who passed, only 30% achieved “good” grades or above. In contrast, the pass rate for University of Cambridge students in their anatomy exams was 96%, with >65% having “good” or ”excellent” grades. Half of the participating anatomists could not confirm the existence of a formal document that stipulates the rules of conduct for medical students within the anatomy course. 70% of anatomists were unfamiliar with the pedagogical concept of Constructive Alignment, widely used in Western European medical programmes. However, after being introduced to this framework, some Central European anatomists have recorded as much as 60% improvement in examination grades achieved by their students. The project also assessed the general mental well-being of participating anatomists. Significant stressors, such as excessive workload, time pressure, and interpersonal communication challenges were prevalent (>20% of anatomists). Burnout was present in one-third of participants, with disengagement being the most commonly reported symptom. Our data point to a need for closer educational collaborations between Western and Central European anatomists which can help in the exchange of best practices in both traditional and student-centred teaching of human anatomy in Europe and beyond. No additional ethical approval was needed for our surveys beyond ERASMUS+ requirements.

Anatomage Presentation

Anatomy at Sheffield - From Scalpel to Virtual Dissection and Beyond

Daniela I. Cacciabue
University Teacher and Anatomy Lead for the School of Biosciences, University of Sheffield, UK

The pedagogical approaches to anatomy have undergone significant transformations throughout history. An exhibition in Sheffield explores this evolution, tracing the journey from traditional methods to contemporary innovations. It outlines the scope of the exhibition, which begins by investigating the new technologies that are revolutionizing anatomy education at the University of Sheffield. It then explores the historical context, examining the challenges and perceptions surrounding anatomy teaching, particularly leading up to its formal establishment at the University in 1904. Concluding the journey, the exhibition showcases centuries-old anatomy textbooks from the Rare Books Collection, highlighting the pioneering scientific contributions of early anatomists and the remarkable technical artistry of their illustrators and printers.

INVITED SPEAKER

Uncovering the strategies of human radial glia using high throughput genomics

Tom Nowakowsk

UCSF, San Francisco, USA

INVITED SPEAKER

Advances in human brain proteomics; Increased-throughput, sub-cellular discovery, and post-translational modifications

Sara Bandiera[1], H Bogetofte[2], P Jensen[2], R Hussain[1], SA Nischal[1], L. Rihova[1], MR Larsen[2], Zoltan Molnár[1], Becky C Carlyle[1]

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In 2017 we published a proteomic survey of the postnatal human brain. We had 77 samples in this study. Sample preparation took over a month, data acquisition took almost half a year, and data processing repeatedly failed over a span of multiple weeks. By carefully combining sample fractionation methods with advanced data processing, we managed to identify just under 9000 proteins from each brain region, and quantify just over 3500. Since then, the throughput of mass-spectrometry proteomics has exploded to the extent that last year, we prepared 525 samples for analysis in two weeks, acquired the data over a long weekend, and processed the data in under 48 hours. With 8 minutes of data acquisition time, we quantified approximately 8000 proteins per sample. These technological developments have brought exciting new capabilities to mass-spectrometry research. In this talk I will cover some of the most major developments in the technology, before focussing in on two techniques we have developed in our labs. Fractionation studies developed in the Carlyle lab allow the assignment of proteins to specific sub-cellular locations, providing increased functional information about novel proteins and disease states. Post-translational modification enrichment methods developed in the Larsen lab can be used to quantify protein regulatory mechanisms offering fresh insight into protein production, modification and regulation. With this talk, we hope to persuade the audience that these development place us at the start of an exciting new era in human brain proteomics, with many opportunities for collaboration and discovery. Ethics statement For the sub-cellular experiments, frozen human dorsolateral prefrontal cortex was collected by the Rush Alzheimer's Disease Research Center and Lieber Institute for Brain Development with full consent for research. Receipt of the tissue occurred under material transfer agreement, and project ethics was approved by the Oxford Tropical Research Ethics Committee (OxTREC 567-22 and 541-23). For post-translational modification experiments, the left hemisphere of a human fetal brain was obtained from a medical abortion at 20 PCW by the Human Developmental Biology Resource (HDBR), University of Newcastle. The tissue was collected with maternal consent and approval from the Newcastle and North Tyneside NHS Health Authority Joint Ethics Committee. The hemisphere was transferred according to the material transfer agreement.

INVITED SPEAKER

Functional Genomics of Human Brain Development and Neuropsychiatric Disorders

Jourdon A[1] *, Mariani J[1]*, Natu A[1]*, Wu F[1]*, Li B, Capauto D[1], Hagy KT[2], Tomasini L[1], Safi A[2], Nelson MP[3], Ramos DM[3], Ward ME[3], Gersbach CA[2], Crawford GE[2], Abyzov A[4], Flora Vaccarino[1#]

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Since the discovery of induced pluripotent stem cell (iPSC) more than a decade ago, iPSCs and brain organoids have become a widely used tool to investigate human brain development, from early patterning of neuroepithelial cells to the emergence of neuronal and glial cell lineages and their interconnections. Cell differentiation involves a complex series of regulatory shifts in chromatin organization where regulatory elements, primarily enhancers and their cognate transcription factors (TFs), activate or repress cell fate genes in a time-dependent manner. We integrated active chromatin and gene expression to build a gene regulatory network (GRN) underlying forebrain neuron differentiation and identified TFs driving major transitions in cell differentiation and cell fate trajectories. Individuals with idiopathic autism spectrum disorder (ASD) exhibited an imbalance in cell fate where ASD with macrocephaly exhibited a relative excess in excitatory cortical neurons, and ASD without macrocephaly an opposite defect in in excitatory cortical neuron differentiation. Using the regulatory network we identified key upstream determinants of ASD-associated differential gene expression. We linked ASD dysregulated genes to hubs of TFs (e.g., BHLHE22, FOXG1, EOMES, NEUROD2) and corresponding enhancers which were dysregulated in opposite directions in ASD with or without macrocephaly. Multiple elements in this vast network (TFs, targeted enhancers and downstream genes) could be responsible for causing imbalances in excitatory and inhibitory neurogenesis in people with autism, in keeping with the heterogeneity of the disorder. The elucidation of biologically distinct disease subtypes could be used as potential stratifying factors in clinical or genetic studies. Ethical statement: Written informed consent was obtained from each participant who donated biospecimens for generating iPSC lines, and all research was approved by the Yale University Institutional Review Board (HIC# 1104008337) and Yale Center for Clinical Investigation at Yale University and was performed in accordance with the Declaration of Helsinki. Human participants' names and other HIPAA identifiers were removed from this presentation. The participants agreed to data sharing of genomic unidentified data using controlled data access.

INVITED SPEAKER

Modelling monogenic epilepsy in human foetal brain slice cultures

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Early infantile epileptic encephalopathies (EIEE) of genetic origin are devastating conditions, but the pathological mechanisms often remain obscure. A major obstacle is the difficulty of studying human cortical brain development, *in utero*. Using a novel approach to maintain developing human brain tissue in the laboratory, we investigated STXBP1 haploinsufficiency—one of the most common genetic causes of EIEE—and previously demonstrated that loss of STXBP1 impaired synaptic function and reduced glutamatergic synapse density at individual neurons (McLeod et al., *Brain*, 2023). To further understand how deficits in STXBP1 affect the early developing brain, we investigated the impact on neuronal networks. Human foetal brain slice cultures were prepared from ethically sourced, 14-17 post conception week cerebral cortex tissue (www.hdbr.org). The gross anatomical structures of the marginal zone, cortical plate and subplate were maintained for several months, while synaptic networks continued to develop. We assessed the impact of shRNA mediated STXBP1 knockdown and the downstream effects on an intact developing human cortical network using three powerful screening tools: (1) multi-electrode array recordings; (2) Ca^{2+} imaging using genetic encoding calcium indicators; (3) gene expression profiles using NanoString nCounter technology. We observed a significant reduction in the frequency of spikes and field potential events in slices with reduced STXBP1 levels. Furthermore, there was a decrease in the amplitude of calcium transients in the subplate and the number of active cells contributing to synchronised calcium activity. Loss of STXBP1 resulted in an upregulation of 81 genes associated glutamate receptor activity, ephrin signalling and vesicle recycling and a downregulation of 47 genes associated with pathways such as apoptosis and oxidative stress. We were able to confirm some, but not all the mRNA expression changes at the protein level by western blot and high-resolution immunofluorescence. Notably, there was an increase in vesicle recycling proteins, perhaps partially compensating for loss of STXBP1, but no significant increase in postsynaptic receptor subunits. In conclusion, intuitively, reduction of excitatory synaptic transmission might be predicted to reduce the likelihood of epilepsy. However, if early disruption and desynchronisation of subplate network activity is the result of STXBP1 haploinsufficiency, including long term changes in gene expression, this could cause a miswiring of cortical synaptic circuitry later in development, leading to seizure susceptibility.

3D printing cortical progenitors to study human brain development

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Traumatic brain injuries (TBI) are common and difficult to treat. Recent studies offer a promising perspective that neural implants may represent a new therapeutic approach. However, significant challenges remain, such as ensuring the survival, maturation, and integration of neurons into the brain. Additionally, these implants often suffer from inadequate vascularization and insufficient support cells. We investigated the therapeutic potential of 3D structures designed to replicate the structural and cellular complexity of the cerebral cortex. Using human neural progenitor cells (hNPCs) and techniques such as 3D bioprinting and microfluidics, we developed three-dimensional structures that simulate features of brain tissue architecture, such as lamination and diverse cellular composition. When implanted in the motor/somatosensory cortex of mice, implants enriched with astrocytes significantly reduced lesion size, increased axonal growth, and improved astrocyte coupling to blood vessels. These results highlight the potential of this approach for treating TBI and other neurological diseases. All animal experiments were approved by a local ethical review committee and conducted under the UK Animals (Scientific Procedures) Act, 1986 (ASPA), under valid personal and project licenses. Funded by: The Oxford Martin School

P1/1 The Many Faces of Imaging: A Collage of the Cover Graphics Submissions for the JoA Special Issue on Biomedical Imaging in Comparative Anatomy

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The May 2025 Issue of JoA (Vol. 246, Issue 5) was a fascinating Special Issue that presented a cross-section through the various imaging modalities currently being prioritised in anatomy pedagogy and research, including computed tomography, magnetic resonance imaging, and diffusion tensor imaging. These enabling imaging techniques, and the Special Issue reporting many of them through its eighteen articles, have caught the attention of readers with a visible popularity among the journal readership. Interestingly, many of the contributing authorial groups also contested for the selection of a suitable journal cover that is visually arresting, and in line with the spirit plus message of this Issue. Although only one of these submissions emerged to be the winner, the other submissions, with plenty of insights, imagination, and ingenuity, were too great to be discarded, and it is unfair not to provide them with some platform for showcasing the great work and passion that resonated through the diaspora of contributing authors. Here, we present a poster where a collage of these cover page graphics, which, despite being great, unfortunately, fell short of making it, will be presented (with due permission from the contributing groups). No ethical approval is necessary, given that the poster will showcase only a few images representing already published articles in JoA, and will not report any new research study or clinical trials.

P1/2 Zbtb20 expression in human fetal ventral forebrain

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During development, interneurons arise from the ventral forebrain, comprised of three ganglionic eminences: medial, lateral, and caudal. The medial and caudal ganglionic eminences give rise to cortical and striatal interneurons (CINs and SINs, respectively), while the lateral ganglionic eminence generates medium spiny neurons and olfactory bulb neurons. This developmental process is controlled by a variety of molecular regulators, which are well established in the mouse brain. Our recent data show that the zinc finger transcription factor Zbtb20, a critical regulator of the hippocampus, is also part of the regulatory molecular network for cortical interneurons in the mouse. In the present study, we aim to elucidate the expression of ZBTB20 in the neurogenic niche of the human ventral forebrain by combining ZBTB20 immunolocalization with stainings for known markers like ASCL1, NKX2.1, LHX6, and pHH3. Our results show that all NKX2.1+ and pHH3+ cells in the ventricular zone (VZ) express ZBTB20. In the subventricular zone (SVZ) LHX6+, present in more committed neuroblasts, do not express ZBTB20, while all proliferative cells (pHH3+) are also ZBTB20 positive. ZBTB20 expression is mosaic when paired with ASCL1: only a portion of the ASCL1+ cells in both the VZ and SVZ express ZBTB20. These results are consistent with the oscillatory behavior shown by ASCL1 and its expression at different stages of neuronal differentiation. These results suggest that ZBTB20 might be involved in the regulatory network for human cortical interneuron genesis. Human fetal brain tissue was obtained from spontaneous abortions that occurred in the Hospital for Obstetrics and Gynecology “Prof. Dimitar Stamatov,” Medical University of Varna (MUV), Bulgaria. Informed written maternal consent following the approval of the local MUV ethics committee.

YOUNG INVESTIGATOR

P1/3 Neurexin1 expression in early human foetal forebrain

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Neurexin1 (NRXN1) is presynaptic terminal protein and candidate neurodevelopmental disorder susceptibility gene. Mutation may upset synaptic stabilization and function .We previously showed by tissue RNA seq, qPCR and immunohistochemistry (IHC) that NRXN1 expression was high in the fetal human cerebral cortex between 8-12 PCW when synaptogenesis is limited . IHC suggested that protein expression was highest in the cortical plate (CP) and progenitor zones , not the synapse containing subplate. In this study we re-examined the location of NRXN1 expression. Transcriptomic data was taken from the following database (solo.bmap.ucla.edu/shiny/webapp/) and NEMO analytic –NeMO Analytics - scRNA workbench) then paraffin sections 8-12 post conceptional week (PCW) were obtained from the human developmental biology resource(HDBR. Org)with maternal consent and ethical approval and used for RNA scope in situ hybridization (ISH) against NRXN1 mRNA. In both cortex and thalamus RNA seq at 18PCW showed highest NRXN1 expression in more mature glutamatergic neurons. Some expression in GABAergic neurons, migrating glutamatergic neurons, non-dividing redial glia, and lowest expression in intermediate progenitors and cycling cells. For ISH ,at 18 PCW Expression was strong in the CP and low in the cortical progenitor zones except for boundary with the ventral telencephalon, where expression was also high in progenitor cell. In the ganglionic eminences, expression was higher in the proliferative zone than in the post-mitotic compartments. In the thalamus , expression was high in both proliferative and post- mitotic compartments and higher than in the pretectum and hypothalamus . This pattern was maintained at older stages (15-21pcw) but, in the cortex , expression increased in proliferative zones. Relatively stronger expression of NRXN1 in was seen in some emergent thalamic nuclei than others . This study confirms that, in the developing human forebrain, NRXN1is likely not to just sub serve synapse formation it is expressed quite strongly in certain proliferative zone but not others. It is most strongly expressed by glutamatergic neurons of the CP and thalamus .NRXN1 may have rolls in cell-cell recognition, migration and axon guidance. All tissue was collected with appropriate maternal consent and approval from the Newcastle and North Tyneside NHS Health Authority Joint Ethics Committee.

YOUNG INVESTIGATOR

P1/4 Investigating the effects of PAX6 haploinsufficiency on functional circuits in human cortical organoids

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Excitatory-inhibitory (E-I) imbalance in neural circuits may underlie some forms of neurodevelopmental disorder (NDD) such as autism spectrum disorder (ASD). Genetic loss of PAX6, which encodes a key transcription factor required for mammalian cortical development, has been implicated in the aetiology of NDD. Some patients with heterozygous PAX6 mutations show clinical manifestations of ASD but how PAX6 mutation might lead to the disorder remains elusive. Previous studies have shown that the loss of Pax6/PAX6 in mice and human models induces a fate change in some dorsal telencephalic progenitors in the developing cerebral cortex; these cells become GABAergic interneurons (INs) instead of glutamatergic neurons. We hypothesize that the presence of these ectopic GABAergic INs may disrupt the E-I balance, thereby affecting the normal functioning of cortical circuits. We aim to investigate the effects of PAX6 haploinsufficiency on functional circuitry and their mechanism using human induced pluripotent stem cell (hIPSC)-derived cortical organoids. We recorded calcium signalling as a readout of neuronal activity in both PAX6 control and mutant organoids, with a focus on examining the excitability of the neurons. The organoids were labelled with a calcium indicator called Fluo-4 AM followed by live imaging using confocal microscopy. Thus far we observed active neurons in our organoids of age Day 90 and above showing spontaneous activity during baseline recordings. Ongoing experiments include the pharmacological administration of compounds including kainate, 4-aminopyridine and potassium chloride to excite the neurons. We further aim to identify the quantity and distribution of GABAergic INs as well as the formation of GABAergic synapses in the organoids to address whether presence of ectopic INs affects neuronal excitability. Findings from this study can potentially reveal the mechanism underpinning ASD linked to PAX6 genetic loss. This work does not require specific ethical approval.

P1/5 Investigating region-specific changes in Srrm4 expression in a mouse model haploinsufficient for the autism-associated gene Chd8

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Autism spectrum disorder (ASD) is a neurodevelopmental condition affecting social communication and behaviour. A potential common mechanism underlying autism is the misregulation of brain-specific microexons that are frequently skipped in autistic individuals. The splicing factor Serine/arginine Repetitive Matrix 4 (Srrm4) is a key regulator of neuronal microexons and has been linked to ASD as its expression is reduced in individuals with ASD. Preliminary evidence suggests the expression of Srrm4 may be altered in mouse models of haploinsufficiency of the autism-associated gene Chd8. We used fluorescent in situ hybridisation (FISH) to determine Srrm4 expression in specific brain regions in this mouse model focusing on prefrontal cortex layer 5 and the hippocampal CA1 region. As synaptic transmission is dysregulated in the prefrontal cortex of Chd8+/- mice, we hypothesised that Srrm4 expression may also be altered in this area. We found a trend for a decrease in Srrm4 expression in prefrontal cortex layer 5 in the Chd8+/- mouse brain, with no changes observed in the CA1 region. Our results suggest that there may be region-specific changes in Srrm4 expression in mouse models of haploinsufficiency of ASD-associated genes. All procedures were done in accordance with the Animals (Scientific Procedures) 1986 Act and in accordance with the relevant project and personal licenses.

P1/6 The impact of β-hydroxybutyrate on glucose deprived neural stem cell health and development

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Glucose is the brains primary energy source during development supporting cell proliferation and differentiation, initially generating ATP by glycolysis and then via oxidative phosphorylation. High demand for glucose during early brain development may exceed its supply, leading to the utilization of ketone bodies, including β-hydroxybutyrate (β-OHB) produced through hepatic ketogenesis, to provide ATP via OXPHOS and the biosynthetic components for cell growth and maturation. Metabolic reprogramming from glycolysis to OXPHOS is essential during brain development and is partly responsible for directing stem and progenitor cell fates; however, the influence of nutrient deprivation and ketone body supplementation on precursor cell growth is unclear. This research examines the impact of anaplerotic and glycolytic input deprivation on precursor cell proliferation, viability and lineage, and investigates the potential of β-OHB to rescue to effects of nutrient deprived conditions in vitro. Neuroblastoma SH-SY5Y and E9 murine cortical neuroepithelial NE4C cell lines were cultured in glucose, low glucose, and glucose, pyruvate and l-glutamine deprived conditions for 96 hr to model the impact of metabolic influence on neuronal progenitor (NPC) and neural stem cell (NSC) cell growth respectively. Cell density, morphology, phenotype, viability and glycolytic activity were measured in nutrient deprived and in 10 mM β-OHB supplementation conditions. Both lines exhibited reduced density, metabolic activity, and L-lactate production under glycolytic input deprivation conditions; however, process length and cell volume were not significantly changed. NE4C cells showed increased sensitivity to nutrient deprivation, when compared to SH-SY5Y cells. Phenotypic analysis showed that nutrient deprivation and β-OHB supplementation did not induce spontaneous differentiation in SHSY5Y and NE4C cells. β-OHB reduced glycolytic activity, indicating a shift toward OXPHOS, yet failed to significantly rescue cell density or viability. These findings highlight the role of glucose in NSC and NPC metabolism and suggest that β-OHB may partially compensate for glucose deprivation by reprogramming metabolic pathways to OXPHOS; however, it does not fully rescue deficits in growth and viability. This research provides insights into the metabolic responses of brain progenitors to nutrient deficiency, and the limited potential of ketone bodies in rescuing the effects of maternal glucose deprivation on NSC and NPC growth.

YOUNG INVESTIGATOR

P1/7 3D Modelling of Neuroblastoma Cells in Aggrewell Plates: A Consideration of Chemotherapeutic Factors Influencing Cell Escapage

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Aggrewell Plates are a novel technology to grow cells, utilizing microwells within each larger well to allow for even spreading of cells and creation of 3D uniform colonies. However, cells have been noticed to “escape” the wells – a phenomenon that is not yet fully explored. Here, we aim to understand factors that influence this escape, exploring how neuroblastoma cells placed in Aggrewell plates are impacted by chemotherapeutics. Oxaliplatin and Vorinostat were mounted at varying concentrations into microwells with Kelly and Kelly-cis neuroblastoma cells. Images of each well and the growth of cells over 6 weeks were captured and stored digitally. The images were then analyzed by hand, and given a score of 0, 1, or 2, based on degree of escapage, with 0 indicating no cell movement away from the center of the well, 1 indicating cell movement within the well, and 2 indicating cell movement outside the cell. The scores were logged electronically, and the total number of microwells falling into each of the three categories was tallied. Out of the 12,661 microwells analyzed from 3 plates, 4547 (36%) scored 0, 594 (5%) scored 1, and 7526 (59%) scored 2, and scores of 2 were higher in plates 2 and 3, whereas scores of 1 were most common in plate 1. Specifically, cells in the control groups escaped the most, while cells in Kelly-Cis Vorinostat escaped the least. These results indicate that cell escape is correlated with the concentration of drug present within the wells – the higher the drug concentration, the lesser the degree of escapage. Though further research is needed to corroborate these results, the study paves the way in understanding how to best maximize efficiency of Aggrewell plates. This also illustrates the necessity for research exploring how cells can be grown without the usage of drugs, which can eventually encourage accurate and precise cell growth among a plethora of stem cells, tumor cells, and more, improving developments and technology in the field. This work was conducted using commercially available cell lines and chemotherapeutic agents. As no human or animal subjects were involved, ethical approval was not required in accordance with institutional guidelines.

YOUNG INVESTIGATOR

P1/8 Optimising Models to allow testing of Bioelectric Modulators to Drive Motor Axon Regeneration in Mouse Models

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Motor neuron diseases (MNDs) results in axonal loss and muscle denervation. The ability to promote axon regeneration is therefore a potential strategy to slow down disease progression and promote recovery. Recent work has shown bioelectric modulators can create a more permissive environment to facilitate axon regeneration, but the concept has not been tested in mammalian systems or in the context of MNDs. In this project, we will test whether bioelectric modulators can promote axon regeneration following peripheral nerve injury and in a regulatable mouse model of amyotrophic lateral sclerosis (ALS). In preparation for these experiments, we must first validate the models of nerve injury and ALS, and verify the optimal time points for the interventional experiments. We have first validated tibial nerve crush injury model in Thy1-YFP mice, which express YFP projection neurons. Tibial nerve crush surgery was performed in 6-week-old mice, and leg tissues were collected 3 days post injury. Lumbrical muscles of the leg were dissected and immunofluorescently labelled. Axon numbers distal to the injury were counted on cross section of tibial nerve. Axon fragmentation, complete endplate denervation and reduction in axonal number are observed 3 days post injury. With regards to the ALS model, we have characterised NMJ loss in the rNLS mice, where the expression of the human TDP43 protein with a defective localisation signal (NLS) can be suppressed by doxycycline. The mice were fed with doxycycline for 5 weeks from birth, followed by taking off doxycycline for either 3 or 5 weeks. Tibialis anterior (TA) and extensor digitorum longus (EDL) were dissected and labelled as mentioned above. After 3 weeks off doxycycline, TA and EDL show 12% and 9% vacant endplates respectively. After 5 weeks, these increase to 43% and 23%, suggesting that TA is more vulnerable in this model. Together, we have validated two models with distal axon degeneration which can be used to test the bioelectric modulators in the future. All experiments were performed in accordance with the UK Animal Scientific Procedures Act (1986) and approved by the University of Edinburgh Bioresearch and Veterinary service.

P1/9 Alterations in the vasculature of the spinal cord in a murine model of motor neuron disease

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The homozygous Wobbler mouse represents a useful model for the investigation of human inherited motoneuron diseases, including amyotrophic lateral sclerosis (ALS). The clinico-pathological features of ALS differ from the Wobbler MND because of the lack of involvement of the human corticospinal tract. Nevertheless the pathogenesis of the mouse and human diseases may have some important common features. Previous pathological reports have indicated that swollen and vacuolated motoneuron cell bodies are the most predominant feature characterising the wobbler mouse motoneuron disease. Here we extend our earlier studies which documented the light and electron microscopical changes in neuronal volumes in the wobbler mutant. In this study we used stereological methods to document the vasculature of the spinal cord in wobbler mutants and control animals at 3 wk (young, stage 1) and 3 months of age (old, stage 4) using stereological methods (n = 6 for each group). All animals were anaesthetised and sacrificed by cardiac perfusion. Material was processed for light and electron microscopy. Parameters estimated included endothelial thickness and the Vv of mitochondria:cell and nucleus:cell. Arithmetic and Harmonic mean thickness of endothelial cells was estimated. Endothelial Microvilli number and dimensions were also estimated. Analysis of variance of the diffusion distance of the grey and white matter of the spinal cord showed a significant effect of location ($P < 0.05$) but no significant effect of age condition or interaction. Ultrastructural studies on the grey matter revealed no significant effect of age or condition on endothelial thickness and the Vv of mitochondria:cell and nucleus:cell. These results highlight the highly conservative nature of the vasculature in the murine spinal cord. There was however a significant effect of Disease on Harmonic mean thickness (Increased) ($P<0.05$). We also documented alterations in the endothelial microvilli primary cilia that may have consequences in blood flow. This study had appropriate ethics committee approval.

YOUNG INVESTIGATOR

P1/10 Anatomical Considerations of Botulinum Toxin Type A Administration: Potential Complications and Strategies to Mitigate Adverse Effects

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Botulinum toxin Type A (BoNT-A) is an injectable neurotoxin widely used for both therapeutic and aesthetic purposes. Due to the complex interconnection of facial muscles, a detailed understanding of facial anatomy is essential to ensure accurate targeting of specific muscle groups, thereby minimising risk of adverse effects. Each region of the face and neck requires tailored consideration, including optimal injection sites, dosages, and techniques, are critical for achieving optimal aesthetic outcomes while reducing complication risk. This systematic review aims to explore the relationship between facial anatomical landmarks in the head and neck regions and the outcomes of BoNT-A treatments, focusing on high-risk areas, including the frontalis, glabellar complex, peri-orbital and peri-oral region, and the platysma. Additionally, this review evaluates common adverse effects ranging in severity and mitigation strategies to enhance patient safety and outcomes. Following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines, a comprehensive literature search was conducted using MEDLINE, Embase and Cochrane library databases to extract relevant studies. A total of 32 studies met the inclusion criteria, highlighting the importance of precise facial anatomical knowledge in BoNT-A administration. The findings reveal that common complications, including brow and eyebrow ptosis, are often associated with improper injection technique and/or incorrect dosage, frequently due to insufficient anatomical knowledge among practitioners. This underscores clinical significance in understanding the relationship between facial anatomy and effective BoNT-A application, the importance of tailored treatment approaches, and addressing potential side effects ranging from mild to severe to reduce the risk of adverse effects. This study provides a foundation for improving clinical outcomes, enhancing overall safety and effectiveness of BoNT-A treatments and no ethical approval was required.

YOUNG INVESTIGATOR

P1/11 Human Schwann cell contributions to keloid scarring

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Schwann cells, the myelinating glia of the peripheral nervous system, are essential for nerve regeneration after injury. Emerging evidence suggests they also contribute to wound healing by activating myofibroblasts and remodeling tissue. Their role in pathological scarring, such as keloids—fibroproliferative lesions marked by excessive fibrosis and inflammation—remains poorly defined. To explore Schwann cell involvement in keloid pathogenesis, we analyzed MPZ expression (a Schwann cell marker) in a publicly available human skin microarray dataset (GSE139300), comparing 150 samples from cheek and body sites. MPZ showed only modest enrichment in facial skin. We then analyzed our bulk RNA sequencing dataset from CD1 mouse skin in homeostasis and at Day 3 post-wounding. These data revealed a two-fold increase in Schwann cell representation in facial versus trunk wounds, suggesting site-specific recruitment during early wound repair. To assess Schwann cell presence in human tissue, we performed immunohistochemistry for S100B on wax-embedded sections of healthy skin and keloid scars. Imaging revealed variability in Schwann cell abundance, morphology, and distribution across patient samples. Future analysis will examine whether these differences correlate with scar-location or severity. Finally, we tested whether keloid fibroblasts exhibit glial plasticity. Primary patient-derived keloid fibroblasts were cultured in Schwann cell progenitor differentiation medium. Cells showed dramatic morphological changes, including arborization and self-assembly, and began expressing Schwann cell markers SOX10 and S100B. Marker expression was confirmed via immunofluorescence, with imaging performed using Operetta high-content system. These findings suggest a capacity for glial-like reprogramming in keloid cells. Primary dermal fibroblasts, both keloid and normal, were taken from adult patients who gave written informed consent. Collection was approved by the National Research Ethics Service UK (14/NS/1073), and the study adhered to the WMA Declaration of Helsinki and the Belmont Report. CD1 mouse work was carried out under the Animals (Scientific Procedures) Act 1986 with Home Office license at King’s College London Biological Services Unit.

Young investigator

P1/12 Deciphering Cell-Type and Temporal-Specific Matrisome Expression Signatures in Human Cortical Development and Neurodevelopmental Disorders via scRNA-Seq Meta-Analysis

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Neurodevelopmental disorders (NDDs) affect approximately 15% of the global population, with the extracellular matrix (ECM) comprising 40% of brain volume playing a critical role in cortical development. Despite its significance, understanding cell-type specific matrisome signatures has been hindered by limitations in computational analysis of single-cell RNA sequencing (scRNA-seq) data. We designed a comprehensive suite of novel computational tools that significantly enhance scRNA-seq meta-analysis. Our custom functions integrate covariate-aware differential gene expression analysis via DESeq2, implement efficient Local Inverse Simpson's Index (LISI) calculation for quantitative assessment of dataset integration quality, and provide robust temporal pattern detection through Pearson's correlation-based regression modelling. These tools and the approach overcome critical limitations of conventional scRNA-seq and existing pipelines by efficiently controlling for batch effects, enabling real-time trajectory analysis, and facilitating detailed cell-cell interaction assessments. We applied this pipeline to integrate scRNA-seq datasets from six independent studies covering human foetal forebrains from gestation weeks 8-26. Our meta-analysis revealed distinctive cell-type specific matrisome signatures, with endothelial cells and astrocytes exhibiting the most extensive profiles (102 and 100 unique markers, respectively), highlighting their importance in cortical development. Temporally, matrisome gene expression peaked during early-second trimester (GW13-19), coinciding with critical neurodevelopmental processes. LGALS3, encoding Galectin-3 (GAL3), emerged as a spatiotemporally regulated gene significantly co-expressed with HOPX in outer radial glia. Through complementary experimental approaches, we validated this co-expression pattern, with immunofluorescence staining confirming that ~71% of HOPX+ cells express GAL3+ primarily in the subventricular zone of human prefrontal cortex during second trimester. Through a series of transcriptomic and image analyses, we demonstrated that LGALS3+ HOPX+ cells position at developmental branch points between radial glia and astrocytes. Our study establishes both a valuable computational toolkit for future neurogenomic research and a comprehensive map of matrisome gene expression during human cortical development. The custom functions developed herein provide researchers with improved capabilities for scRNA-seq analysis across diverse biological contexts. Meanwhile, our characterisation of LGALS3 reveals its potential role in astrogenesis, offering insights into mechanisms underlying neurodevelopmental disorders linked to ECM dysfunction and establishing a foundation for future functional studies of matrisome contributions to brain development. Ethics statement: Foetal tissues from elective, normally progressing pregnancies are collected under the Scottish Advanced Fetal Research (SAFeR) study (NCT04613583). The collection process is approved by one of the 12 Scottish National Health Service Research Ethics Committees (REC 15/NS/0123) and follows the Declaration of Helsinki guidelines.

YOUNG INVESTIGATOR

P1/13 Mediation analysis of Bullying, Brain Development and Psychopathology: a longitudinal MRI study

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Bullying victimisation during childhood and adolescence has been linked to significant long-term mental health and cognitive impairments, with effects often persisting into adulthood. Adolescence, as a critical neurodevelopmental period, is particularly vulnerable to disruptions caused by chronic stressors such as bullying. Previous research has shown that bullying victimisation can lead to structural changes in the brain, including alterations in subcortical regions, with sex-specific differences in brain development. However, the relationship between these brain changes and the onset of psychopathology remains underexplored. This study investigates whether bullying-related disruptions in brain development mediate the relationship between childhood bullying and the onset of psychopathology, and whether these effects differ by sex. Data from the IMAGEN study, a three-timepoint longitudinal cohort of 2,094 adolescents (1009 females) across the ages of 14 to 23, were used for secondary analysis. Bullying victimisation was assessed using a Likert scale adapted from the Olweus Bully/Victim Questionnaire, and brain development was evaluated using structural MRI scans obtained at all three time points. MRI data were processed using FreeSurfer software to extract cortical thickness, surface area, and volume measures across brain regions, including the hippocampus, amygdala, thalamus, hypothalamus, and brainstem. A causal mediation analysis framework, combined with mixed-effects modelling, was used to assess whether changes in brain volume mediated the association between bullying and psychopathology. Confounding variables such as age, sex, socioeconomic status, and intracranial volume were controlled for, and bootstrapping was used to improve inference robustness. Significant mediation effects were observed for hyperactivity/impulsivity symptoms through reduced volume in the right medial orbitofrontal cortex (8% mediation, $p = 0.018$), left supramarginal gyrus (5.4%, $p = 0.028$), rostral middle frontal gyrus (4.1%, $p = 0.016$), and total grey matter volume (5.3%, $p = 0.05$). Emotional problems were mediated by reduced volume in the left pallidum (3.57%, $p = 0.03$). No additional significant mediation effects were identified. These findings suggest that specific structural brain changes partially mediate the long-term mental health effects of bullying and may inform neurobiologically targeted interventions. Ethical approval was obtained by the IMAGEN consortium from local research ethics committees at each recruitment site, and written informed consent was provided by all participants in accordance with the Declaration of Helsinki.

YOUNG INVESTIGATOR

P1/14 Investigating the role of PPT1 using ovine models - a multi organ morphological and molecular study to inform therapeutic targeting.

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The neuronal ceroid lipofuscinoses (NCL), or Batten Disease are a group of inherited neurodegenerative disorders that predominantly affect children and young adults (commonly called 'childhood dementia'). This umbrella term constitutes 13 known genetically distinct variants categorised based on time of symptom onset and pathology. All NCLs are inherited lysosomal storage disorders which are caused by genetic alterations resulting in altered lysosomal function. In this study, we will focus on CLN1, an aggressive form of the disease with an early symptom onset developing from 12-24 months of age. Clinical manifestations include blindness, psychological and motor deterioration and seizures with an average life expectancy of 9-12 years old. CLN1 disease is caused by defects in the gene encoding palmitoyl protein thioesterase (PPT1). In the absence of PPT1 function, granular osmiophilic deposits accumulate in the CNS and other tissues. There is no cure for CLN1 in part due to poor understanding of the regional nature of the disease and a lack of readily available biomarkers. We have generated a CLN1 ovine model to bridge the translational gap from small animal models to preclinical trials. We aim to understand: 1. Why is the nervous system preferentially affected at early disease stages? 2. What impact is there on other organ systems? 3. How can (and/or should) we predict disease staging and track progression? So far, we have carried out proteomic analysis on differentially affected brain regions and identified protein candidates which likely underpin regional vulnerability. In due course, we plan to carry out proteomic analysis of multiple organ systems and bodily fluids to help identify molecular consequences of altered PPT1 throughout the body. Imaging modalities (MRI of the nervous system and full-body CT scans) will be used to indicate gross morphological changes throughout disease progression. We believe this study will play a significant role in informing preclinical therapeutic trials on regional targeting and timing of intervention. All experiments performed and tissues collected from the ovine model in this project has been reviewed by the appropriate Animal Welfare and Ethical Review Board (AWERB) and carried out with approval from the Home Office under PPL number: PP2318334.

P1/15 An anatomical investigation of the insula in a South African population: An MRI-based study

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The insula is a small yet complex cortical region buried deep within the lateral sulcus of the brain. It is involved in a wide variety of functions, ranging from sensory and emotional processing to higher-level cognition. Due to its concealed location and intricate anatomical structure, the insula has long posed a surgical challenge. Comprehensive knowledge of the insular anatomy is therefore integral to preoperative planning and safe interventional procedures. Since magnetic resonance imaging (MRI) is a favoured modality for the identification of cerebral structures, this study aimed to investigate the morphology and morphometry of the insula in a South African population, using MRI scans. One-hundred MRI studies of insulae (n=200 hemispheres) were retrospectively analysed for morphological features and morphometric parameters. The insulae were predominantly trapezoidal in shape (Laterality: Left: 82%; Right: 78%; Sex: Male: 84%, Female: 76%). The central insular sulcus was almost always “well seen” (Laterality: Left: 97%; Right: 99%; Sex: Male: 99%, Female: 97%). The middle short insular gyrus (MSG) was most variable in visibility, especially when compared across the sexes (p=0.004). Insular gyri widths were comparable in both cerebral hemispheres; the posterior long gyrus (PLG) presented with the smallest mean widths. Anterior lobule (AL) widths were larger than those of the posterior lobule (PL). Widths of the insular gyri and lobules were generally larger in males than in females. The MSG and PLG widths in the left hemisphere, AL width in the right hemisphere, and the PL width in both hemispheres were significantly larger in males than in females (p=0.001; p=0.005; p=0.041; p=0.001, p=0.015, respectively). This study concludes that MRI scans may be used to accurately interpret insular anatomy. The data obtained may aid neurosurgeons in performing safe insula-related surgical procedures. Ethical approval for this study was obtained from the Biomedical Research Ethics Committee of the University of KwaZulu-Natal (BREC/00004502/2022). This study utilized retrospective MRI scans, posing no risks to the patients. The data obtained was anonymized.

YOUNG INVESTIGATOR

P1/16 Basicranial Sexual Dimorphism in Modern Homo sapiens

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Homo sapiens exhibit reduced sexual dimorphism compared to earlier hominins, yet residual differences in skeletal morphology remain critical for anthropological sex estimation in post-mortem contexts. While sexually dimorphic traits in craniofacial regions are well-documented, the basicranium remains relatively understudied. This is surprising given its clinical and forensic significance, as well as its frequent preservation in fragmented remains due to protection by surrounding soft tissue. Addressing this gap, the current study investigates sexual dimorphism in basicranial size and shape using three-dimensional geometric morphometrics (3D-GM). Using the New Mexico Decedent Imaging Database (NMDID), 3D crania of 100 decedents (50 male, 50 female; average age = 47.47 years, age range = 15–88 years) were segmented from post-mortem CT scans via semi-automated methods. Each model was then landmarked using 32 fixed landmarks and 78 semi-landmarks placed on homologous basicranial loci. As a proxy for size, this study found statistically significant sex differences in endocranial volume (ECV) ($p = 0.003$, mean Male ECV = 1470.68; mean Female ECV = 1297.11). These findings support the hypothesis that Males tend to have larger basicranial dimensions, aligning with trends in skeletal 'robusticity' associated with greater functional demands and muscle mass. Landmark-based shape analysis is ongoing, and will use Generalised Procrustes Analysis (GPA) and Principal Components Analysis (PCA). Results will be completed by June 2025. This research has implications in three key areas: (1) enhancing precision in clinical procedures such as trans-sphenoidal surgery; (2) offering insight into how evolutionary pressures have shaped cranial morphology; and (3) improving forensic and archaeological sex estimation for fragmented human remains. Full ethical approval was granted by the Department of Archaeology, University of Cambridge. The anonymised dataset is securely stored on an encrypted external hard drive accessible only to primary researchers. The thesis is scheduled for submission in June–July 2025.

YOUNG INVESTIGATOR

P1/17 Anatomical Variation in Vertebral Artery Morphology: Observations from an Irish Cadaveric Population and Implications for Cerebral Development

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The vertebral arteries (VAs) are known key contributors to posterior cerebral blood circulation, supplying blood to the brainstem, cerebellum, and occipital lobes, which are vital for Cortical integration, balance, equilibrium and visual processing This study investigated VA morphology in an Irish Cadaveric population, across all four of its segments, V1 (pre-foraminal), V2 (foraminal), V3 (Atlantic/extradural), and V4 (intradural/intracranial), specifically focusing on variations in the V4 segment and its potential implications for cerebral development. Standard posterior approach dissection methods were employed to reveal the arteries from their subclavian origin to their intracranial junction at the basilar artery. Measurements included vessel diameter, trajectory, and lateral dominance throughout all segments. Variability was observed at various levels such as differences in transverse foramen entry points in V2, tortuosity or looping in V3, and prevalent asymmetries and angulations in the V4 segment. Intracranially, differences in diameter and convergence angle were notably pronounced, with some specimens displaying significant lateral dominance or medial deviation. While direct evidence linking vertebral artery morphology to cortical development is limited, the V4 segment's role in supplying blood to posterior cerebral areas, known for supporting early cortical processing and structural maturation, implies it may affect developmental perfusion dynamics. Subtle variations in posterior circulation may influence neuronal migration, circuit formation, or vulnerability to ischemic injury during essential stages of brain development. These findings underscore the imperative of doing a thorough evaluation of the vertebral arteries, as changes may arise at any segment and together impact perfusion. It also acts to promote increased awareness of vertebral artery variations in developmental neurobiology and clinical applications, including neuroimaging, vascular surgery, and cerebrovascular risk evaluation. This research has been conducted on human cadavers from the University College Cork Anatomical Donor Program. All donors in the program have consented to the use of their bodies for medical education, research, and training in accordance with the Anatomy Act and in line with the Irish Medical Council Guidelines.

P1/18 The morphological study of the frontal process foramina and maxilla foramina in dry skull

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There are foramina found in the maxillary bone called, frontal process foramina and maxilla foramina. This study aimed to investigate the morphological features of the frontal process foramina and maxilla foramina. The 56 dry skulls from Department of Anatomy, Faculty of Medicine, Khon Kaen University, Thailand, were used in this study. The external surface of the maxilla bone and the internal surface of the nasal bone were examined, and the number of frontal process foramina and maxilla foramina of maxilla were recorded. The frontal process foramina are most common found for 20 skulls in one non-connected opening. The maxilla foramina are mostly found with no external opening for 38 skulls. Results from cadaver found 51 frontal process foramina and 18 maxilla foramina. The presence of differences in the frontal process foramina and maxilla foramina classification and size in Thai populations. According to this finding, this information provides suggestions to be careful in surgery or injections around this area. Ethical approval for this study was granted by the Center for Ethics in Human Research, Khon Kaen University (HE661581).

P1/19 Three-Dimensional Topography of the Superficial Temporal Artery and Its Branches in Thai Cadavers: A Cadaveric Dissection and Photogrammetry Study

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Understanding the detailed anatomy of the superficial temporal artery (STA) is essential for optimizing surgical outcomes and minimizing procedural risks, particularly cerebral embolism associated with filler injections in the temporal region. Although morphometric data exist for several ethnic populations, anatomical information specific to Thai individuals is lacking. This study aimed to characterize the STA and its branches in Thai cadavers to support safer surgical and aesthetic procedures. Twenty hemifaces from embalmed Thai adult cadavers (14 male, 6 female) were dissected using standardized anatomical techniques. The STA, frontal, parietal, and zygomatico-orbital arteries (ZOA) were measured using digital calipers and referenced to defined surface landmarks. To enhance anatomical visualization, photogrammetry was performed on one dissected specimen. This technique involved capturing photographs from multiple angles and processing them with specialized software to generate a life-size, photorealistic three-dimensional digital reconstruction of the STA and its branches. In 90% of cases, STA bifurcated above the zygomatic arch. The mean STA diameter was 3.29 ± 1.08 mm, larger than reported in American (2.03 ± 0.33 mm), Taiwanese (2.14 ± 0.45 mm), and Egyptian (2.75 ± 0.53 mm) populations. Frontal and parietal branch diameters averaged 2.59 ± 0.78 mm and 2.51 ± 1.09 mm, respectively. The ZOA was present in 90% of specimens, more frequently than in Turkish (77.78%) and Korean (22.8%) studies. Its average diameter was 1.24 ± 0.46 mm, closely matching Chinese data (1.2 ± 0.2 mm) and Korean findings (1.1 ± 0.5 mm). The STA bifurcation was located 30.13 ± 10.82 mm superior to the zygomatic arch and 22.38 ± 6.64 mm medial to the tragus. The ZOA originated 19.36 ± 9.45 mm from the jugale, similar to Chinese values (20.9 ± 6.4 mm), but shorter than Korean data (29.6 ± 4.6 mm). These findings suggest anatomical similarities between Thai and East Asian populations, particularly Chinese. This study provides the first detailed morphometric analysis of the STA in Thai cadavers and supports population-specific surgical guidelines. This study was approved by the Siriraj Institutional Review Board (SIRB Protocol No. 696/2567, Exempt).

P1/20 Exploring cortical trajectory of the lumbar vertebrae: a morphometric study in dry skeletons: a retrospective study in Thailand

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The cortical bone trajectory (CBT) is a novel approach for vertebral screw fixation aimed at addressing spinalinstability associated with spinal disorders. The morphometry of the lumbar vertebrae is crucial in tailoring screw design for each CBT application, given the significant variations in optimal screw sizes, lengths, and angles among populations. This study aimed to explore the morphometry of the Thai lumbar vertebrae. A total of 300 dried lumbar columns were used to measure the pedicle height (PH) and width (PW), length for cortical bone trajectory (LCT), cephalad screw angle (CSA), axial cortical bone trajectory angle (ACA), and possible cortical zones for the CBT.The following average values were calculated: PH in L1, 15.09±1.44 mm; PW in L5, 16.96±2.42 mm; LCT in L3, 35.75±2.61 mm; CSA in L1, 20.85°±2.30°; and ACA in L5, 21.83°±2.49°. Women generally had shorter PH and PW than men, with significant differences across lumbar levels. The LCT was significantly shorter in women and was notably different between the left and right sides. The CSA and ACA varied significantly between sexes and sides, with specific lumbar levels showing wider angles in one sex over the other. The most common cortical zones for screw tips were Z3 and Z10, with high incidences across all lumbar levels. This study presents detailed lumbar vertebral morphometry data specific to the Thai population. The results are essential for CBT application in screw fixation procedures. This information will contribute to the production of optimally designed screws for Thai patients in the future. This study was approved by the Khon Kaen University Ethics Committee for Human Research (approval no., HE641512).

P1/21 The comparison of fetal body parameters in second and third trimester of gestation

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The study of fetal growth patterns and body parameter dynamics is an actual task of both human prenatal biology and obstetrics. Numerous clinical studies have been conducted on these parameters, but they are solely based on sonography data or extremely rare and outdated radiographic data. The technical errors that occur when measuring linear parameters and the impossibility of direct measurement of fetal weight are major disadvantages of ultrasound studies. The most reliable and valid data can be obtained only with direct instrumental measurements. The study aim is to identify the prenatal time of manifestation of sex differences in weight, body length, torso length, and BMI. The material consisted of retrospective anonymized data from standard medical autopsy protocols, age determination based on fetal growth tables. The analysis used data of direct instrumental weight measurements with an accuracy of 500 mg and the crown-heel length and the crown-rump length measurements with an accuracy of 1 mm. The analysis and application of retrospective data have been permitted by the Local Ethics Committee of the REAVIZ Private University October 28, 2024 7th protocol. The material ranging from 14 to 33 weeks was divided into two age groups: the second trimester group (N=127) and the third trimester group (N=112). In the first group, data from 55 female and 72 male fetuses and in the second group of 51 female and 61 male fetuses were analyzed. Weight's sexual differences in the second trimester were only. The difference in the weight was detected already in the second trimester and was 72.4 grams ($p<0.053$). In the third trimester, the differences between two groups were 0.34 grams in weight (1001±408♂ vs 858±216♀, $p<0.026$), 1.1 cm in CRL (23.3±2.68♂ vs 22.2±1.78♀, $p<0.018$), and 1.5 cm in CHL (35.0±3.58♂ vs 33.5±2.63♀, $p<0.02$), respectively. The BMI of both groups was the same. The obtained results indicate a decrease in the difference in weight by almost two times in the third trimester compared to the second trimester. The manifestation of statistically significant sexual differences in the third trimester indicates heterochrony of the prenatal dynamics of the linear and weight parameters of the fetus.

YOUNG INVESTIGATOR

P1/22 Comparative analysis of embryonic limb muscle bundle formation in chick, mouse, and human development

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The musculature of the human limb has been well described since the late 15th and early 16th century. Despite this, how this anatomy is sculpted through development remains poorly understood. Using Optical Projection Tomography (OPT) and immunohistochemistry labelling, we rendered 3D forelimb muscle bundles across chick, mouse, and human development. This was achieved using OPT imaging to generate TIFF stacks which were reconstructed through Horos software. These reconstructions were combined with serial cryosections to provide a quantitative dataset documenting the volumetric dimensions of muscle bundles, alongside their fibre diameter and number. We found that at equivalent stages of forelimb development between species, the average diameter is between 3.4 to 3.9µm despite any size differences of the bundles themselves. Furthermore, analysis of the Extensor Metacarpi Radialis (EMR) across days 7.5-11 of chick embryonic development demonstrated that size increase through growth was not due to increased fibre diameter (*e.g.,* as seen in post-natal muscle growth through hypertrophy) but instead due to increased fibre number. Fibres composing the EMR stay within 3.4 to 3.9µm through day 7.5-11, but fibre number increases dramatically from 91 to 733. Thus, the key finding from our comparative approach suggests muscle bundle size is not defined by fibre diameter or the starting size of muscle bundles, but by the number of fibres recruited. This comparison is reflected in both size differences between different species, alongside differences seen in the same species at different developmental stages. Our findings are of importance to regenerative therapies addressing congenital limb defects affecting musculature, where the field has advanced enough to generate muscle cells in vitro, but remains unable to assemble functional muscles of appropriate size. Ethics: Chick embryos were harvested no later than 11 days. Pre-existing OPT lab data sets were used for the human analysis which were originally generated using CS18 and CS22 embryos obtained from the Medical Research Council–Wellcome Trust Human Developmental Biology Resource (HDBR) (MR/R006237/1). All regulated work using mice was carried out under the appropriate UK Home Office Animal (Scientific Procedures) Project Licence (Holder: Malcolm P.O. Logan) and was reviewed and approved internally through the local Ethical Review Panels (ERP) at King's College London.

YOUNG INVESTIGATOR

P1/23 The Ligament of the Head of the Femur: A Study of its Anatomy in the Dog, Sheep and Goat

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The ligament of the head of the femur connects the head of the femur to the acetabulum and contains blood vessels within its collagen bundle. Functionally, it is linked to stability of the hip joint and the blood supply to the femoral head. This study examined the comparative features of this ligament in an athletic species (dogs) with well-developed gluteal muscles and in sheep and goats which are more sedentary and have only a small gluteal muscle mass. Samples of the ligament were collected from canine (n=6), ovine (n=4) and caprine (n=3) cadavers and fixed in formalin. Ligaments were photographed measured prior to sampling. Routine histological staining was conducted and the vascular area of each specimen was calculated and photographed. Cross sections of ligaments were studied using image analysis (ImageJ software) to calculate the vascular area relative to the cross-sectional area of the ligament. All data were collated and subjected to statistical analysis. The study found that the mean vascular area relative to the cross-sectional area of the ligament was 0.027% in dogs and 0.028% in both sheep and goats. We conclude that the lack of statistical difference in these results indicates that the degree of vascularity of the ligament of the head of the femur is unrelated to muscle mass or athleticism. Ethical approval was granted for this work (AREC-E-21-19-Kilroy) by the university research ethics committee.

YOUNG INVESTIGATOR

P1/24 Sex Determination Using Discriminant Function Analysis of Northeastern-Thai Occipital Bones.

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In forensic investigations, facial bones are often damaged or missing, making the occipital bone (OB) a valuable alternative for sex determination. Previous studies have reported high accuracy using the OB in various populations. This study aimed to modify and apply 12 occipital bone measurements for sex determination in Northeastern Thai skulls. Discriminant function analysis and descriptive statistics were employed. Results indicated that all parameters such as hormion-basion length, bi-lower part of temporo-occipital suture breadth, bi-asterion breadth, opisthion-lambda length, foramen magnum breadth, foramen magnum length, right-lower part of temporo-occipital suture to opisthion length, left-lower part of temporo-occipital suture to opisthion length, right-asterion to basion length, left-asterion to basion length, right-asterion to lambda length, and left-asterion to lambda length were significantly greater in males than in females ($P < 0.01$). Among the univariable analyses, the temporo-occipital suture breadth (TOB) showed the highest classification accuracy (75.4%). In the multivariable stepwise method, a combination of hormion-basion length (HBL), TOB, and left asterion–basion length (Lt. ABL) yielded the highest accuracy rate (78.8%). These findings suggest that TOB, HBL, and Lt. ABL are reliable parameters for sex determination using dry occipital bones in the Northeastern Thai population. Ethical approval for this study was granted by the Center of Ethics in Human Research, Khon Kaen University (HE651222).

P1/25 Gender Bias and Representation in Anatomy Teaching: Insights from a Second-Year Medical Module on Reproduction and Development.

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Gender bias in medical education, particularly in anatomy teaching, remains a longstanding issue, with male anatomy receiving greater emphasis than female anatomy. This study aimed to investigate the perceptions of students and staff at the University of Birmingham regarding the representation of male and female anatomy in the second-year RED (Reproduction, Endocrinology, and Development) curriculum. A mixed-methods approach was employed using two surveys: one for second-year medical students and one for anatomy staff. Both surveys explored content adequacy, representation and inclusivity in teaching resources, and identified barriers in teaching female and male reproductive anatomy. Results from 28 student and 10 staff responses indicated significant disparities, with male external genitalia taught in greater detail. Female students expressed a stronger need for comprehensive teaching of female reproductive anatomy, especially external genitalia, which was underrepresented. Staff reported discomfort and a lack of confidence in teaching female and intersex anatomy, citing insufficient training and cultural barriers. These findings highlight the ongoing gender bias in medical education, pointing to the need for curriculum revision, enhanced staff training, and more inclusive resources. Future research should explore the intersectionality of gender, race, and other social factors in anatomy education, and assess the impact of revised teaching methods on student learning outcomes and perceptions of inclusivity. The study received ethical approval from the Department of Biomedical Science Ethics Committee at the University of Birmingham (reference number: BMSRP_2025_EDU014).

P1/26 The Art, Language, and Legacy of Anatomy: Teaching with Depth and Purpose

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Human anatomy is a foundational component of education for medical, nursing, and allied health professionals. Traditionally, it is delivered through a structured syllabus focusing on systems, structures, and clinical relevance. While essential, this approach often overlooks the rich historical and linguistic heritage of the discipline. A more holistic model—blending historical context and linguistic foundations—can enhance understanding, foster engagement, and support long-term retention. The history of anatomy is more than a timeline of discoveries; it reflects humanity's enduring curiosity about the inner workings of the body. From early dissections and Leonardo da Vinci's anatomical sketches to 3D flap-based textbooks and stereoscopic atlases such as the Edinburgh collection, anatomy has always represented a union of science and art. Incorporating this perspective into teaching cultivates a deeper appreciation for the subject and rekindles intrinsic motivation. Equally integral is the language of anatomy, rooted in Latin and Greek. These classical languages form the basis of standardized medical terminology and connect students to the discipline's historical roots. Teaching the etymology of anatomical terms can enhance conceptual clarity and memory, strengthening the association between structure and function. Anatomy education should tell a story that includes the evolution of anatomical knowledge, the artistry of its representation, and the linguistic precision that underpins professional communication. Educators are responsible for inspiring curiosity and preserving this intellectual and cultural legacy. To promote this integrative approach, I hosted "Anatomy Jargon Dissected" in collaboration with the Bodleian Library. Attendees from linguistics, history, and medical sciences explored the origins of anatomical language and knowledge. A curated exhibition featured rare texts, including: Thomas Willis' Cerebri Anatome (1664), Gautier d'Agoty's Suite d'Anatomie (1745), William Cheselden's Osteographia (1733),Henry Gray's Anatomy (1858), Vesalius' De Humani Corporis Fabrica (1543), Remmelin's Catoptrum Microcosmicum (1639), featuring layered flap illustrations. This was reflected in participant feedback: "Interactive and speakers very engaging. Opportunity to interact with people across the University and from very different fields." "I liked the exhibition of the anatomy books from hundreds of years ago and the explanation of this exhibition."

P1/27 Implementation of a Clinical Anatomy Course using New Digital and 3D Resources through a Blended Approach, Results to 7 years of Teaching Experience in a New Career of Medicine from Chile.

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In 2015, new digital and 3D technological resources were acquired for the Anatomy Laboratory of the new School of Medicine of the Universidad de Tarapacá, in Arica-Chile, to start teaching its first undergraduate students in 2016. The aim was to analyze the academic performance in the subject anatomy of the first 7 cohorts exposed to new digital and 3D technologies. We used a SECTRA® digital dissection touch table and its workstation (connected to the IDS7® portal), a Syndaver® synthetic cadaver for the study of human macroscopic anatomy, a set of Erler-Zimmer® high fidelity 3D prints to study small details of human cadaveric anatomy. The teaching-learning process was through participatory activities such as: inverted class, problem-based learning, directed reading of scientific articles, digital dissection and review of digital topographic anatomy, prospection of synthetic and 3D printed anatomical models, review of radiological anatomy and a digitized cadaver using the VH Dissector® program installed on the SECTRA® table to orient the reviewed contents towards its clinical utility. The final annual grade point averages were 5.55 in 2016, 5.32 in 2017, 5.24 in 2018, 5.69 in 2019, 5.99 in 2020, 6.22 in 2021 and 5.80 in 2022 on a scale of 1.0 to 7.0 equivalent to 79.29%, 76.00%, 74.86%, 81.21%, 85.57%, 88.86% and 82.86% respectively. Failure of the subject was 3.33% in 2016 and then 2.63%, 5.40%, 3.33%, 2.70%, 0.00% and 0.00% successively. ANOVA analysis revealed a statistically significant difference in the mean grades of different years with $F=24.7474$ and p-value< 0.000. Pearson's correlation analysis between the first and second semester grades during the period 2016 to 2022 revealed a correlation coefficient of $r = 0.4695$ ($p < 0.0001$). This value indicates a statistically significant moderate positive correlation between the two semesters. In conclusion, the teaching of anatomy through a blended approach, using new technological and didactic resources focused on the student, allows optimizing the student's performance, achieving a good final performance and with a low failure rate of the subject. Ethical statement: The study followed international regulations in accordance with the Declaration of Helsinki. This work used an anonymized local database and did not require ethics and scientific committee approval.

P1/28 Evaluation of medical students' feedback on ultrasound integration for anatomy teaching

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There is a growing interest in the integration of ultrasound into undergraduate medical education, particularly within anatomy teaching. Ultrasound offers a dynamic, real-time imaging of living anatomy, which complements traditional dissection, 3-D models and atlas modalities. This study aims to evaluate students' perceptions of an ultrasound-based session, focusing on its usefulness, relevance, and educational impact. A total of 158 first-year medical students attended the session, and 85 students returned a completed feedback form. The workshop consisted of a 60-minute small group teacher-led US session on the musculoskeletal system. After the session, the students were asked to fill in an anonymous feedback form. Most of the students found the session both useful (93%) and interesting (98%). Ninety-three percent acknowledged that they have learned something new. The session enhanced the anatomical understanding of 94% of the participants, and 97% endorsed ultrasound as a valuable tool for learning anatomy. Furthermore, 97% considered that ultrasound sessions should become a regular component of the anatomy curriculum. Fifty percent of the students preferred an ultrasound session duration between 30 and 45 minutes and 28% between 45 and 60 minutes. The students particularly appreciated the interactivity, the application of their previous knowledge, the opportunities for learning and skill-building, the high standard of teaching, and the visualization and spatial comprehension. This study supports the incorporation of ultrasound into preclinical medical education. The findings highlight the educational value of ultrasound in anatomy teaching and its potential as an effective and engaging pedagogical approach. Ethics approval was not required for this study.

YOUNG INVESTIGATOR

P1/29 Effects of PACAP deficiency on immune dysfunction and integrity of Peyer's patches in young and aging mice

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Pituitary adenylate cyclase-activating polypeptide (PACAP) is a neuropeptide with known cytoprotective, anti-apoptotic and anti-inflammatory functions. While its involvement in systemic immunity has been extensively investigated, its specific role in gut-associated lymphoid tissue (GALT), particularly Peyer's patches (PPs), remains insufficiently characterised. This study aimed to investigate the impact of PACAP deficiency on immune cell composition and checkpoint molecule expression in PPs of young and aging mice to better understand its role in intestinal immune homeostasis. Wild-type (WT) and PACAP knockout (KO) mice were examined at two age points (3, and 12–15 months). PPs were first isolated and evaluated macroscopically. Subsequently, 3-µm-thick sections were prepared and stained with haematoxylin and eosin for histological analysis. Flow cytometry was then employed to characterise T-cell subsets (CD3+, CD4+, CD8+), activation markers (CD69), cytotoxic effectors (perforin, granzyme B), and immune checkpoint molecules (PD-1, PD-L1, TIM-3, Galectin-9) derived from PPs. The number of PPs declined with age in WT (young: 12.40 ± 2.72, aging: 10.20 ± 1.69) but not in PACAP KO mice (young: 10.46 ± 1.69, aging: 10.11 ± 1.81). Aging WT mice showed a reduced CD8+ T-cell frequency (5.03 ± 2.27, $p = 0.006$) and altered checkpoint expression (e.g., increased TIM-3 (30.94 ± 8.33, $p<0.001$), reduced CD69 (7.53 ± 1.52, $p<0.001$), and Gal-9 (10.32 ± 8.12, $p<0.001$), indicative of immune aging. In contrast, PACAP KO mice displayed more profound immune dysfunction with aging: both CD4+ and CD8+ T cells exhibited lower PD-1 (19.88 ± 7.75, $p = 0.018$), PD-L1 (30.51 ± 8.38, $p = 0.004$), CD69 (9.46 ± 6.54, $p<0.001$), and Gal-9 levels (14.97 ± 10.06, $p<0.001$), and higher granzyme B expression, particularly in CD8+ cells (71.13 ± 15.99, $p<0.001$). Despite similar PP histology, functional markers revealed impaired immune regulation in KO mice. These findings demonstrate that PACAP deficiency leads to significant age-related dysregulation in T-cell phenotype and checkpoint molecule expression within PPs, compromising mucosal immunity. This underscores PACAP's crucial role in maintaining intestinal immune homeostasis and its potential relevance in immunosenescence and inflammatory bowel disease. Ethical approval: BA/73/00452-6/2023. Grants and support: ÚNKP-21-3-I-PTE-1193, ÚNKP-22-3-II-PTE-1438

YOUNG INVESTIGATOR

P1/30 Characterising Cellular Biology in Paediatric Scoliosis

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Adolescent Idiopathic Scoliosis (AIS) is a lateral curvature of the spine diagnosed in patients aged below 18. It affects 1-3% of adolescents and is the leading cause of paediatric scoliosis. While the exact pathology behind AIS is poorly understood, its impact on local cellular biology has recently received increasing attention. This project aims to investigate the impact of AIS on the osteogenic potential of vertebral MSCs, and assess its impact on different vertebral harvest sites, comparing apical to non-apical and lumbar to thoracic vertebrae. Three AIS patients, yielding four samples, were included in this study. The expression of well-established MSC markers in the isolated cells was assessed through flow cytometry. Osteogenic potential was assessed by overexpression of osteogenic genes and matrix mineralisation. Apical and non-apical vertebrae from the same patient were compared, revealing that MSCs from the non-apex vertebra showed greater expression of CD90, a key stem cell marker. Similarly, differences in osteogenic gene expression were noted, with non-apical vertebrae displaying an overexpression of osteopontin. They also showed greater matrix mineralisation, suggesting a relationship between CD90, osteopontin expression and osteogenic potential. Interestingly, comparison of thoracic and lumbar vertebrae - from different patients - showed that although lumbar vertebrae exhibited the greatest levels of stemness markers, thoracic vertebrae had higher levels of matrix mineralisation and osteogenic potential. In conclusion, our study provides further evidence that the effect of AIS on MSCs function is not uniform throughout the spine and can vary based on harvest location - specifically, that non-apical vertebrae appear to exhibit higher osteogenic potential. Since this project was limited to 8 weeks, only a small number of patients could be assessed. However, it is included in a much larger scale project with greater patient and sample numbers. Further research will aim at comparing vertebral MSCs to non-vertebral, iliac crest MSCs to better understand the local effects of AIS, allowing for a better understanding and more targeted, effective treatment against the condition. Ethical approval and informed patient consent were obtained from Crumlin Children's Hospital. This project was supported by the School of Medicine, RCSI Translational Seed Fund, and NuVasive.

YOUNG INVESTIGATOR

P1/31 Studying the development and evolution of teleost electroreceptors using the channel catfish, *Ictalurus punctatus*.

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The lateral line system of fishes and amphibians consists of mechanosensory and electrosensory divisions. Lines of neuromasts in the skin contain mechanosensory hair cells (very similar to vestibular inner ear hair cells) that detect local water movement. Many non-teleost fishes and amphibians also have electrosensory ampullary organs on the head: these sense weak, low-frequency electric fields in water and are primarily used for hunting. Previous studies in a non-teleost bony fish (paddlefish) and a cartilaginous fish (skate) have shown that ampullary organs, like neuromasts, develop from embryonic lateral line placodes and suggest that non-teleost electroreceptors evolved via the modification of lateral line hair cells. Electroreception was lost in the bony fish lineage leading to teleosts, but a few teleost groups are electroreceptive, including the Mormyrids (elephantfishes), Gymnotiformes (knifefishes) and Siluriformes (catfishes). Teleost electroreceptors are physiologically different from non-teleost electroreceptors and are thought to have evolved independently, also via modification of neuromast hair cells. To test this hypothesis, we studied the expression of candidate genes in channel catfish (*Ictalurus punctatus*) embryos and larvae using wholemount *in situ* hybridisation and immunostaining. Some candidates were selected from a putatively electroreceptor-enriched gene-set, arising from differential RNA-seq analysis of skin transcriptome data from the black ghost knifefish (*Apteronotus albifrons*), in a sister group to catfishes. Many candidate genes examined are expressed in both neuromasts and ampullary organs in catfish, including transcription factors (e.g., Sox2, Eya1, Klf5a, Msx2b) and a calcium-dependent cysteine proteinase subunit (Capns1) that was highly enriched in the knifefish dataset. Shared gene expression supports a close developmental (and potentially evolutionary) relationship between neuromasts and ampullary organs. The transcription factor Foxe1 (also from the knifefish dataset) was expressed in ampullary organs but not neuromasts, potentially giving insight into the specification of electroreceptors versus hair cells. Furthermore, the expression in catfish ampullary organs of candidate genes from the knifefish dataset may support the hypothesis that ampullary organs evolved in the common ancestor of knifefishes and catfishes. Overall, these results shed new light on the development and evolution of electroreceptors in teleost fishes. No ethical approval was required for this project.

P2/1 The Human Developmental Biology Resource and the HDBR Atlas

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The Human Developmental Biology Resource (HDBR) is an MRC/Wellcome funded biobank providing embryonic and fetal samples to global researchers. Based at Newcastle University and UCL tissue from 3 weeks through to post-natal is collected under an HTA research tissue bank licence with REC approval, meaning UK based researchers do not need to apply for separate ethics to use the material in their research. Since 1999, tissue has been supplied to over 800 individual research projects resulting in over 600 publications, many in high impact journals. HDBR are a major tissue provider to the Human Developmental Cell Atlas and the Wellcome-funded Human Developmental Biology Initiative. Registered projects receive fixed, frozen or fresh tissues that can be used to gain insights into unique aspects of human development as well as validate findings from cell culture and animal studies. Bespoke dissections of organs of interest can be requested, and the tissue prepared to users' unique requirements, including dissociated cells preparations; sectioned to microscope slides; or RNA, cDNA or protein extractions. The HDBR Atlas is a unique, freely available online resource which aims to facilitate the understanding of early human development. It includes 3D models, annotated histology sections from Carnegie stages, gene expression patterns, and 3D models of developing organ systems. The gene expression portal offers the most comprehensive collection of human embryonic/fetal gene and protein expression data freely available. HDBR also offer a bespoke service conducting experimental analysis on your behalf using human developmental tissues. Support is provided throughout the project, beginning with guidance on the initial experimental design and continues through to assistance with the interpretation of the final results and publication. Following publication, data will be shared via our gene expression portal to support our commitment to open access science. Utilising techniques such as multiplex and base specific in situ hybridization, simultaneous RNA and protein localisation, single cell RNA sequencing, multiplexed RNA in situ imaging (Xenium), and spatial transcriptomics (Visium HD and Curio Seeker). The HDBR has received favourable ethical review from North East - Newcastle & North Tyneside 1 Research Ethics Committee (23/NE/0135 – Newcastle University) and London - Fulham Research Ethics Committee (23/LO/0312 – UCL). All tissue is collected following appropriate material consent.

YOUNG INVESTIGATOR

P2/2 Expression of the candidate dyslexia susceptibility gene CADM2 in the human fetal forebrain

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CADM2, a cell adhesion molecule, promotes cell aggregation and trans-synaptic adhesion in the central nervous system. A recent genome-wide association study identified CADM2 as a dyslexia susceptibility gene. We explored its expression pattern in early human forebrain to understand how mutations in CADM2 might lead to developmental dyslexia. Tissue (hdbr.org/expression) and single cell RNAseq (nemoanalytics.org) revealed that CADM2 mRNA expression was in the top 50% of protein coding genes in the cerebral cortex with peaking at 12 post-conceptual weeks (PCW). ScRNAseq localised expression to principally glutamatergic neurons and oligodendrocyte precursor cells in cerebral cortex and thalamus. CADM2's primary binding partner is CADM1 from the same gene family. Its cortical expression level was in the top 25% of protein coding genes and it was similarly expressed by glutamatergic neurons but also by GABAergic neurons. Immunohistochemistry and RNAScope in situ hybridisation on paraffin sections of human fetal forebrain provided by the Human Developmental Biology Resource (hdbr.org) revealed expression of CADM2 protein and mRNA in post-mitotic neuron cell bodies (beta tubulin positive) of the cortical plate at 8 PCW. By 17 PCW, CADM2 was also strongly co-expressed with the axon growth marker GAP43 in specific axon pathways, most notably in thalamocortical axons within the subplate and internal capsule. Co-expression was also evident in corpus callosum axons, especially those bordering the indusium griseum, which plays a role in guiding the trajectory of callosal axon growth. CADM1 immunoreactivity co-localised with CADM2 at 8 PCW in the cortical plate. As expected CADM2 immunoreactivity localised more to the cell surface and neurites, surprisingly CADM1 appeared strongly localised to the cell cytoplasm and nucleus, like what we have observed for other synaptic markers NRXN1 and CASK at this developmental stage. CADM1 and CADM2 mRNA were co-expressed in cells of the neocortical plate and hippocampus at 16 PCW. In conclusion, CADM2 is highly expressed in early developing human forebrain showing protein localisation to axons suggesting a role in axon growth guidance. All tissue received from the HDBR was collected with appropriate maternal consent and approval from the Newcastle and North Tyneside NHS Health Authority Joint Ethics Committee.

YOUNG INVESTIGATOR

P2/3 Investigating the effect of PAX6 haploinsufficiency on cortico-cortical projections using human cerebral assembloids.

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The human cerebral cortex relies on precise molecular regulation during development to establish complex neural circuits underlying cognition. The transcription factor PAX6 is a critical regulator of cortical patterning, neuronal differentiation, and axon guidance. In humans, heterozygous mutation in PAX6 is associated with agenesis of corpus callosum. In mouse models, PAX6 deficiency has been linked to reduced numbers of SATB2-expressing upper-layer cortical projection neurons. Given the differences between humans and mice in cortical development like cell type composition, distribution of different neurons and cortex folding, human-specific models are required to understand the role of PAX6 in structural connectivity of the brain. We utilise cortico-cortical assembloids which are derive from fusing two human induced pluripotent stem cell-derived cerebral organoids with control (PAX6+/+) and heterozygous (PAX6+/-) genotypes to model the impact of PAX6 on cortical projections. To do so, we first quantify SATB2-expressing cells using QuPath semi-automated cell counting method. We then visualise the neural projections using DiI&DiO lipophilic tracers, neurofilament immunostaining, and retrograde AAV-based labelling, followed by whole tissue clearing and 3D imaging using light-sheet microscopy. Preliminary data so far indicate there is a difference in total number of SATB2-expressing cells in heterozygous (PAX6+/-) organoids compared to control (PAX6+/+) organoids. Regarding the projections, they are predominantly intra-organoid rather than inter-organoid across both genotypes. Ongoing analysis aim to investigate the effect of PAX6 on projection morphology and trajectory. Moreover, to determine whether earlier fusion timepoints will have an effect on the formation of cortico-cortical projections. These findings may provide a human-specific model for further functional neural circuit studies and may offer insights into neurodevelopmental disorders associated with PAX6 dysregulation.

P2/4 Role of proteoglycans in cerebral cortex development and microcircuitry specification in human

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The specific brain proteoglycans (PG) and their spatial-temporal expression and reorganization during development were researched at the level of protein and transcriptomics using immunohistochemical and RNA-seq analysis in 50 postmortem fetal and perinatal human brains. The results show that the PGs' expression patterns are highly dynamic in humans between the mid-fetal period and the end of the first postnatal year. The chondroitin-sulfate proteoglycans diffuse expression in the intermediate zone shifts to the subplate zone and then to the cortical plate around 33 gestation weeks, defining the sublamina of future cortical layers. The versican and keratan-sulfate expression specifies the limbic supra-callosal region and marginal zone at the midfetal period. They downregulate around 35 gestation weeks, concordant with versican upregulation around some neuron populations, forming the earliest perineuronal nets. The glycosylation type of the PGs revealed by a set of different lectins (WFA, LEL, DSL, and WGA) shows the region and lamina-specific expression patterns, confirming the specific glycosylation contributing to the future cerebral cortex region and circuit specification. A significant downregulation of all diffusely expressed PGs in the third trimester of the fetal period affects the imaging signal intensity in MRI of the fetal and early postnatal brain, placing the knowledge on spatial-temporal PG developmental expression essential for perinatal medicine diagnostic approaches, and therapeutic strategies. The Ethical Committee of the School of Medicine, University of Zagreb and the Ethical Committee of the University Hospital Centre Zagreb (approvals No.:251-59-10106-24-111/170, Class: 641-01/24-02/04, and No.:380-59.10106-19-111/210, Class: 641-01/19-02/10) approved the human brain samples collection for studies of human brain development (IP-2019-04-3182; IP-2024-05-4135) led by Prof. Dr. Natasa Jovanov-Milosevic.

YOUNG INVESTIGATOR

P2/5 Inflammatory disruption of human cortical interneuron development in a 3D ex vivo model

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GABAergic neurons originating from the ventral subpallium play a critical role in human cortical development. While animal studies have shown that both genetic and environmental disruptions to interneuron development can contribute to neurodevelopmental disorders such as autism spectrum disorder, the cellular and molecular effects of early environmental insults on human cortical interneuron progenitors remain poorly understood. Unravelling the underlying mechanisms by which the establishment of cortical circuits are disrupted requires human-specific models of cortical interneuron development. To investigate this, we have established a 3D ex vivo culture system of the human foetal brain, termed dorsoventral cerebroids, focusing on the early development of the medial ganglionic eminence (MGE), the principal source of cortical interneurons in humans. We performed immunofluorescence staining for neural stem cell markers SOX2 and NESTIN; NKX2.1, a marker for MGE-derived progenitor cells; DCX, an intermediate progenitor marker; DLX2 and LHX6, which promote differentiation of GABAergic interneurons; and Ki67 to assess proliferation. We demonstrate that dorsoventral cerebroids maintain the expression of key cellular markers of interneuron development as well as the cytoarchitectural organisation of the human MGE. With this novel model system, we are studying the impact of the pro-inflammatory cytokine IL-17A, a key mediator thought to underlie brain abnormalities associated with maternal immune activation. Dorsoventral cerebroids were maintained in a free-floating culture for 7 days, with doses of IL-17A administered regularly. Afterwards, the tissue was fixed for immunofluorescence. Our preliminary results indicate that IL-17A exposure may alter the timing and regional identity of MGE development, providing insight into how inflammatory signals may impact interneuron development in the human brain and lead to excitation/inhibition imbalance. The collection of foetal tissue from electively terminated normally progressing pregnancies conducted as part of the Scottish Advanced Fetal Research (SAFeR) study (NCT04613583) has been approved by the North of Scotland Research Ethics Committee (REC reference: 15/NS/0123) and with written informed consent obtained from participants. Participant recruitment was carried out by NHS Grampian healthcare professionals acting independently of the SAFeR research team.

YOUNG INVESTIGATOR

P2/6 Molecular and structural features of human neocortical layer I during infancy

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During gestation, the marginal zone represents a dynamic compartment marked by multiple transient phenomena, reflected in a profound structural changes over time. In primates, by the end of the second trimester, the marginal zone is populated by numerous cells and serves as one of the primary routes for tangentially migrating neurons. In contrast, the adult neocortical layer I – occupying the zone directly beneath the pia mater that corresponds spatially to the fetal marginal zone – is a relatively acellular, around 200-micron-thick layer. However, the precise timing of its maturation and the cessation of neuronal migration through this region remain unclear. To determine whether layer I retains transient developmental features after birth, we analyzed its cellular composition and molecular profile in postmortem human brain tissue from adults, and from infants up to three months of age. Immunohistochemistry and RNAscope in situ hybridization were applied to samples from the frontal and occipital associative cortex. Layer I was subdivided into two distinct zones: an upper sublayer that was relatively sparse in neurons, and a lower sublayer with a higher density of NeuN-positive cells. These neurons express the vesicular transporter for either GABA (VGAT) or Glutamate (VGLUT1). Approximately 20–50% of NeuN-positive neurons expressed calretinin, a pattern consistent with the molecular profile observed in the adult cortex. Calbindin-, parvalbumin-, and somatostatin-positive neurons were only sporadically detected, further aligning with the adult phenotype of layer I. However, in infant brains, the density of NeuN-positive neurons appeared markedly higher than in adults. In addition, intensely stained calretinin-reactive Cajal-Retzius cells were observed just beneath the pia, along with sporadic small cells exhibiting immature morphology, potentially indicative of residual migratory activity, dispersed throughout the rest of layer I. These findings suggest that during early postnatal development, layer I shows both adult-like organization and residual features of the fetal marginal zone, a transient compartment essential for early cortical patterning and neuronal migration. The work was supported by Croatian Science Foundation under the project number HRZZ-IP-10-2022-8943 which was approved by University of Zagreb School of Medicine Ethics Committee.

YOUNG INVESTIGATOR

P2/7 Gene Expression Mapping in the Human Fetal Subplate at 21 Gestational Weeks

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The subplate (SP), a transient layer unique to mammalian cortical development, is critical for guiding neuronal migration and establishing thalamocortical connections. In humans, the SP is thicker and anatomically subdivided compared to rodents, yet the functional roles of its sublayers and subplate neuron (SpN) subtypes remain elusive. Using spatial transcriptomics (Visium platform), we mapped gene expression in formalin-fixed paraffin-embedded sections of human fetal brains at 21 gestational weeks, targeting superficial and deep frontal lobes, temporal lobe, and insular cortex. Seurat integration and clustering of 12,982 spatial spots revealed 17,943 expressed genes, with transcriptional domains aligning with anatomical structures.The SP exhibited distinct transcriptional sublayers. Differentially expressed genes (DEGs) in superficial SP were enriched for synaptic transmission (e.g., C1QL3, WNT7B), while deep SP DEGs were associated with extracellular matrix organization (e.g., HAS3,GFAP). These findings suggest functional specialization across SP depth, supporting diverse SpN roles in cortical circuit formation. This molecular heterogeneity provides a foundation for identifying human-specific SpN subtypes, advancing our understanding of cortical development and potential neurodevelopmental disorders.This study was approved by ethics committees at Osaka National Hospital, Kyoto Prefectural University of Medicine, and Tokyo Metropolitan Institute of Medical Science, with inter-institutional collaboration from the University of Tokyo.

P2/8 Orchestrated changes and spatiotemporal relationships between different transient compartments during precocious cortex-type specification in the human fetal pallium

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Early development of human pallium is characterized by dynamic laminar compartment-specific processes regulating the formation of distinct cortical types. Despite growing evidence on molecular changes in transient cytoarchitectonical compartments, cellular and molecular relationships between individual compartments leading to the cortex-type specification, remain poorly understood. In this study, we followed spatiotemporal differences in expression of proliferative, neuronal, fibrillar and synaptic markers in the subventricular zone (SVZ), postmigratory cortical plate (CP) and connectivity rich subplate (SP), and marginal zone (MZ) on serially sectioned postmortem fetal brain (tissue is part of the Zagreb Neuroembryological Collection, with ethical permission from the Internal Review Board of the Ethical Committee of the University of Zagreb, School of Medicine) during following phases: preplate (7-7.5 PCW), initial CP formation (8 PCW), primary CP condensation (8.5-11 PCW), secondary CP-SP formation (12-14 PCW) phases, and typical lamination period (15 PCW). Appearance of medial pallial hem is marked with an expanded plexiform MZ containing TBR2+, TBR1+, cells and tangetial medial fiber system. Allocortex primordium is also clearly defined at caudal ganglionic eminence outlining the future ventral division. In the preplate phase, dorsal neopallium shows massive invasion of TBR1+ reactive neurons. During next phase, disc shaped CP is formed showing basal to dorsal gradient in thickness of postmigratoy compartments alligned with SVZ gradient. Concomitantly, ventral allocortex displays an MZ enlargement, absence of CP in hippocampal primordium, SVZ thinning, and TBR2+ progenitors accumulation in MZ which merges with mesocortical SVZ. For the first time, CP is well defined in ventral hippocampal anlage (9.5-10 PCW). Despite the fact that CP is formed in allocortex later than in neopallium, since then hippocampal formation shows an accelerated differentiation where by 13 PCW is possible to distinguish all hippocampal fields, dentate gyrus and medial and lateral entorhinal pallium. Our findings suggest that establishment of the blueprint of cortex-type divisions is an orchestrated process involving coordinated interactions between different cellular and fibrillar compartments. We have observed that allocortical regions have unique developmental patterns from early embryonic development. This study contributes to filling a gap in understanding of cortex-type-specific lamination, and tectogenetic gradients of molecular and connectivity-based regionalization. This work was supported by the Croatian Science Foundation under the project number HRZZ-IP-2024-05-7157 (IK) and HRZZ-IP-2022-10-5975 (ŽK).

YOUNG INVESTIGATOR

P2/9 Endothelial-specific SMN Deficiency Drives Retinal Hypovascularization in a Novel SMA Mouse Model.

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Spinal Muscular Atrophy (SMA) is a genetic neuromuscular disorder caused by the loss of the SMN1 gene, resulting in decreased survival motor neuron (SMN) protein production. While traditionally considered a motor neuron disease affecting the spinal cord's ventral horn, recent evidence supports a broader, multisystemic pathology involving peripheral organs and tissues. In particular, growing data from both SMA patients and animal models indicate defects in the microvasculature. To explore the contribution of endothelial dysfunction to SMA pathology, we examined retinal vascular development in a newly developed endothelial-specific SMA mouse model (Endo SMA), in which SMN is selectively deleted in endothelial cells. Retinal vasculature was compared between Endo-SMA, full-SMA model mice, and controls. Whole-mount retinal immunohistochemistry was performed at postnatal day 7 using anti-PECAM1 to label endothelial cells. Vascular networks were quantified using AngioTool software to assess a range of parameters, including vessel outgrowth, density, endpoints, and lacunarity. Data showed significant differences across parameters using one-way ANOVA followed by Tukey's post hoc test (n = 3 per group), specifically a reduction in microvascular density in Endo SMA retinas (28.61±1.189 % Mean±SD) compared to control littermates (39.18±1.214%, $p<.0001$), confirming that endothelial SMN depletion alone is sufficient to impair vascular development. Interestingly, while the Endo SMA mice exhibited marked hypovascularization, this was not as severe as that observed in the full SMA model (19.07±1.115%, $p <.001$), suggesting a cumulative or synergistic effect of SMN deficiency across cell types. These findings highlight a key role for endothelial SMN in maintaining retinal vascular integrity and underscore the importance of targeting vascular components in future therapeutic strategies for SMA. Mice were maintained at and obtained from the University of Aberdeen Animal House, held under the personal licence of JMC (PP5319455). This followed the internal ethical approval from the University of Aberdeen.

YOUNG INVESTIGATOR

P2/10 An investigation into SKOR1 as a potential therapeutic target to prevent α-synuclein-induced degeneration in cellular models of Parkinson's disease.

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Parkinson's disease (PD) is a neurodegenerative disorder caused by αSynuclein (αSyn) accumulation and degeneration of nigrostriatal dopamine (mDA) neurons, resulting in motor impairments. There are currently no disease-modifying therapies for PD, making it crucial to identify new targets for neuroprotective therapy. Previous analysis highlighted SKI Family Transcriptional Corepressor 1 (SKOR1) as the most upregulated gene in the αSyn rat model of PD. SKOR1 overexpression has been shown to impair neurite growth, but it is unknown whether knockdown of SKOR1 can protect against αSyn. SH-SY5Y cells were co-transfected with 500ng of either a GFP or GFP-αSyn plasmid as well as 10nM of siRNA for SKOR1 knockdown (siSKOR1) or control siRNA. For the 6-OHDA model, cells were transfected with siSCR or siSKOR1 and then treated with 10nM 6-OHDA, or vehicle as a control, daily for 3 days. Transfected cells were cultured for 72hr before live imaging of GFP-positive neurites, and fixation for immunocytochemical staining. Effects of alterations in SKOR1 levels on neurite length, cell soma area and cell viability were measured. The negative effect of SKOR1 overexpression on neurite length was comparable to that caused by αSyn overexpression. siSKOR1 had a neuroprotective effect on neurite length in αSyn-overexpressing cells. Immunocytochemical staining showed that this neuroprotective effect was not due to changes in αSyn levels between groups. SiSKOR1 did not have a neuroprotective effect on neurite length in 6-OHDA-treated cells. This suggests that the neuroprotective effect of SKOR1 in SH-SY5Y cells is dependent on interaction with αSyn.SKOR1 is known to be a negative regulator of the BMP-SMAD pathway, but its mechanism is unknown. Modulation of SKOR1 levels did not impact levels of phosphorylated SMAD (pSMAD) in SH-SY5Y cells, which suggest that SKOR1 may act at the transcriptional level. To investigate this, we used a SMAD-GFP reporter assay, which indicated an inverse relationship between SKOR1 levels and transcriptional activity, suggesting that SKOR1 acts to negatively regulate BMP transcription. These data provide information on the mechanism of action of SKOR1 in dopamine neurons, and highlights SKOR1 as a novel target for a-Syn-focused therapies for PD.

P2/11 Understanding the Role of the Retrosplenial Cortex in Parkinson's Disease using Rodent Models and Human Brain Tissues

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Recent research has identified metabolic differences in the retrosplenial cortex (RSC) that differentiate cognitively normal people with Parkinson's disease (PD) from those with cognitive impairment. There remains relatively little investigation of this pathway in PD, despite the potential importance of this pathway to the manifestation of cognitive dysfunction. Therefore, this project sought to (1) validate the impairment in the RSC in PD; (2) use neuroanatomical tracing to identify the origin of the catecholaminergic innervation to the RSC; and (3) investigate the anatomical and functional characteristics of catecholaminergic denervation of the RSC. To achieve this, we (1) characterised the loss of tyrosine hydroxylase (TH+) innervation in two rodent models of PD, as well as in human post-mortem brain tissue; (2) used fluorogold retrograde tracing, co-labelled with TH to identify the source of the afferent projection, and (3) investigated the functional consequences of catecholaminergic denervation of the RSC using a rodent model. (1) A significant reduction in TH+ projections to the RSC was identified in two rodent models and, importantly, this loss was validated in human post-mortem brain tissues. (2) The RSC receives TH+ projections predominantly from the locus coeruleus, with no appreciable contribution from the ventral tegmental area or substantia nigra. (3) Loss of catecholaminergic innervation into RSC impaired short-term memory in the object recognition test and induced long-term spatial memory impairments in a spatial discrimination task. Catecholaminergic projections from the locus coeruleus to the RSC are implicated in PD and may contribute to cognitive features of the disease, such as short-term memory deficits and spatial memory dysfunction. Ethics Statement: All animal experiments were conducted in compliance with the UK Animals (Scientific Procedures) Act 1986 under Home Office Licence No. PP7595333 and with the approval of the local Cardiff University Ethics Review Committee. Human post-mortem tissue was obtain via the Parkinson's Tissue Bank at Imperial College London, which has been approved as a Research Tissue Bank by the Wales Research Ethics Committee (Ref. No. 18/WA/0238).

YOUNG INVESTIGATOR

P2/12 Epithelial-Neuronal Transdifferentiation in the Hypothalamo-Pituitary Axis in Acromegaly

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Developmental plasticity in cell lineage development in humans may be recapitulated in neoplastic transformation of cells. Here, we illustrate this phenomenon in the context of acromegaly caused by clonal transformation of somatotroph neuroendocrine cells of the pituitary. In rare instances of acromegaly, so-called 'collision tumours' have been described, comprising a presumed hypothalamic gangliocytoma or hamartoma and pituitary adenoma. However, we suggest that transdifferentiation of adenoma cells into neuronal ganglion cell-like phenotypes is a more likely explanation. We examined three examples of this rare phenomenon using immunohistochemical and epigenomic analyses. We find that cells that clearly exhibit ganglion cell-like morphological features co-express neuronal and epithelial markers (NeuN, neurofilament, cytokeratins) that are mutually exclusively expressed in normal hypothalamic and anterior pituitary cells. Specifically, fibrous bodies composed of low-molecular weight cytokeratins, which are pathognomonic to certain somatotroph adenoma subtypes, were clearly present in neuronal-like cells. Application of an epigenomic brain tumour classifier that identifies cell-lineage methylation signals and clearly distinguishes classes of gangliocytoma and pituitary adenoma, classified the lesions as somatotroph pituitary adenomas. In summary, these rare lesions seem to represent a naturally occurring example of the potential for cell-type and lineage plasticity in humans. Single cell transcriptomic experiments are underway to further resolve the dynamic trajectory of this phenomenon, since it remains unknown whether cell-intrinsic or microenvironmental signals drive this phenotytpic cellular plasticity. This research used human brain tissue samples. Ethical approval for this project is in place via Oxford-sponsored MRC Brain BioLink research funding. The authors for this study have no conflict of interest.

YOUNG INVESTIGATOR

P2/13 Developing and evaluating cephalometric measurements to accurately identify the location of the thalamus for neurosurgical procedures

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Cephalometric techniques, which use head measurements to locate brain structures, have been used since the late 1800s. Today, more advanced techniques such as neuronavigation are commonly used to localise brain areas accurately. However, knowledge of the cephalometric techniques used to locate brain structures is still useful for neurosurgeons when undertaking pre-operative planning and intra-operative navigation. Neurosurgical trainees are encouraged to use cephalometric techniques rather than solely relying on neuronavigation technology. Our review of the literature showed that while cephalometric methods are widely used for locating cerebral structures, there are no such methods to locate the thalamus, a structure often thought of as the centre of the brain. Therefore, we created two novel cephalometric techniques, technique 1 (Cavanagh) and technique 2 (Leonard), which located the thalamus using simple and easy-to-reproduce measurements between existing external landmarks. The accuracy of our techniques was evaluated on 78 3D-reconstructed magnetic resonance imaging (MRI) scans, two cadaveric heads and one living volunteer. Our results show that both of these techniques successfully locate the thalamus to a high degree of accuracy. Technique 1 aimed to locate the centre of the thalamus and was able to do so within 6.88mm (±2.58mm), 4mm and 24mm, and 3.0mm in the MRI, cadaveric and living volunteer studies respectively. Technique 2 aimed to locate the superior border of the thalamus and did so within 4.89mm (±2.85mm) in the MRI stage and to a high degree of accuracy in the cadaveric study. We conclude that our techniques are valuable additions to the existing cephalometric measurements used by neurosurgeons to locate brain structures. The location of the thalamus on the surface of the head will allow for orientation around a central point, which, when used alongside neuronavigation, has the potential to improve pre-operative planning and intra-operative navigation of neurosurgical procedures. The central point also provides opportunities to locate surrounding brain structures, allowing visualisation on the surface of the head to further support trainees with the localisation of brain areas. Bequeathed human cadaveric material were maintained as per the Anatomy Act 1984 (as amended by HTA (Scotland) Act 2006).

YOUNG INVESTIGATOR

P2/15 Head in the clouds: How Do Particulate Matter Pollution and Early-Life Stressors Influence Zebrafish Neurodevelopment?

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Urban particulate matter (UPM), a mixture of solids, gases and aerosols, is associated with ~7 million premature deaths annually. Early-life UPM exposure impacts upon cognition, memory and behaviour, yet it is not known if UPM is directly responsible or primes the nervous system to respond adversely to other environmental challenges. As a vertebrate model with conserved neurodevelopmental pathways, zebrafish offer a powerful system for gaining mechanistic insight into how UPM may disrupt early human brain development. This model was used to test the hypothesis that repeated exposure to lower levels of UPM and additional stressors are required to induce neurodevelopmental deficits. Zebrafish embryos and larvae were treated with different concentrations of UPM (30 and 100µg/ml) ± Cortisol (1µM), which mimics elevated hormonal stress levels. Treated larvae were assessed for alterations in morphometry using microscopy, and the functional impact of potential neurodegeneration assessed by behavioural analyses using a DanioVision machine. Embryos incubated in UPM showed significantly reduced movement at 5dpf. Significant differences were found in other behavioural metrics relating to larvae orientation, e.g., angular velocity. The same pattern was also observed in morphometric measurements of the larvae head width, a proxy for forebrain/midbrain growth, and pigmentation. Neuronal architecture was examined using immunohistochemistry and confocal microscopy, showing qualitative differences in axonal connections across the brains of individual larvae. A computational approach in topological data analysis (TDA) was used on a selection of these confocal images—specifically the zebrafish midbrain—to independently assess structural changes relating to neuronal topology. No significant differences were found between zebrafish exposed to either UPM and/or Cortisol. This may reflect limitations of TDA for confocal images, though further analysis of other brain regions and ongoing TUNEL experiments are needed to evaluate its relevance to neurodevelopment. This study offers insight into how UPM and co-occurring stressors affect nervous system development, using a whole-animal model to inform strategies for mitigating pollution-related neurodevelopmental risks in humans. This project has been approved by the RVC Animal Welfare and Ethic Review Board and is being conducted under Home Office Project License PP5309866. Zebrafish larvae were euthanised using a Schedule 1 method.

YOUNG INVESTIGATOR

P2/16 Investigating the Microbiomes Influence on a Zebrafish Larval Model of Neuronal Ceroid Lipofuscinosis Type 2 (CLN2) Disease

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The microbiome has been linked to various neurodevelopmental conditions such as autism and epilepsy but the impact of the microbiome on many neurodevelopmental disorders has not been fully explored. Neuronal ceroid lipofuscinosis type 2 (CLN2) disease is caused by mutations in the Tripeptidyl-peptidase-1 (Tpp1) enzyme, resulting in accumulation of waste within lysosomes and extensive neurodegeneration across the cortex. The age of onset of CLN2 disease is 2-4 years old with seizures, followed by progressive loss of motor and cognitive skills and premature death by age 13. To identify whether microbiome manipulations may modify symptoms, the microbiome was removed from a zebrafish larval model of CLN2 disease (tpp1-/- larvae), generating germ-free tpp1-/- larvae. Various phenotypes were explored such as behaviour, lysosome levels and cell death within the brain area. Whilst some measurements did not significantly change with the removal of the microbiome, tpp1-/- larvae raised in a germ-free environment until 3dpf exhibited an increased mean velocity, suggestive of increased seizures. Despite this, with delayed microbiota colonisation until 3dpf, an increased mean meandering was observed at 5dpf, suggesting an improvement in the loss of locomotion phenotype normally observed in 5dpf tpp1-/- larvae. Tpp1-/- larvae raised in a germ-free environment until 5dpf had an intraocular distance more comparable to wildtype larvae, a measurement suggestive of forebrain size. A reduction was also observed in the number of TUNEL clusters in 5dpf delayed colonisation and germ-free tpp1-/- larvae compared to conventionally raised controls, suggesting a reduction in cell death within the brain. 3dpf RNAseq analysis, suggested genes related to the forebrain, eyes, pigment and iron transport/metabolism are altered by the absence of a microbiome and are returned to levels commensurate with control larvae. This data collectively suggests that microbiome manipulation can impact CLN2 disease phenotypes and may identify potential therapeutic approaches for this neurodevelopmental disorder. This PhD project is Anatomical Society funded, is being conducted under Home Office PPLs PCAF13DEE and PP5309866 and has been approved by RVCs AWERB.

YOUNG INVESTIGATOR

P2/17 Morphometric analysis of the lateral pterygoid plate in human dry skulls and its role in the surgical approaches of trigeminal neuralgia through foramen ovale

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Trigeminal neuralgia is managed surgically through percutaneous needle insertion through the foramen ovale (FO) to access the trigeminal ganglion. While this technique is minimally invasive, variations at the skull base can hinder needle trajectory, leading to reduced procedural success and increased complications. The posterior border of the lateral pterygoid plate (LPP) is commonly used as a guide to locate the FO, but morphological differences in LPP can create physical barriers during cannulation. Iwanaga et al. categorised skulls into four types based on the spatial relationship between the FO and the posterior border of the LPP and described that the removed type may be more prone to procedural failure. This study investigated whether additional morphometric characteristics of LPP in removed skull types also increases the likelihood of obstruction while targeting foramen ovale. A total of 38 human dry skulls (76 sides) were examined, with 60 sides meeting inclusion criteria. Each skull was classified into one of the four FO types, and nine morphometric parameters were measured: LPP breadth at five evenly spaced levels, LPP height, distances from the LPP to medial pterygoid plate and articular tubercle, and the lateral deflection angle of the LPP. Measurements were obtained using digital vernier calliper, two-pin spacer, and goniometer. The results revealed that skulls with medial FO type exhibited significantly greater LPP breadth in the mid-to-proximal regions and increased LPP height ($p < 0.05$), suggesting that LPP may be a more prominent anatomical barrier. However, distances to adjacent landmarks and the lateral deflection angle showed no significant differences between FO types. These findings indicate that in medial type skulls, the LPP may pose a greater risk of obstructing needle access to the FO, potentially leading to deviation or failure of procedure. This challenges the previous assumption that the removed type is the most obstructive, which was based only on the posterior border of LPP. Incorporating this detailed morphometric evaluation of LPP into preoperative planning may improve the accuracy of procedures and reduce recurrence rates. The specimens used for this study were sourced through the donor registration program at the University of Birmingham (license number 11236).

YOUNG INVESTIGATOR

P2/18 Volumetric representation of carpal bones in the study of anatomical variations in primate wrists – a novel way to assess small, complex bone structures

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Carpi are small and have highly irregular - function depending shape. This makes it difficult to identify meaningful ways to compare them across closely related taxa. This study explores the use of volumetric representation of small irregular-shaped bones by investigating volumetric variation in carpi and their functional columns across 34 species of extant primates, as a complementary factor in the evolution of the primate wrist. This study first aims to confirm the between-group differences of carpi and their functional columns across primate taxa. Then, to investigate patterns of variation in observed variation (correlation test and PCA), also, the relationship between variation and locomotor in a phylogenetic framework (PGLS). These analyses were also conducted on the three columns of carpi. In which pisiform and triquetrum were grouped as ulnar column; capitate, hamate, and lunate as central column, and the combination of scaphoid and centrale (SCE), trapezoideum, and trapezium as radial column. From correlation test, at family level, only in Hominidae, radial column is independent from the other columns. From PCA, PC1-PC3 represent 75.69% of variations from carpi volume across 34 species of primates. The two carpi of ulnar column make significant contribution to PC1, and the three carpi of central column make significant contribution to PC2. Finally, the two carpi of radial column (trapezoideum and SCE) and the hamate of central column make significant contribution to PC3. PGLS models indicate that both PC1 and 2 are significantly correlated with locomotor. Results from this study 1. Supports the use of volume as a quantifiable parameter in the study of primate carpi. 2. Carpus series can be viewed as the ulnar, central, and radial columns, and such grouping of the carpus is of functional relevance. Overall, this study reports interesting findings of how the variations seen in the primate carpus can be summarised into three PCs and mostly overlap with the functional column. The result of the study supports the use of volumetric parameters as a way of studying primate carpi variation, as well as providing new insights in future studies concerning the integration and modularity of the carpi in wrist evolution.

YOUNG INVESTIGATOR

P2/19 Nerve distribution patterns across the human orbicularis oculi muscle: Implications for facial reanimation surgery

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Voluntary eyelid closure and the blink reflex are mediated by distinct anatomical segments of the orbicularis oculi (OOc) muscle. However, the distribution of facial nerve branches supplying these segments remains undefined. Given the challenges in re-establishing a natural blink, despite achieving voluntary eyelid closure, in facial reanimation procedures, this study aims to characterise the macro- and microscopic innervation patterns of the OOc to explore its anatomical and functional complexity. Sixteen OOc dissections were performed on 8 human soft-embalmed cadavers (4 male, 4 female; mean age: 85 years) by an experienced supermicrosurgeon. The OOc was divided into three Zones: orbital (A), pre-septal (B) and pre-tarsal (C). Transition and penetration points were mapped using a cartesian coordinate system to determine nerve location, direction of travel and the point of entry into muscle. Statistical analysis compared the distribution of nerves in Zones A-C (Kruskal-Wallis test; Dunn's post-hoc analysis). Nerve diameter and morphological characteristics were recorded, and histological analysis was performed with Haematoxylin and Eosin stained slides and S100 immunostaining. A total of 521 nerves were identified: Zone A (42.91%), Zone B (37.81%), and Zone C (18.62%). In Zone A, the highest nerve density was aligned with the intercanthal midpoint, with 47% of branches transitioning to Zone B. Zone B was densely innervated near the medial canthus, while Zone C displayed a remarkably different innervation pattern, with minimal contribution from Zones A and B. Statistical analysis showed significant differences between Zones A and C, and Zones B and C ($p<0.05$). Histological analysis supported the pre-tarsal distribution and confirmed the intramuscular nerve dense regions. Orbital and pre-septal nerve distributions seem largely interlinked and are essentially terminal branches of periocular muscles, such as the corrugator supercilii, frontalis and zygomaticus major. The innervation of the pre-tarsal segment, crucial for the blink response, is independent of the orbital and pre-septal OOc. These findings expand on the anatomical basis of rapid, involuntary blinking, and the synkinesis and co-contractions associated with gentle and forced eyelid closure. The donors were bequeathed for anatomical education and research at Brighton and Sussex Medical School, in compliance with the Human Tissue Act (2004).

P2/20 Role of the spatial relationship of the foramen ovale to the adjacent neurovascular structures in different human skull types for percutaneous trigeminal neuralgia interventions

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The foramen ovale (FO) is an important anatomical landmark at the base of the skull used in percutaneous procedures for trigeminal neuralgia (TN). The lateral pterygoid plate (LPP) is an anatomical landmark to access FO. However, the anatomical relationship between the FO and the LPP varies across individuals, leading to four distinct skull types: lateral, medial, direct, and removed. Complications like internal carotid artery haemorrhage, nerve palsy, and facial weakness have been reported in percutaneous intervention for TN. To avoid complications during procedures, it is necessary to determine the position of FO to adjacent neurovascular structures in different skull types. Therefore, this research aimed to assess whether specific skull types pose a higher risk during surgical interventions due to the proximity of FO to the neurovascular structures. Thirty human dry skulls (60 sides) were examined and classified into one of the four types based on the position of the LPP relative to the FO. Using a vernier caliper, measurements were taken from the FO to adjacent anatomical landmarks: the spine of sphenoid bone, foramen spinosum, alveolar tuberosity, foramen lacerum, carotid canal, inferior orbital fissure, and foramen of Vesalius. Most of the skull types showed less or no significance in the position of the FO in relation to surrounding structures. However, the removed type was significantly farther from the inferior orbital fissure, and the direct type was notably closer to it ($p < 0.005$). While previous literature has suggested that the removed type poses challenges during needle insertion, our findings highlight that the direct type may pose a greater risk of complication due to its proximity to the inferior orbital fissure—increasing the chance of nerve injury and subsequent diplopia or blindness. Since the direct skull type is the most common, clinicians should be aware that injury to the inferior orbital fissure is more likely in such types, emphasizing the importance of the relationship of FO to the adjacent structures. The consent for images of the human dry skulls used in this research were obtained through the donor registration programme at the University of Birmingham (license number 12236).

YOUNG INVESTIGATOR

P2/21 Understanding The Medical And Surgical Implications Of Accessory Spleen In Homo Sapiens

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An accessory spleen is a congenital condition resulting in splenic tissue forming in ectopic sites in the abdomen. This literature review aims to identify the common sites of accessory spleen (AS) formation and its occurrence in the population. It will also include why AS is relevant to surgeons when diagnosing masses found in abdominal scans of patients with acute abdominal pain. This study examined case reports from PubMed and Google Scholar, and results were discussed, showing that AS was frequently misdiagnosed as a neoplasm. Cadaveric studies were also included in this review to see how the results from case studies compare to studies where the sample size is larger, when looking at the site and prevalence of AS . Some comparisons made were that the most common sites of AS formation were at the spleen's hilum and the pancreas's tail. Prevalence of AS in the cadaveric studies ranged from 0% to 23%, and in both case reports and cadaveric studies, cases of multiple AS were reported. AS can often be asymptomatic or result in pathologies such as torsion, which patients can present with in the emergency department. SPECT-CT and histology examination were identified as a potentially accurate diagnostic tool for AS pre-operatively. No ethical approval was required for this literature review, as all research papers included (that involved cadaveric studies or live patients) were found on search engines.

P2/22 Altitude-related anthropometric differences between Highlander and Lowlander Bhutias of Uttarakhand

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Jad Bhutia is an indigenous transhumant tribe of Uttarakhand, India. They have permanent settlements at Dunda in Uttarkashi at an altitude of 1158 meters, Bagori in Harsil valley (2745meters) and seasonally migrate to Jadong (3824 meters) for pasture. Living at varying altitudes they exhibit notable differences in anthropometric and craniofacial characteristics. This study aimed to compare facial and general anthropometric parameters of the indigenous Bhutia tribe, residing in Harshil Valley at altitudes of 2745 metres, and Dunda Valley at 1158 meters, in Uttarakhand, India. This cross-sectional study included 24 highlanders (6 males, 18 females) from Harshil Valley and 32 lowlanders (5 males, 27 females) from Dunda Valley, belonging to the same indigenous Bhutia tribe. Anthropometric parameters of body, craniofacial features, skinfold thickness, age, weight and height along with other demographic data were recorded after informed consent. Significant variations were noted in craniofacial characteristics with Highlander males having considerably greater head length ($p = 0.007$) and smaller zygomatic distance ($p < 0.028$). Significant differences were also seen in ear and upper lip measurements with lowlander males having wider and longer ears and broader upper lip ($p = 0.035$). Highlander females had greater head length ($p < 0.001$), head breadth ($p = 0.016$) and face length ($p = 0.029$). However, Lowlander females had wider zygomatic distance ($p < 0.001$) and malar breadth ($p =0.007$). Significant differences were also seen in ear, nose, eyes and lip measurements with Lowlander females having broader ears with wider canthal distance. Highlander females had more elevated but less broad nose. The mid-arm circumference of Highlander females had reduced skinfold thickness ($p < 0.001$). Possible altitude-related adaptations are suggested by the reported anthropometric differences between Highlanders and Lowlanders, especially in terms of body, craniofacial and skin features. These discoveries add to the expanding corpus of research on how human phenotypes might adapt to these changes and could be helpful in planning facial reconstructive surgeries and/or other health related care. This study was a part of Extramural Project sanctioned by UCOST- Uttarakhand, with Principal Investigator from department of Physiology and Institutional Ethical approval (AIIMS/ IEC/18/70).

YOUNG INVESTIGATOR

P2/23 Bony anatomical differences for the sex disparity in anterior cruciate ligament injury: a human cadaveric morphometric study

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Anterior cruciate ligament (ACL) injuries are common in the young and active population, with female athletes experiencing up to an 8-fold higher incidence rate than male athletes. The cause of this increased incidence is likely multifactorial, comprising of anatomical, physiological and environmental factors. Anatomical factors which have been examined in previous studies include differences in bony morphology between males and females, notably the femoral intercondylar width (ICW), femoral bicondylar width (BCW) and tibial plateau slope (TPS). However, these studies often produce contradicting results. The present study investigated the bony features on the distal femur and proximal tibia using 12 cadaveric donor knees to account for the sex discrepancy in ACL injury rates. Values were obtained through direct measurements of the width, height and depth of the distal femur and proximal tibia features using digital callipers, and a goniometer to measure the TPS. The ICW and BCW were found to be significantly smaller in females relative to males, along with lateral femoral condylar width and height, and the total, medial and lateral tibial plateau widths. However, the TPS was not significantly different. Non-contact ACL injury typically results from a valgus force exerted on a flexed knee. During this motion, a smaller ICW may impinge the ACL against the notch wall and a smaller BCW may permit greater rotation of the knee, increasing stress on the ACL. These findings highlight the need for specific training programmes for the separate sexes to strengthen muscles around these bony differences to reduce the ACL injury incidence rate. Additional functional testing on the ACL replicating the forces that occur during an ACL injury may identify the position and angle of the bony features which produce strain on the ACL. Tibial plateau dimensions have received limited attention in previous research and is a factor that should be explored in greater detail in the future. All cadaveric research was conducted in full compliance with relevant anatomical legislation under the University of Birmingham's Human Tissue Authority Licence for Anatomical Examination 12236. All donors gave their consent in accordance with the Human Tissue Act (2004).

YOUNG INVESTIGATOR

P2/24 Morphometric Analysis of Knee Ligaments and Menisci: A Cadaveric Study of Sexual Dimorphism and its Implications for the Disparity in ACL Injury Incidence

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Females sustain anterior cruciate ligament (ACL) injuries at disproportionally higher rate than males. Although these injuries are widely recognised as multifactorial, there remains limited consensus on sex- based morphological variation of the ACL and supporting knee structures. This study aimed to investigate morphometric differences in the ACL, posterior cruciate ligament (PCL), medial collateral ligament (MCL), lateral collateral ligament (LCL), and the menisci between male and female donors. Seven donor-derived knee joints (3 female, 4 male) were dissected by two independent observers. Length, width, thickness and circumference of the ligaments were measured. Cross-sectional areas (CSA) were calculated at the midsubstance, femoral origin, and tibial insertion. Meniscal curved length and slope at the posterior horn were recorded. All measurements were analysed in absolute terms and normalised to donor height using unpaired t-tests. Significant sex-based differences were identified across several parameters. Male ACLs presented greater values in ACL width, midsubstance CSA, and tibial footprint area. Similar patterns were observed in the PCL, MCL, and LCL. However, this trend was reversed following height normalisation, with females presenting significantly greater direct and area measurements. No statistically significant differences were found in meniscal posterior horn slopes. Whilst males generally presented larger ligament dimensions, the reversal of this trend following height normalisation complicates interpretation, challenging both the initial hypotheses and prevailing assumptions in the literature. These findings highlight methodological and theoretical limitations in sex- based anatomical research, reinforcing the need for more refined approaches to understanding ACL injury risk.All cadaveric research was conducted in full compliance with relevant anatomical legislation under the University of Birmingham's Human Tissue Authority License for Anatomical Examination 12236. All donors gave their consent in accordance with the Human Tissue Act (2004).

P2/25 Understanding the breakdown of hair follicle integrity in hidradenitis suppurativa

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Hidradenitis suppurativa (HS) is a devastating inflammatory skin disease with poorly understood pathogenesis but a distinct anatomical presentation in the groin, armpits and inframammary regions with terminally differentiated hair follicles are present. These hair follicles appear to be the site of disease initiation through their aberrant infundibular plugging, intradermal rupture and subsequent inflammation which becomes chronic. Our research aims to better understand the diseases' pathogenesis using a combination of ex vivo human hair follicle culture, single-cell transcriptomic datasets and immunohistochemical analysis of fresh and cadaveric skin specimens (all human). We are using these approaches to understand the inflammatory and neuroimmune factors which may govern the disruption of the distinct anatomical regions of the hair follicle, with a particular focus on the infundibulum with early results indicating known interleukins such as IL-17 may causes a hyperproliferation in this region. In addition, we are building a transcriptomic map of HS hair-follicle vulnerability, by precisely taking multiple hair follicle samples from axillar resections and performing bulk and single-RNAseq from multiple samples/patient. The single-cell cell samples will identify cells types in the deconvoluted bulk RNAseq, increasing the power of the dataset. All research is conducted with appropriate ethical oversight from participating institutions local ethics committees.

P2/26 Variation in the Origin of radial artery: An Ultrasound anatomy study

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Typically, the radial artery arises as a branch from the brachial artery at the level of the neck of the radius in the distal antecubital fossa. Anatomical variations in the radial artery are relatively common. Published literature demonstrates wide variability in the prevalence of high originating radial artery (0.5-14.27%). The literature also shows inconsistent and vague nomenclature when describing the arterial system in cases of the high originating radial artery. This study aimed to investigate the incidence of a high originating radial artery in vivo through the use of ultrasound. 300 upper limbs from 150 individuals were investigated using GE LOGIQ e and SonoSite MicroMaxx ultrasound machines with 12L-RS & A L38e 10-5MHz transducer, respectively. The radial artery was initially identified and followed proximally to its origin and then distally to the wrist, noting its course and relationships to other anatomical structures. The radial artery was identified through the use of ultrasound in the antecubital fossa in all 60 participants as an anechoic structure in cross-sectional axial ultrasound images. High originating radial arteries were found in 23/300 (7.6 %) upper limbs . In the participants studied, the high originating radial arteries were found to occur unilaterally predominantly on the left side (15/23 cases).Variations in the anatomical course and relationships of the radial artery are pertinent to surgeons, radiologists and anatomists. The presence of a high originating radial artery has both clinical and surgically significance in procedures, such as arterial grafting and cardiac catheterisation. Due to its superficial course, it is more vulnerable to injury due to trauma or during cannulation and drug administration. Bedside ultrasound techniques can not only be of benefit in identifying variations prior to such procedures but also for future anatomical studies. This ultrasound study was performed with the understanding and written consents of all participants. This study was approved by Institutional review board of Northumbria University, United Kingdom.

YOUNG INVESTIGATOR

P2/27 Evaluating the learning efficacy and perceptions of 3D-printed cranial structures in undergraduate anatomy education: a mixed methods study

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Anatomical education is dynamic and ever-changing, with rapid advancement occurring in three-dimensional modelling and printing. The advent of three-dimensional printed models (3DPM) offers a novel substitute to traditional anatomical models. Additionally, it provides the opportunity for modelling rare and pathological specimens which are otherwise unsuitable for large cohort undergraduate teaching. This mixed-methods study investigated the integration of in-house printed 3D models of skull bones and hydrocephalus pathologies as teaching resources at University of Birmingham (UoB), focusing on student and staff perceptions as well as the learning efficacy. A total of 245 out of 425 first-year students enrolled in the UoB MBChB programme and nine staff members completed a Likert-scale questionnaire and were invited to include open-text responses following interaction with 3D printed sphenoid models. Additionally, normal lateral ventricles, hydrocephalic lateral ventricles and hydrocephalic skull 3DPMs were created using publicly available MRI data and 3D scans of archived hydrocephalic skull specimens. These models were used to compare learning outcomes against traditional bony specimens. As part of a randomised controlled trial, 12 first- and second-year volunteers were randomised into three active learning session groups involving either 3DPMs, bony specimens or a combination. Knowledge retention was assessed by pre-session and post-session tests. Responses from the sphenoid model Likert questionnaire were overwhelmingly positive, with content analysis of open-text responses highlighting enhanced visualisation and educational value. UoB students and staff agreed that 3DPMs should serve as an adjunct to real specimens. All groups from the randomised controlled trial showed improved test scores, with the 3DPM group demonstrating the greatest average improvement from pre-session to post-session test score (4.38 points), while the combination group portrayed the least improvement (2.25 points). The differences in improvement between the three groups were not statistically significant indicating no superiority of any single resource. Overall, this study confirms the value of 3DPMs in settings when traditional materials are limited if implemented effectively, whilst reinforcing the importance of multimodal learning approaches in anatomy at UoB. Additionally, it highlights the benefits and feasibility of the incorporation of 3DPMs generated from MRI patient-specific data and 3D scans of pathological specimens into teaching at UoB. Ethical approval was granted by the School of Biomedical Science Ethics Committee of the College of Medical and Dental Sciences (UoB). The Ethics Committee reference number is BMSRP_2025_Lab044.

P2/28 Exploring student perceptions of underrepresented bodies in anatomy education using 3D printing and wax modelling

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The underrepresentation of cisgender female, transgender female, and intersex bodies in anatomical education limits inclusivity and can affect clinical competence and equitable care. This study explored how hybrid 3D-printed wax models and sketches showing variations in internal and external genital anatomy could improve knowledge, confidence, and views on inclusivity among medical students and anatomy teaching staff. An interactive session was delivered to 19 second-year MBChB students and eight staff members at the University of Birmingham. Participants completed pre- and post-session surveys with Likert-scale and open-ended questions assessing confidence, comfort, and perceptions of the curriculum. Before the session, students reported high confidence in cisgender anatomy but significantly lower confidence in transgender and intersex anatomy ($p < 0.01$), with no significant differences in comfort. Staff also reported lower confidence and comfort with teaching transgender and intersex anatomy compared to cisgender anatomy, with some differences reaching significance ($p < 0.05$). Post-session, both groups showed improved confidence and comfort, though most changes were not statistically significant. However, staff showed a significant increase in confidence related to intersex anatomy ($p < 0.05$), suggesting targeted impact. Both students and staff supported using inclusive anatomical models in education and highlighted gaps in current curricula, especially in representing anatomical diversity beyond the gender binary. This study shows that inclusive anatomical resources can enhance confidence and raise awareness of curriculum limitations. Integrating such tools into medical education offers a practical way to support gender- and sex-inclusive healthcare training. Ethical approval: University of Birmingham BMS Ethics Committee (Ref: BMSRP_EDU015).

P2/29 Creating inclusive perineal anatomy models using 3D printing and wax modelling techniques

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Anatomical education has historically lacked representation of gender- and sex- diverse bodies, limiting student understanding of diversity in bodies. This project aimed to (1) develop models of the cisgender female, transgender female, and intersex perineum, and (2) design an autonomous learning session to promote engagement with underrepresented anatomies. Over a four-week period, nine hybrid anatomical models were created using a combination of 3D printing and wax sculpting techniques. A digital model of the bony pelvis was sourced from Sketchfab, modified in Tinkercad to retain perineal structures and incorporate the perineal membrane, and printed using BCN3D Epsilon printers. External genitalia were sculpted in terracotta and white wax, then painted to represent a range of skin tones. The final collection included four cisgender, two transgender, and three intersex models, each depicting variations in anatomical structures such as the clitoris, labia, and superficial perineal pouch structures commonly seen post-vaginoplasty or in intersex presentations. Supplementary resources, including labelled sketches, case studies, and explanations of terminology, accompanied the models to support self-directed learning. Survey responses from a self- selected sample of twenty-seven participants (students n = 19, staff n = 8) indicated that the models improved understanding of anatomy, provided inclusive representation of intersex and transgender bodies, and should be integrated more broadly into medical education. This project demonstrates how combining 3D printing and wax modelling can enhance representation of diversity in anatomy education and promote inclusive and reflective learning. Ethical approval was granted by the Department of Biomedical Sciences Ethics Committee (Ref: BMSRP_EDU015)

P2/30 Investigating Medical Students' Perceptions of Gender Bias in Clinical Pain Management Observations

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Gender bias in pain management can impair diagnosis and treatment, often leading to the psychologisation and undertreatment of women's (cisgender and transgender) pain. While policies promote equitable care, little is known about how early-stage medical students perceive and internalise such biases. This study aimed to quantify perceptions of gender differences in pain management among first-, second- and third-year medical students, explore how biases are observed in practice, and evaluate perceived curriculum adequacy. In this mixed-methods pilot, 22 medical students completed a 17-item paired-Likert survey, six open-ended reflections, and three semi-structured interviews. Wilcoxon signed-rank tests compared mirrored female and male pain scenarios, while thematic analysis was applied to qualitative data. Students agreed that women's pain is more often attributed to psychological causes ($p=0.0078$) and that women must advocate more strongly for analgesia than men ($p=0.0027$). Only 14% felt prepared by the curriculum to address gender bias, while 91% called for further training. Although 55% reported confidence in identifying bias, interviews revealed that power dynamics created hesitancy in challenging clinicians. Students recognised gender disparities in pain management but felt underprepared to address them due to limited formal training. These preliminary findings suggest potential value in incorporating interactive, bias-focused education into the medical curriculum, developing tools to track bias awareness over time, and including more diverse patient scenarios in teaching. Further research is needed to explore the feasibility and impact of such measures, including the potential development of an NHS audit tool to monitor clinical gender bias. Approval was granted in March 2025 by the Department of Biomedical Science Ethics Committee, University of Birmingham (Reference Number: BMSRP_2025_EDU17).

P2/31 Medical Students' Perceptions of Gender and Ethnic Bias in Pain Management: A Mixed Methods Study

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Disparities in pain management based on gender and ethnic background have been widely documented; however, limited research has explored how medical students perceive these biases in relation to their own demographic characteristics. This cross-sectional mixed-methods pilot study hypothesised that medical students, particularly those from marginalised backgrounds, would recognise both gender and ethnic bias in clinical pain management. Twenty-two medical students from years one to three of the University of Birmingham completed a bespoke questionnaire combining Likert-scale items, open-ended questions, and follow-up interviews. Quantitative data suggested that while students recognised gender and ethnic bias separately, they struggled to identify their intersection. A significant finding was that students perceived female patients as needing to advocate more strongly for pain relief compared to males ($p = 0.0036$), though no significant differences were observed in treatment outcomes. Thematic analysis of qualitative responses suggested that although students expressed confidence in detecting bias, they reported infrequent observation of such incidents in practice, and no clear pattern was found linking student gender or ethnicity with bias recognition. This may indicate that systemic biases are internalised regardless of the students' own demographic background. These initial findings suggest value in expanding this research to a larger cohort and support further investigation into how structural and educational changes might better equip students to recognise and address intersectional bias. Approval was granted in March 2025 by the Department of Biomedical Science Ethics Committee, University of Birmingham (Reference Number: BMSRP_2025_EDU17)