SABV SYMPOSIUM 2026

ABSTRACT BOOK

Sex as a Biological Variable (SABV)

From discovery to translation: Embedding sex-inclusive frameworks in preclinical and clinical research

23 - 24 June 2026 • Zurich, Switzerland

Dear Colleagues,

Welcome to the SABV Symposium 2026 in Zurich! What started as a small symposium four years ago in Bern has now grown into a biennial event, and I am excited to host its third edition this year.

This international symposium remains dedicated to raising awareness of why it is important to consider biological sex and to study it appropriately in basic and preclinical research. The scope this year extends to clinical research as well, looking not only at biological sex but also at gender, and bringing female health into the spotlight, an area that remains strikingly understudied, undervalued, and underfunded. To shed light on these topics, the program brings together internationally renowned speakers who will share the latest evidence on how sex shapes biological processes, from the molecular level all the way to the whole organism. It also features selected abstracts, and this year's especially high number of submissions resulted in an impressive poster session, making the selection of the eight flash talks no easy task.

This symposium is made possible by the support of the EU-SABV COST Action grant (CA24168), which I was awarded last year and which enabled the creation of the first open European network of researchers dedicated to understanding how biological sex shapes health and disease, and most of these researchers are here with us today. I would also like to thank the Philas Foundation and Roche Research Education and Development in Switzerland (REDS), who awarded me grants in support of this event. A big thank you also goes to Merck, Inotiv, and Novogene for their sponsorship, and to the University of Zurich and University Hospital Zurich for hosting us. Last but not least, my thanks go to the Swiss 3R Competence Centre (3RCC), which has supported this symposium since its very first edition four years ago in Bern.

I hope you will enjoy the symposium, find the talks inspiring for your own work, and leave feeling more empowered to account for both biological sex and gender in your future research. I wish you a productive and enjoyable time in Zurich and thank you for your participation.

Dr. Ivana Jaric
Organizer of the SABV Symposia
Group Leader, Neuroendocrinology group, Institute of Laboratory Animal Science (LTK)
University of Zurich
Chair of EU-SABV COST Action (CA24168)

Please complete the short survey to assist in improving the SABV symposium. Your feedback will help determine if similar symposia and workshops should be offered as future continuing education courses.

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The SABV Symposium 2026 is co-organized by the EU-SABV COST Action (CA24168), the European Initiative to Enhance the Current SABV Policy in Preclinical Biomedical Research, funded by the European Cooperation in Science and Technology (COST). Learn more about the EU-SABV COST Action at action webpage: https://sabv.eu

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Symposium venue

University Hospital Zurich (USZ)
Frauenklinikstrasse 10
8091 Zurich

Building NORD 1
Large lecture hall
(Room number D 304)

Free Wi-Fi at the venue

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Continuing education certificate

The SABV Symposium 2026 has been officially accredited by the Federation of Swiss Cantonal Veterinary Officers (VSKT) as **2 days of continuing education** for the following professional categories:

- Study directors and involved persons
- Animal welfare officers
- Heads of animal facilities and animal caretakers
- Members of cantonal commissions

Swiss national railways (SBB)

Timetables for airport-to-city trains and Zurich public transport: **www.sbb.ch/en**

Zurich public transport

Local timetables, network maps, and ticket options for city trams, buses, and boats: **www.zvv.ch**

Zurich public bikes

Map of self-service bike stations and app setup for short-term bicycle and e-bike rentals: **www.publibike.ch/en/zurich**

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SABV SYMPOSIUM 2026

PROGRAM

Day 1 • 23 June

Day 1 • 23 June 2026

8:00 – 8:50	Registration
8:50 – 9:00	Welcome address ***Dr. Ivana Jaric**, Symposium organizer - University of Zurich, Switzerland*

Session 1: Sex-inclusive research - Bridging the 3Rs framework and study design
Chair: Dr. Ivana Jaric, University of Zurich, Switzerland

9:00 – 9:30	**Addressing cultural and knowledge barriers to enable preclinical sex-inclusive research** ***Dr. Natasha Karp**, AstraZeneca, UK*
9:30 – 10:00	**Half the biology, half the insight: Accounting for sex in your experimental design** ***Prof. Dr. Penny S. Reynolds**, University of Florida, USA*
10:00 – 10:20	**The 3R framework for sex-inclusive animal research** ***Dr. Fernando Gonzalez Uarquin**, University Medical Center Mainz, Germany*
10:20 – 10:30	**Swiss 3RCC: A national platform for the promotion of the 3Rs** ***Dr. Homare Yamahachi**, Swiss 3R Competence Center*
10:30 – 11:00	Coffee break

Session 2: Sex differences in brain structure, function and disease
Chair: Prof. Dr. Charlotte Cornil, University of Liège, Belgium

11:00 – 11:25	**Sexual dimorphism in astrocyte-dependent synaptic pruning: implications for health and major depressive disorder** ***Prof. Dr. Barbara Di Benedetto**, University Hospital Regensburg, Germany*

Day 1 • 23 June 2026

Session 2 - continued

11:25 – 11:50 **Why should sex-dependent differences be considered for an optimized therapeutic approach of central nervous system demyelination?**
***Dr. Elisabeth Traiffort**, Inserm, Paris-Saclay University, France*

11:50 – 12:15 **Addressing the sex differences in Alzheimer's disease**
***Prof. Dr. Ivan Nalvarte**, Karolinska Institutet, Sweden*

12:15 – 12:40 **Different roles of brain uroguanylin and brown adipose tissue in males and females**
***Prof. Dr. Aleksandra Dugandzic**, University of Zagreb, Croatia*

12:40 – 14:00 Lunch break

Session 3: Sex differences across organ systems
Chair: Dr. Christina Boyle-Neuner, University of Zurich, Switzerland

14:00 – 14:25 **Role of sex hormones in lung disease manifestation**
***Dr. Valentina Biasin**, Medical University of Graz, Austria*

14:25 – 14:50 **Sex differences in kidney health and disease**
***Prof. Dr. Stefanie Steiger**, LMU Hospital Munich, Germany*

14:50 – 15:15 **Role of sex differences in the cardiac proteome and early graft recovery in donation after circulatory death**
***Prof. Dr. Sarah Longnus**, University of Bern, Switzerland*

15:15 – 15:40 **Sex differences in pharmacokinetics of anticancer drugs - why does that even matter?**
***PD Dr. Berna Ozdemir**, University Hospital Bern, Switzerland*

15:40 – 16:00 Flash talks selected from the abstracts 1
Chair: Prof. Dr. Michelle Roche, University of Galway, Ireland

Chronic unpredictable stress during the adolescent sensitive period induces sex-specific prefrontal microglial remodeling and differential astrocytic responses to extracellular vesicles in vitro
***Narimane Bouzourène**, Université de Lausanne, Switzerland*

Sex differences in a mouse model of chronic kidney disease
***Oriana Nobus**, Ghent University, Belgium*

Male mice rupture patellar tendon struts more often than females, with failure possibly attenuated by running
***Nicole A. Chittim**, Balgrist University Hospital, Switzerland*

Biological sex influences the physiological response to anesthesia in rats
***Maria Arnold**, Bern University Hospital, Switzerland*

16:00 – 17:00 Coffee break and poster session

Plenary talk 1
Chair: Dr. Ivana Jaric, University of Zurich, Switzerland

17:00 – 17:45 **Pain, sex, and death**
***Prof. Dr. Jeffrey Mogil**, McGill University, Canada*

SABV SYMPOSIUM 2026

PROGRAM

Day 2 • 24 June

Day 2 • 24 June 2026

8:10 – 8:50 Registration

Session 4: From evidence to action - Economics, innovation, and preclinical research
Chair: Dr. Ivana Jaric, University of Zurich, Switzerland

8:50 – 9:10 **The economic consequences of systemic underinvestment in women's health**
***Dr. Valentina Sartori**, McKinsey Health Institute*

9:10 – 9:20 **Accelerating innovation through sex-inclusive R&D**
***Dr. Juliana Bessa**, Roche Innovation Center Basel*

9:20 – 9:50 **PAINDIFF recommendations for the study and inclusion of sex and gender in research**
***Prof. Dr. Michelle Roche**, University of Galway, Ireland*

Plenary talk 2
Chair: Dr. Ivana Jaric, University of Zurich, Switzerland

9:50 – 10:30 **Sex, stress and high estrogen levels- a toxic hippocampal cocktail?**
***Prof. Dr. Tallie Z. Baram, MD**, University of California, Irvine, USA*

10:30 – 11:00 Coffee break

Session 5: Sex, hormones, and brain function
Chair: Dr. Jodi Pawluski, Universite De Rennes I, France

11:00 – 11:30 **Sex- and oestrous-dependent plasticity in midbrain circuits controlling survival instincts**
***Dr. Vanessa Stempel**, Max Planck Institute for Brain Research, Germany*

11:30 – 12:00 **SABV considerations in sleep loss-induced memory loss**
***Prof. Dr. Nicole Gervais**, Rijksuniversiteit Groningen, Netherlands*

12:00 – 12:30 **Hormonal contributions to depression in women; implications for precision prevention and treatment**
***Prof. Dr. Vibe G. Frokjaer**, Copenhagen University, Denmark*

Day 2 • 24 June 2026

Session 5 - continued

12:30 – 13:00 **Regulatory effects of antidepressant exposure on maternal–fetal signaling**
Prof. Dr. Jocelien Olivier, *Rijksuniversiteit Groningen, Netherlands*

13:00 – 14:00 Lunch break

Session 6: Female hormones and disease susceptibility
Chair: Prof. Dr. Christina Dalla, National and Kapodistrian University of Athens, Greece

14:00 – 14:30 **The estrous cycle stage affects mammary tumor sensitivity to chemotherapy**
Dr. Laura Bornes, *Leiden University Medical Center, Netherlands*

14:30 – 15:00 **The many faces of perimenopause: why are we still so bad at understanding the menopausal transition?**
Doc. Dr. Ljiljana Marina, *University Clinical Centre of Serbia, Faculty of Medicine, University of Belgrade, Serbia*

15:00 – 15:30 **Harnessing big data to study female brain and mental health**
Prof. Dr. Claudia Barth, *Charité, Universitätsmedizin Berlin, Germany*

15:30 – 16:00 **Adolescent exposure to contraceptive hormones alters biomarkers associated with depression in female rats**
Dr. Jesse Lacasse, *Centre for Addiction and Mental Health, Canada*

16:00 – 16:20 Flash talks selected from the abstracts 2
Chair: Prof. Dr. Michelle Roche, University of Galway, Ireland

Sex-specific antidepressant and anxiolytic effects of GPER1 activation in rats
Pavlina Pavlidi, *National and Kapodistrian University of Athens, Greece*

APOE4 drives opposing neuroimmune responses in females and males with distinct implications for Alzheimer's immunotherapy outcomes
Nikoleta Delivanoglou, *Mayo Clinic, USA*

EcoSplit reveals a female-specific immune–stromal program with androgen receptor sensitisation and adverse prognosis across cancers
Ekaterina Petrenko, *Israel Institute of Technology, Israel*

Sex differences in immune response to an MVA-based vaccine against Middle East respiratory syndrome (MERS)
Tamara Zoran, *University Medical Center Hamburg-Eppendorf, Germany*

16:20 – 17:00 Coffee break and poster session

Plenary talk 3
Chair: Dr. Ivana Jaric, University of Zurich, Switzerland

17:00 – 17:45 **Unlocking the complexities of endometriosis**
Dr. Brett McKinnon, *University of Queensland, Australia*

17:45 – 18:00 Closing ceremony and poster awards
Dr. Ivana Jaric, *University of Zurich, Switzerland*

18:00 – 19:00 Aperitif & networking

TALK SUMMARIES AND SPEAKERS

Day 1 • 23 June

Session 1: Sex-inclusive research - Bridging the 3Rs framework and study design

Dr. Natasha Karp

AstraZeneca, UK

Addressing cultural and knowledge barriers to enable preclinical sex-inclusive research

A culturally embedded practice of studying only one sex in preclinical research biases the scientific knowledge base and contributes to poor translation and irreproducible findings. Although scientists recognise sex as important, many still view sex-inclusive research as too difficult to implement. I will present research on barriers to inclusion and use change management theories to contextualise strategies we have implemented to drive change. One such strategy, the Sex Inclusive Research Framework, evaluates in vivo proposals using a traffic light classification. By supporting researchers, ethics boards, and funders, it enables rigorous assessment and helps shift research practice beyond embedded sex bias.

Prof. Dr. Penny S. Reynolds

University of Florida, USA

Half the biology, half the insight: Accounting for sex in your experimental design

Despite the widespread adoption of Sex as a Biological Variable (SABV) principles in preclinical research, implementation remains largely superficial. Key shortcomings include limited sex-specific analyses and inadequate application of rigorous statistical methods. Reframing inference around signal-to-noise discrimination rather than p-values highlights the importance of Design of Experiments (DOE) for identifying true sex effects and controlling unwanted variation. Experimental designs such as factorial, nested, split-plot, and optimal designs are particularly well suited to SABV research, enabling efficient evaluation of sex effects and interactions whilst improving validity, reducing animal and resource use, and enhancing reproducibility and translational relevance.

Dr. Fernando Gonzalez Uarquin

University Medical Center Mainz, Germany

The 3R framework for sex-inclusive animal research

A culture of care embedded in everyday practice strengthens implementation of the 3Rs (Replacement, Reduction, and Refinement), sex-inclusive research, and scientific quality. Focusing on refinement, I show how collaborative decision-making uncovers sex-specific welfare needs and shapes responses to experimental procedures. I further examine how refining experimental conduct with sex in mind advances the 3Rs while deepening the integration of sex as a biological variable. By connecting refinement practices to measurable improvements in data quality, I argue that a 3R culture of care is not an add-on, but foundational to sex-inclusive and ethically robust animal research.

Dr. Homare Yamahachi

Swiss 3R Competence Center

Swiss 3RCC: A national platform for the promotion of the 3Rs

This talk introduces the Swiss 3R Competence Centre and how it supports Replacement, Reduction and Refinement in Switzerland. It will give a brief overview of the 3RCC's work, from research funding and education to communication, monitoring and networking, showing how these activities help bring the 3Rs into everyday research practice.

Session 2: Sex differences in brain structure, function and disease

Prof. Dr. Barbara Di Benedetto

University Hospital Regensburg, Germany

Sexual dimorphism in astrocyte-dependent synaptic pruning: implications for health and major depressive disorder

How does biological sex influence the developing brain? During critical postnatal windows, sex-specific hormonal signals sculpt neural circuits, yet the cellular mechanisms remain largely unknown. We explore astrocytes as key mediators of synaptic refinement, investigating how hormone-dependent pathways regulate synapse elimination and the emergence of the excitatory/inhibitory (E/I) structural balance. Combining human brain tissue, animal models, organotypic cultures, high-resolution imaging, and 3D reconstructions, we map astrocyte–synapse interactions across development. By focusing on the astrocyte-dependent synaptic phagocytosis, we uncover how astrocytes translate hormonal cues into sex-specific circuit architecture, offering new insights to investigate the developmental origins of neuropsychiatric disorders.

Dr. Elisabeth Traiffort

Inserm, Paris-Saclay University, France

Why should sex-dependent differences be considered for an optimized therapeutic approach of central nervous system demyelination?

While sexual dimorphism of the most common demyelinating disease of the central nervous system, multiple sclerosis (MS), is well-known at the clinical level, it is much less characterized at the cellular and molecular levels. We now provide evidence for the exclusive and potent anti-inflammatory role exerted by the male sex hormones in microglia of demyelinated females (not males). We also suggest that normalizing these hormones in women with MS and taking into account the sex of MS patients should contribute to a therapeutic approach aimed at optimizing the regeneration of the disrupted myelin.

Prof. Dr. Ivan Nalvarte

Karolinska Institutet, Sweden

Addressing the sex differences in Alzheimer's disease

Two-thirds of people with Alzheimer's disease are women, who often experience faster and more severe progression than men. This sex difference likely reflects complex interactions between declining sex hormones during aging and environmental and genetic factors. Ivan Nalvarte, Associate Professor at Karolinska Institutet, studies these interactions across the lifespan. His research combines epidemiological, biomarker, and experimental approaches to identify factors influencing Alzheimer's risk and resilience differently in men and women. This work aims to improve understanding of disease mechanisms and support more equitable prevention and management strategies.

Prof. Dr. Aleksandra Dugandzic

University of Zagreb, Croatia

Different roles of brain uroguanylin and brown adipose tissue in males and females

Obesity and type 2 diabetes mellitus (T2DM) are major burdens on global health today. A novel therapeutic approach is increasing postprandial glucose and fatty acid utilization through the activation of brown adipose tissue (BAT). Due to the different physiological and pathophysiological functions of BAT and its activators in males and females, the introduction of BAT activators as a therapy for obesity and T2DM must take sex and phase of estrous cycle into account.

Session 3: Sex differences across organ systems

Dr. Valentina Biasin

Medical University of Graz, Austria

Role of sex hormones in lung disease manifestation

Sex differences are a prominent but incompletely understood feature of systemic sclerosis–associated lung fibrosis and may extend to other fibrotic lung diseases. This work investigates how testosterone influences disease progression through metabolic regulation. Using animal models and patient-derived data, we show that reduced testosterone is associated with enhanced fibrosis and altered lipid metabolism. Testosterone may promote fatty acid–dependent pathways that influence fibroblast fate, favoring a lipofibroblast phenotype and limiting collagen production. These findings highlight a sex hormone–metabolism axis as a potential driver of fibrosis, with relevance beyond systemic sclerosis, including idiopathic pulmonary fibrosis.

Prof. Dr. Stefanie Steiger

LMU Hospital Munich, Germany

Sex differences in kidney health and disease

Why do men and women experience kidney disease differently? Growing evidence shows that biological sex influences kidney function, injury, repair, and long-term outcomes. While female kidneys appear more resilient in experimental models, the picture in humans is far more complex. Women are more likely to develop chronic kidney disease, yet men progress more rapidly to kidney failure and face higher mortality. My talk explores the biological mechanisms underlying these differences, from hormones and immunity to inflammation and fibrosis, and discusses their implications for research and clinical care. Understanding sex-specific pathways may be key to developing more precise and effective kidney disease therapies.

Prof. Dr. Sarah Longnus

University of Bern, Switzerland

Role of sex differences in the cardiac proteome and early graft recovery in donation after circulatory death

Why do some donor hearts recover better than others after circulatory death? In this talk, I'll share findings from our rat model of donation after circulatory death (DCD), where we compared cardiac recovery in male, female, and ovariectomized hearts following warm ischemia. Ventricular functional recovery was significantly higher in female hearts compared to males. Diving into the proteome and phosphoproteome, we uncovered strikingly different molecular responses, male hearts leaned on coagulation and energy pathways, while female hearts activated anti-inflammatory, pro-survival programs. I'll discuss what this means for how we think about sex and hormones in organ preservation, and where this could lead for DCD heart transplantation.

PD Dr. Berna Ozdemir

University Hospital Bern, Switzerland

Sex differences in pharmacokinetics of anticancer drugs - why does that even matter?

Sex differences in anticancer drug pharmacokinetics are a largely overlooked source of variability in treatment efficacy and toxicity. Evidence from multiple drug classes shows clinically relevant differences in drug exposure between female and male patients, contributing to higher rates of adverse events in women. I will discuss the implications of these findings for dose optimization and how sex-informed dosing strategies could improve the therapeutic index of cancer therapies.

Plenary talk 1

Prof. Dr. Jeffrey Mogil
McGill University, Canada

Pain, sex, and death

Pain researchers have now come to some consensus regarding the existence of sex/gender differences in the sensitivity to and tolerance of pain in humans. In addition, evidence is rapidly emerging that the sexes may differ *qualitatively* in their biological mediation of pain. Different genetic factors, neural circuits, neuromodulators, and immune cells appear to be relevant to pain processing in males and females. I will present several research stories suggestive of fundamental sex dimorphism in pain processing, the effects of pain on mortality, and the interaction between pain and social behaviour.

TALK SUMMARIES AND SPEAKERS

Day 2 • 24 June

Session 4: From evidence to action - Economics, innovation, and preclinical research

Dr. Valentina Sartori

McKinsey Health Institute

The economic consequences of systemic underinvestment in women's health

Women spend 25% more of their lives in poor health than men, a gap that, if closed, could add over 1 trillion dollars annually to the global economy by 2040. Dr. Valentina Sartori from the McKinsey Health Institute presents findings from their landmark report with the World Economic Forum, examining nine conditions, from cardiovascular disease to endometriosis and menopause, that account for a third of this gap. She'll unpack why nearly half of relevant research lacks sex-disaggregated data, and outline a blueprint for closing the gap, making the case that investing in women's health is not only a matter of equity, but a major economic opportunity.

Dr. Juliana Bessa

Roche Innovation Center Basel

Accelerating innovation through sex-inclusive R&D

Developing innovative medicines is a high-risk and costly journey. Analyzing sex-based differences in biological pathways and biomarkers early in R&D is crucial to reducing Phase 3 attrition. Roche is strongly committed to inclusive research and aims to align clinical trial representation with the actual disease incidence in women.

Prof. Dr. Michelle Roche

University of Galway, Ireland

PAINDIFF recommendations for the study and inclusion of sex and gender in research

Sex and gender are important variables in research, yet they are often explored inconsistently. I will present the findings from the international PAINDIFF Network who have made thirteen recommendations for the study and inclusion of sex and gender as variables in pain research, which have relevance across the full spectrum of biopsychosocial research. Five universal recommendations apply to the majority of research studies, with an additional three recommendations specifically for preclinical studies, and five further recommendations for human and clinical studies. Wide adoption and implementation of these recommendations will reduce variability, improve reproducibility, and enhance translatability of research findings.

Plenary talk 2

Prof. Dr. Tallie Z. Baram, MD

University of California, Irvine, USA

Sex, stress and high estrogen levels - a toxic hippocampal cocktail?

It is increasingly recognized that acute traumatic events (mass shootings, natural disasters) can provoke enduring memory deficits and generalization of trauma cues, and these are more common in women. We investigated the underlying mechanisms and sex differences in mice, focusing on the sex hormone 17β-estradiol and its receptors in hippocampus. Surprisingly, high physiological hippocampal estrogen levels, observed in male and proestrus female mice were required for stress--induced memory problems. High estrogen levels generated a permissive chromatin state, allowing both adaptive plasticity and vulnerability to acute concurrent stresses, Local conditional knockout mice, pharmacology and epigenomics showed that stress-vulnerability involves estrogen receptor (ER)α in males and ERβ in females. The study has implications to women's health and cognitive aging.

Session 5: Sex, hormones, and brain function

Dr. Vanessa Stempel

Max Planck Institute for Brain Research, Germany

Sex- and oestrous-dependent plasticity in midbrain circuits controlling survival instincts

The midbrain periaqueductal gray (PAG) is an evolutionarily conserved brainstem region that controls the initiation of most instinctive behaviours. In particular, it is critically involved in the execution of defensive behaviors, such as risk assessment and escape from threat. These behaviors are modulated by sex and the reproductive cycle of females, however we do not currently know if the PAG itself undergoes plasticity in a manner that depends on these factors. In this talk I will discuss recent proteomic and electrophysiological data, highlighting the importance of sex and the reproductive cycle in shaping PAG proteome composition and its neuronal properties.

Prof. Dr. Nicole Gervais

Rijksuniversiteit Groningen, Netherlands

SABV considerations in sleep loss-induced memory loss

Women experience poorer sleep quality than men, and yet almost all of what is known about its consequences for brain health is derived from male rodents. Findings from the Memory, Sleep and Hormones (MeSH) lab challenge the assumptions about the role of sleep in cognition by addressing SABV in humans and rodents. In this presentation, I will share our recent findings that demonstrate the resilience of the hippocampus in females based on hormone state. The relevance of these findings for AD risk among females will also be discussed.

Prof. Dr. Vibe G. Frokjaer

Copenhagen University, Denmark

Hormonal contributions to depression in women: implications for precision prevention and treatment

Why are women nearly twice as likely as men to experience depression? This talk explores how fluctuations in sex hormones across reproductive transitions, the menstrual cycle, pregnancy, postpartum, and perimenopause, shape brain function and mood. Drawing on neuroimaging, neuroendocrine, and clinical evidence, I will show that individual sensitivity to hormonal change, rather than hormone levels themselves, may underlie vulnerability to depression. Special focus will be given to the serotonin system and stress pathways as key mediators. These insights point toward sex-stratified, hormone-informed approaches to prevention and treatment, positioning hormonal profiling as a critical, underused tool in precision psychiatry.

Prof. Dr. Jocelien Olivier

Rijksuniversiteit Groningen, Netherlands

Regulatory effects of antidepressant exposure on maternal–fetal signaling

How does a mother's gut microbiome shape brain development in her offspring, and could these effects differ between males and females? Serotonin, a key regulator of neurodevelopment, is largely produced in the gut and influenced by both the microbiota and commonly prescribed antidepressants such as SSRIs. In this talk, I will present findings showing that maternal SSRI treatment alters the gut microbiome, affects offspring social behavior, and changes the expression of myelin-related genes in brain regions critical for emotion and cognition. These findings highlight maternal serotonin signaling as a potential driver of sex-specific developmental trajectories.

Session 6: Female hormones and disease susceptibility

Dr. Laura Bornes

Leiden University Medical Center, Netherlands

The estrous cycle stage affects mammary tumor sensitivity to chemotherapy

Breast cancer response to neoadjuvant chemotherapy (NAC) varies even within the same molecular subtype. Here, we identify the oestrous cycle as a contributor to this heterogeneity. Across three mouse models and retrospective premenopausal human cohorts, initiating NAC during dioestrus/ luteal phase reduced treatment response compared with oestrus/ follicular phase. Mechanistically, dioestrus was associated with increased EMT, reduced tumour vessel diameter, and elevated macrophage presence, all linked to chemoresistance. Although NAC disrupted the oestrous cycle, macrophage abundance persisted, and macrophage depletion restored sensitivity. These findings identify the oestrous cycle as a determinant of chemosensitivity and warrant future clinical trials to optimize treatment-timing.

Doc. Dr. Ljiljana Marina

University Clinical Centre of Serbia, Faculty of Medicine, University of Belgrade, Serbia

The many faces of perimenopause: why are we still so bad at understanding the menopausal transition?

Perimenopause affects millions of women worldwide, yet it remains one of the least understood phases of female reproductive aging. In this lecture, we will explore why medicine continues to struggle with understanding the menopausal transition. Through the lenses of women's health research, terminology, and neuroendocrine biology, we will discuss how static diagnostic frameworks fail to capture a highly dynamic biological process. Finally, we will examine emerging data-driven approaches that may help define meaningful perimenopausal phenotypes and improve care for women navigating this transition.

Prof. Dr. Claudia Barth

Charité, Universitätsmedizin Berlin, Germany

Harnessing big data to study female brain and mental health

Big data and machine learning are opening new windows into the female brain.Big data and machine learning are opening new windows into the female brain. In this talk, I show how female-specific factors, such as reproductive history, shape brain aging. To capture this, I use the brain age gap, a marker derived through machine learning, applied to large-scale data from the UK Biobank. I make the case that moving beyond sex-neutral approaches is essential. It is what we need to build mechanistic models of sex differences in disease, and to deliver the personalized mental health care that half the population deserves.

Dr. Jesse Lacasse

Centre for Addiction and Mental Health, Canada

Adolescent exposure to contraceptive hormones alters biomarkers associated with depression in female rats

Hormonal contraceptives (HCs) are used by more than 300 million women worldwide, yet some users, particularly adolescents, appear more vulnerable to adverse mental health outcomes during exposure. In this talk, I will present preclinical evidence examining whether adolescence represents a sensitive window for HC-induced changes in stress biology. Using a female rodent model, we investigated endocrine, neural, and neuroimmune responses to stress following HC exposure. Our findings suggest adolescence may confer heightened sensitivity to HC-related alterations in stress responsivity and brain network organization, with implications for understanding mechanisms linking HC exposure and depression risk.

Plenary talk 3

Dr. Brett McKinnon

University of Queensland, Australia

Unlocking the complexities of endometriosis

Endometriosis is a chronic gynaecological disease that affects one in ten women and is a leading cause of chronic pain and infertility, yet its underlying biology remains poorly understood. It is widely believed that the endometrium is the source of endometriotic lesions. The endometrium undergoes profound cyclical changes driven by ovarian hormones, making the menstrual cycle a critical biological variable in disease risk. This presentation will explore how integrating menstrual cycle biology with spatial transcriptomics and advanced three-dimensional endometrial models reveals disease heterogeneity, uncovers mechanisms of pathogenesis, and highlighting the importance of dynamic female biology in biomedical research.

POSTER PRESENTATIONS

List of posters in numerical order (1–63)

Poster No.	Presenter	Title
1	Narimane Bouzourène	**Chronic unpredictable stress during the adolescent sensitive period induces sex-specific prefrontal microglial remodeling and differential astrocytic responses to extracellular vesicles in vitro**
2	Faure Mélanie Clémence	**Astrocytic Cdk4 regulates hypothalamic functions in a sex dependent manner**
3	Bárbara Canijo	**Different sex-dependent trajectories in Early Life Stress outcomes**
4	Lan Zhou	**Sex Differences in the Association Between Childhood Adversity and Psychosis: A Meta-Analysis**
5	Irina Kovlyagina	**Trait- and Sex-Dependent Modulation of Threat-Memory Extinction by Conditional FAAH Knockout**
6	Pavlina Pavlidi	**Sex-specific antidepressant and anxiolytic effects of GPER1 activation in rats**
7	Mohsin Zafar	**Paclitaxel-induced neuropathy in CD-1 mice induces cognitive, anxiety, and depressive-like alterations: investigating sex-specific differences**
8	Bucaro Ivana	**Sex-dependent vulnerability to early-life adversities and cognitive development in preschool children**
9	Palanza Paola	**Sex Differences in Neurodevelopmental Vulnerability to a Real-Life Endocrine Disruptor Mixture**
10	Susanne Ott	**Predicting Sex- and Gender-Sensitive Psychological Distress After Spinal Cord Injury Rehabilitation: A Risk Prediction Model**
11	Manuela Valencia	**Sex- and gender-sensitive dynamics in mental health outcomes in individuals with physical disability: a systematic review**
12	Bernd Lenz	**Sex-Specific Perspective on Alcohol Use Disorder: From Epidemiology to Everyday Patient Care**
13	Ljerka Delac	**Sex-specific signatures of CYP46A1 overexpression in App knock-in mouse models of Alzheimer's Disease pathology during aging**
14	Daniel Ruiz-Gabarre	**Proteomic profiling of three different brain regions in the Atp11bKO model of small vessel disease — a focus on sex differences**

Poster No.	Presenter	Title
15	Özlem Tuğçe Çilingir-Kaya	**The effects of intermittent fasting on neurogenesis in rats with genetic absence epilepsy in terms of sex differences**
16	Sofija Vojvodic	**Sex differences in stroke outcomes, treatment efficacy and mechanisms in animal models of focal cerebral ischemia: a systematic review and meta-analysis**
17	Ozge Selin Çevik	**Investigation of the effect of cage placement on social interaction behavior in female rats exposed to postnatal stress**
18	Marta Anna Mazurkiewicz	**Bridging metabolism and pain: transcriptomic evidence for a key role of spinal oligodendrocytes**
19	Marija Glisic	**Sex-Specific Patterns of Polypharmacy Following Traumatic Spinal Cord Injury**
20	Sierra Arn	**Reproductive Ageing and Physical Activity in Later Life (REALL-Q) Questionnaire: Development, Validation and Analysis**
21	Stefania Del Prete	**Sex-Bias Immune Aging and its Interplay with X-Inactivation Escape Genes at Single-Cell Level**
FLASH TALK 22	Nikoleta Delivanoglou	**APOE4 drives opposing neuroimmune responses in females and males with distinct implications for Alzheimer's immunotherapy outcomes**
FLASH TALK 23	Ekaterina Petrenko	**EcoSplit reveals a female-specific immune–stromal program with androgen receptor sensitisation and adverse prognosis across cancers**
24	Cristina Conde Lopez	**Characterizing Sex Chromosome Dosage Differences in Head and Neck Squamous Cell Carcinoma Microenvironment**
25	Katrien De Roeck	**Interrogating Mechanisms of Sex Bias in IPO8-related Thoracic Aortic Aneurysm**
FLASH TALK 26	Tamara Zoran	**Sex Differences in Immune Response to an MVA-Based Vaccine Against Middle East Respiratory Syndrome (MERS)**
27	Giulia Germena	**Exercise-induced cardioprotection through sex-specific remodelling in ageing murine hearts**
28	Georgia Beer	**A brief period of cold, static preservation affects cardiac graft recovery in a rat model of donation after circulatory death (DCD) in a sex-specific manner**
29	Anja Helmer	**Sex-dependent recovery of left ventricular function and corresponding gene expression in a rat model of donation after circulatory death (DCD)**
FLASH TALK 30	Maria Arnold	**Biological Sex Influences the Physiological Response to Anesthesia in Rats**

Poster No.	Presenter	Title
31	Goretti España-Irla	**Mapping the Female Brain Across the Menopause Transition: A Multi-Site Cross-Sectional Mega-Analysis**
32	Małgorzata M. Tybuszewska	**Menopausal Hormone Therapy in Schizophrenia**
33	Enriqueta Vallejo-Yagüe	**Guidance for sex- and gender-related data collection in chronic diseases: The Sex and Gender Data Item Set**
34	Maxine Sokolowski	**Estrous cycle-dependent modulation of inhibition in the mouse midbrain**
35	Simón Comerma-Steffensen	**Impact of a non-invasive oestrous synchronisation protocol on sexual behaviour in Sprague-Dawley rats**
36	Simeunovic Valentina	**Adolescent Dietary Restriction Alters Behavior and Disrupts the Estrous Cycle in Aging Female Wistar rats**
37	Rosie Longster	**Neurological and behavioural effects of ovarian hormone cycle suppression**
38	Clair A. Enthoven	**Estimating the Effect of Combined Oral Contraception on Adolescent Mental Health**
39	Elena Kutsarova	**The impact of sex and environment on the proteomic landscape of the midbrain periaqueductal gray and superior colliculus**
40	Pishan Chang	**Sex- and Age-Dependent Regulation of circadian and Infradian Rhythms**
41	Ilya Smolensky	**Sex-specific effects of ketogenic diet on metabolism, behavior, and circadian activity of male and female BDNF-deficient mice**
42	Srdjan Sokanovic	**Sex-specific and shared function of PTPRN and PTPRN2 in the regulation of reproduction, growth, and melanotroph development in mice**
43	Gabriela Neubert da Silva	**Sexual dimorphism in the leptin-signalling system**
44	Charlotte A. Cornil	**Region and testosterone-dependent transcriptomic sex differences in the brain of Japanese quail**
45	Jutta Schillings	**Establishing a novel rat model for mimicking human postmenopausal obesity with impaired glucose homeostasis**
46	Elena Pavicic	**The influence of sex-hormone deprivation and black cohosh treatment on hippocampal and hypothalamic gene expression profiles in ovariectomized rats**

Poster No.	Presenter	Title
47	Andrea S. Leuthardt	**Impact of current breeding practices on the health of breeding mouse dams**
48	Kristina Saravinovska	**The impact of estrogen on the gut microbiome: a systematic review and meta-analysis**
49	Hanne Haslene-Hox	**Establishment and characterization of patient derived endometriosis organoids for high throughput screening**
50	Roberta Tassinari	**Mediterranean Phytochemicals as Emerging Therapeutic Strategies against Endometriosis**
51	Sandra Calvo Blanco	**Gender-affirming hormone therapy initiated in early puberty affects the hepatic and whole body metabolic response to a dietary challenge in a mouse model of adolescent gender transition**
52	Bart Wouters	**Uncovering the effects of adolescent gender transition on skeletal muscle using mouse models**
53	Vanessa Dubois	**Feminization of the male liver transcriptome drives adaptive and functional remodeling in a weight cycling mouse model of MASLD**
54	Boya Zhang	**Unraveling sex differences in the hepatic response to androgens**
55	Torkild Visnes	**Sex Hormones Shape Drug-Induced Liver Cell Phenotypes**
56	Agathe Iannone	**Sex Disparities in Human Lung Cancer Cell Line Availability and Use: A Call for Attention**
FLASH TALK 57	Oriana Nobus	**Sex differences in a mouse model of chronic kidney disease**
58	Stefan Rudloff	**Baseline fetuin-A shapes sex-dependent responses in acute kidney injury**
59	Yan Xu	**Cardiometabolic Disease Burden in Women with Spinal Cord Injury: The Role of Menopausal Status**
FLASH TALK 60	Nicole A. Chittim	**Male mice rupture patellar tendon struts more often than females with failure possibly attenuated by running**
61	Qiuya Shao	**Sex as a variable in mitochondrial diseases**
62	Camila Peres Rubio	**Changes in saliva due to social stress in pigs: the influence of sex**
63	Marlotte Loyens	**Structural vascular alterations in intra-uterine growth restricted piglets: cross-sectional area of umbilical cord, aorta and pulmonary artery**

POSTER AWARDS

This year's SABV Symposium will recognize outstanding posters through two main awards and two special prizes for omics-related research. All winners will be announced at the closing ceremony.

Audience Choice Award

Vote for your favorite poster by scanning the QR code below. This will open a brief Google Form where you can submit your choice.

Voting will be open until **24 June at 17:00**.

Committee Award

The committee will visit and evaluate posters during the afternoon sessions:

Posters 1–30	Day 1 16:00 – 17:00
Posters 31–63	Day 2 16:20 – 17:00

Presenters are kindly requested to be available at their respective poster boards during these times.

Novogene Omics Awards

Two sequencing vouchers sponsored by Novogene will be awarded to outstanding posters incorporating omics methodologies (e.g., genomics, transcriptomics, proteomics, metabolomics). Winners will be selected by the scientific committee.

Poster 1

Chronic unpredictable stress during the adolescent sensitive period induces sex-specific prefrontal microglial remodeling and differential astrocytic responses to extracellular vesicles in vitro

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2 Leenaards Memory Center, Lausanne University Hospital (CHUV) and University of Lausanne, Lausanne, Switzerland

Chronic mild unpredictable stress (CMUS) during adolescence, a developmental window of heightened prefrontal-limbic plasticity, triggers sex-dependent trajectories: externalizing manifestations are more frequently reported in males, while internalizing phenotypes predominate in females. The biological mechanisms underlying these divergent outcomes remain poorly understood, particularly regarding sex-specific neuroimmune responses. We therefore investigated stress-induced prefrontal microglial remodeling and, since extracellular vesicles (EVs) carry molecular cargo reflecting the physiological state of their tissue of origin, tested whether PFC-derived EVs from stressed animals modulate astrocytic responses in vitro. Wistar Han male and female rats were exposed to a CMUS paradigm during adolescence. Disinhibited behavior was assessed using the Elevated Plus Maze. Ex vivo microglial morphology was analyzed in the PFC. EVs were isolated from the PFC and applied to primary astrocyte cultures monitored for up to 72 h. EV protein cargo was profiled using quantitative proteomic approaches. CMUS induced behavioral disinhibition in males only. Ex vivo analyses revealed more pronounced stress-induced microglial morphological remodeling (ameboid shape) in female PFC. Proteomic analyses of PFC EV cargo further revealed sex-dependent compositional shifts following stress. Preliminary astrocyte assays showed that EVs from stressed males elicit more pronounced cellular responses compared to female donors. Our findings demonstrate that adolescent stress produces sex-dependent prefrontal neuroimmune adaptations encompassing microglial morphological remodeling and altered astrocytic responses to stress-derived EVs. These results highlight sex as a critical biological variable shaping the neuroimmune consequences of adolescent adversity and support the use of PFC-derived EVs as molecular probes of sex-specific stress vulnerability.

Poster 2

Astrocytic Cdk4 Regulates Hypothalamic Functions in a Sex-Dependent Manner

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Astrocytes regulate hypothalamic neuronal circuits controlling reproduction, stress and metabolism, and display sexually dimorphic features across hypothalamic regions. However, the astrocytic factors underlying these differences remain poorly understood. We recently identified the kinase Cdk4 as a potential sex-dependent regulator of neuroendocrine functions using a full-body Cdk4-KO model. In the hypothalamus, Cdk4 is predominantly expressed in glial cells, including astrocytes. Beyond its classical role in cell-cycle control, Cdk4 also regulates cellular plasticity and metabolism in peripheral tissues. Although hypothalamic Cdk4 deletion/inhibition alters systemic metabolism, its role in the adult hypothalamus remains unclear. We hypothesize that astrocytic Cdk4 modulates adult neuroendocrine functions through sex-specific effects on astrocyte metabolism and/or plasticity. To test this, we generated an astrocyte-specific Cdk4 knockout model (Cdk4flox/flox hGFAP-CreERT2) and induced recombination with tamoxifen. Female AstroCdk4KO exhibited disrupted estrous cycles, although fertility remained intact in both sexes. Under a chow diet, increased body weight gain and adiposity were observed only in males. In contrast, under a 60% high-fat diet, these genotype differences disappeared in males but emerged in females. Under chow diet and exposure to a mildly stressful novel environment, both sexes displayed reduced food intake and body weight, while males exhibited elevated corticosterone levels. Behavioural assessments revealed sexually dimorphic vulnerability: females displayed altered anxiety-like and decision-making behaviours, whereas males showed no major behavioural changes. Altogether, our findings suggest that astrocytic Cdk4 regulates energy homeostasis and behavioural adaptation to stress in a sex-dependent manner. Ongoing studies will assess astrocyte numbers, morphology and molecular pathways affected by Cdk4 loss, before investigating the underlying mechanisms.

Poster 3

Different sex-dependent trajectories in Early Life Stress outcomes

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Early life stress (ELS), characterized by disrupted maternal care, significantly impacts brain development. These environmental insults occur during critical periods of neuronal wiring, often leading to lasting emotional and cognitive deficits. While ELS is known to cause sex-specific behavioral and circuit alterations, the role of hormonal-driven brain organization in these sexual dysmorphisms remains under-explored. We employed the Maternal Separation and Unpredicted Stress (MSUS) protocol to mimic ELS in the post-natal period (PND2-14). To explore hormonal influence, females received testosterone injections and males received letrozole (an aromatase inhibitor) at PND0–1. Serum and brain tissue were collected at PND5 and PND40 for molecular and cellular analysis. Behavioral phenotypes were assessed via Open Field, Elevated Plus Maze, and Delay Aversion tests. Additionally, shotgun mass spectrometry was used to analyze ganglioside content in the prefrontal cortex (PFC). Unpublished data of our group indicate that MSUS adolescent males exhibit hyperactive, impulsive, and risk-taking behaviors, with altered inhibitory drive in the medial orbital PFC and changes in myelination. MSUS females appear resilient to these changes, demonstrating clear sexual dysmorphism. Interestingly, MSUS females treated with testosterone showed a tendency for increased impulsivity, mirroring the male phenotype. Both sexes showed alterations in early ganglioside profile, specifically in ganglioside species essential for proper myelination. These findings highlight how early hormonal environments lead to sex-specific responses to stress. Furthermore, identifying ELS-induced ganglioside deficits suggests that nutritional supplementation could serve as a potential strategy to mitigate the adverse neurodevelopmental outcomes of ELS.

Poster 4

Sex Differences in the Association Between Childhood Adversity and Psychosis: A Meta-Analysis

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Childhood adversity is a well-established risk factor for psychosis, but whether this association differs by sex remains unclear. Clarifying potential sex differences is important for understanding underlying mechanisms and informing targeted prevention strategies. We conducted an updated multi-level meta-analysis synthesizing four decades of research on childhood adversity and psychosis. Random-effects models were used to estimate overall and sex-stratified associations across trauma subtypes. Meta-regression analyses were conducted to examine sex differences. Exposure to any type of childhood adversity was associated with a markedly increased risk of psychosis (OR = 2.80, 95% CI = 2.18–3.60; k = 183; N = 349,265). Sex-stratified analyses showed comparable associations in males (OR = 2.48, 95% CI = 1.72–3.57; k = 33; N = 144,179) and females (OR = 2.62, 95% CI = 1.98–3.46; k = 36; N = 169,740), with no significant sex difference (QM = 0.13, p = 0.72). Subtype analyses showed no significant sex differences. For sexual abuse, the odds ratio was 2.71 in females (95% CI = 1.74–4.22; k = 9; N = 4,332) and 1.76 in males (95% CI = 0.93–3.30; k = 5; N = 3,636), with no significant difference (QM = 1.17, p = 0.28). For physical abuse, estimates were also similar in females (OR = 2.35, 95% CI = 1.48–3.75; k = 6; N = 813) and males (OR = 2.36, 95% CI = 0.70–7.96; k = 3; N = 314; QM = 0.06, p = 0.81). The association between childhood adversity and psychosis appears largely consistent across sexes, suggesting similar effects in males and females. However, subtype-specific analyses were based on relatively small samples and should be interpreted with caution.

Poster 5

Trait- and Sex-Dependent Modulation of Threat-Memory Extinction by Conditional FAAH Knockout

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Anxiety and stress-related disorders show marked inter-individual variability in symptom severity and treatment response, motivating the adoption of precision-oriented approaches in psychiatry. The endocannabinoid system has been shown to modulate major neurotransmitter systems in a state- and sex-dependent manner, making it a promising therapeutic target. In particular, inhibition of fatty acid amide hydrolase (FAAH), the primary enzyme responsible for terminating endocannabinoid signalling, has been associated with facilitated extinction learning and reduced anxiety-like behaviour. Using TRAP, we selectively deleted FAAH in auditory aversive conditioning (AAC) activated neurons, simultaneously labelling these ensembles with GFP. Male (n=64) and female (n=55) mice subjected to AAC were stratified according to their trait anxiety using sex-specific machine-learning-based classifiers. This approach distinguished phasic and sustained responders and enabled evaluation of intervention effects at the group and subgroup levels across an extensive behavioural phenotyping pipeline. In females, GFP-labelled nuclei from the amygdala (n=20) and hippocampus (n=20) were collected after final retrieval for transcriptomic analysis. After conditioning, females showed consistently higher freezing across retrieval (R1-4) and extinction (Ext1-3) trials compared to males. In females, group-average comparisons revealed FAAH-KO effects on threat memory extinction, whereas stratification along the phasic-sustained axis attributed enhanced extinction primarily to the phasic phenotype. In males, knockout effects were restricted to the first extinction-training trial. Transcriptomic analysis is ongoing. These findings indicate that FAAH-KO modulates threat-memory extinction in a sex- and trait-dependent manner. Resolving latent endophenotypes provides a methodological foundation for precision-oriented preclinical anxiety research.

Poster 6

Sex-specific antidepressant and anxiolytic effects of GPER1 activation in rats

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Mood and anxiety disorders disproportionately affect women, while current treatments such as selective serotonin reuptake inhibitors remain ineffective in many patients, contributing to Treatment Resistant Depression. G protein-coupled estrogen receptor 1 (GPER1) has emerged as a promising target implicated in depression and anxiety, potentially overlapping with the rapid antidepressant mechanisms of glutamatergic agents such as esketamine. This study investigated the therapeutic potential and sex-specific effects of GPER1 activation in adult male and female Wistar rats following systemic or intrahippocampal administration of the GPER1 agonist G1. Behavioural responses were assessed using the open field, splash, novelty-suppressed feeding, and forced swim tests. Neurochemical profiling and Western blot analyses evaluated monoamines, amino-acids and intracellular signalling pathways associated with synaptic plasticity. Pharmacological inhibitors of PI3K/Akt and MEK/ERK pathways were administered intrahippocampally to examine GPER1-mediated mechanisms. A separate cohort underwent chronic mild stress (CMS) to assess the effects of chronic G1 treatment on anhedonia and hippocampal neuroplasticity. Acute local and systemic G1 administration produced rapid anxiolytic- and antidepressant-like effects selectively in females, reducing feeding latency and increasing grooming behaviour. These effects were abolished by PI3K/Akt inhibition, but not MEK/ERK inhibition, indicating sex-dependent intracellular signalling requirements. Acute GPER1 activation also revealed sex-biased coupling to distinct Gα subunits, differential engagement of hippocampal Akt, mTOR, ERK, and PKA Cα signalling, and enhanced dopaminergic activity in the female prefrontal cortex. Chronic G1 treatment reversed CMS-induced anhedonia and restored hippocampal dendritic complexity. Together, these findings identify GPER1 as a sex-dependent modulator of mood and a promising rapid-acting antidepressant target.

Poster 7

Paclitaxel-induced neuropathy in CD-1 mice induces cognitive, anxiety, and depressive-like alterations: investigating sex-specific differences

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Neuropathic pain is a chronic condition that disrupts nociceptive signalling and progressively alters emotional and cognitive functions. Although substantial evidence shows that sex critically influences neuropsychiatric outcomes, it remains inadequately incorporated in research. Therefore, this study aimed to investigate sex-specific differences in pain sensitivity, depressive-like behaviours, and cognitive dysfunctions in a paclitaxel-induced mouse model of neuropathy. CD-1 male and female mice were administered with paclitaxel to induce neuropathy. Pain hypersensitivity was assessed using cold plate and paw pressure tests, while anxiety-related behaviours were evaluated through the open field, hole board, and elevated zero maze tests. Depressive-like behaviour was examined by the splash, tail suspension and forced swim test. Cognitive impairment was evaluated with the novel object recognition test. Paclitaxel-treated mice of both sexes developed a neuropathic phenotype, exhibiting hyperalgesia and allodynia. In the open field test, sex-specific differences were observed, with CD-1 female mice showing greater time spent in the centre and more centre entries, as well as increased number of nose poking in the hole board test, suggesting lower baseline anxiety-like behaviour in this strain. In the depressive-like domain, sex-specific effects emerged, as paclitaxel-treated female mice showed higher immobility frequency and reduced swimming frequency in the forced swimming test, as well as longer latency to first lick in the splash test. Moreover, paclitaxel administration attenuated recognition memory and disrupted cognitive functions in the novel object recognition test in both sexes. Paclitaxel was able to induce neuropathic hypersensitivity and cognitive deficits in both sexes, while depressive-like behaviours showed a sex-specific pattern, being more prominent in females. These findings highlight sex as a critical biological variable and support the development of sex-specific therapeutic strategies for neuropathic pain.

Poster 8

Sex-dependent vulnerability to early-life adversities and cognitive development in preschool children

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Early life adversities (ELAs) are violations of the expected environment that takes the form of biological and psychosocial hazards and occur during critical and sensitive periods of development. These stressors may disrupt neurodevelopmental trajectories contributing to long-term alterations in cognitive functioning. However, it remains unclear whether these outcomes differ systematically between males and females. This contribution presents the theoretical framework and research design of an ongoing project investigating sex-dependent vulnerability to two relevant sources of ELA: prenatal exposure to endocrine-disrupting chemicals (EDCs) and preterm birth. EDCs can mimic, block, or alter the synthesis, transport, and metabolism of endogenous hormones, thereby interfering with endocrine signalling essential for brain development, especially during highly vulnerable neurodevelopmental windows. Preterm birth, similarly, represents a significant disruption of typical developmental timing and has been associated with long-lasting effects on brain structure and function. These alterations may negatively affect cognitive development and intellectual functioning, while also increasing the risk of neurodevelopmental disorders and behavioural difficulties. The project includes two complementary cohorts: children with quantified prenatal EDC exposure and preterm-born children and is designed to examine group differences and sex-by-exposure interactions across cognitive domains, with particular focus on socio-emotional and visuospatial functioning, which are consistently associated with sex-related differences. Overall, the project aims to advance understanding of early neurocognitive vulnerability within a sex-sensitive framework.

Poster 9

Sex Differences in Neurodevelopmental Vulnerability to a Real-Life Endocrine Disruptor Mixture

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Males and females differ in their susceptibility to environmental stressors during critical developmental periods. Endocrine disruptors (EDs) are widespread environmental chemicals that interfere with hormonal signaling and may induce sex-specific neurodevelopmental, reproductive and metabolic alterations. We investigated the effects of perinatal exposure to a real-life ED mixture (LM-MIX) in a mouse model. The LM-MIX composition was defined based upon biomonitoring data from pregnant women enrolled in the European Life MILCH project (www.lifemilch.eu). Pregnant CD-1 females were orally fed corn oil (control) or LM-MIX at three different concentrations (1×, 10×, and 100× of levels detected in pregnant women) from gestational day 12 to postnatal day 12. Spontaneous maternal behavior was assessed during the first postnatal week, while offspring were evaluated for growth, endocrine-sensitive endpoints, sex-specific pubertal markers and early neurobehavioral development. Exposure to the 10× LM-MIX altered maternal behavior, increasing pup-related activities. Neurodevelopmental reflexes were affected in all exposed offspring, regardless of sex. Sex-specific effects emerged in body weigh growth, with increased body weight in the male offspring but no effects in females. Low LM-MIX doses altered male reproductive endpoints (e.g., gonadal weight) and puberty onset in both sexes. Ongoing analyses are investigating sex-specific alterations in emotional and social behaviors, together with structural and functional changes in hormone-sensitive brain regions. By integrating experimental findings with human biomonitoring data, this study may provide novel insight into how environmentally relevant ED mixtures shape neurodevelopment through sex-dependent mechanisms, emphasizing the importance of incorporating sex as a biological variable in ED research and risk assessment.

Poster 10

Predicting Sex-and Gender-Sensitive Psychological Distress After Spinal Cord Injury Rehabilitation: A Risk Prediction Model

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The transition from initial rehabilitation to the community setting is associated with substantial psychological challenges for individuals with spinal cord injury (SCI). While psychological distress is already present during inpatient care, the prevalence of psychological disorders increases after returning home, particularly among women. However, it remains unclear which factors are associated with psychological distress during this transition. This study aims to develop a risk prediction model of psychological distress during the transition using sex- and gender-sensitive contextual predictors. Data from the Swiss Spinal Cord Injury Cohort Study, including n=410 individuals, were analyzed at discharge from initial rehabilitation and one year after SCI onset. Extreme Gradient Boosting was used to estimate psychological distress during the transition phase, capturing potential non-linearities and interactions among sex- and gender-sensitive predictors. Stepwise linear regression assessed linear relationship between sex-and gender-sensitive predictors and psychological distress, with performance evaluated via cross-validation. No sex differences between women and men were found. However, gender-sensitive analyses showed that lower psychological distress at discharge, higher self-esteem at discharge, higher support from friends, lower strain and lower posttraumatic growth during initial rehabilitation were associated with lower psychological distress after returning home. Psychological distress after rehabilitation can be identified using psychological distress at discharge, social support from friends, strain and posttraumatic growth assessed during rehabilitation. Early, sex- and gender-sensitive interventions targeting psychosocial resources may reduce psychological distress and support successful reintegration back into everyday life.

Poster 11

Sex-and gender-sensitive dynamics in mental health outcomes in individuals with physical disability: a systematic review

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Physical disabilities significantly affect daily life, functioning, and social participation, increasing the risk of negative mental health outcomes that may worsen functional impairments, reduce treatment adherence, and elevate healthcare burden. Despite evident sex and gender differences in the cause, incidence, and mental health, current rehabilitation guidelines often overlook these disparities, limiting rehabilitation strategies for both men and women. We conducted a systematic review and reported results following PRISMA guidelines to synthesize evidence on sex and gender differences in negative mental health outcomes, such as depression, anxiety, psychological distress, and social isolation, among individuals with physical disabilities, including spinal cord injury (SCI), traumatic brain injury (TBI), and multiple sclerosis (MS). Among 59 studies, most included individuals with MS (37.3%) and TBI (35.6%). Most studies examined depression (88.1%), followed by anxiety (40.7%), and psychological distress (20.3%), while a few investigated other negative mental health outcomes. Women with MS more frequently reported anxiety and emotional symptoms, whereas men showed higher depressive symptom burden in several studies. Women with TBI demonstrated greater affective symptom burden, while men more often exhibited externalizing symptom patterns. In SCI, women experienced greater depression, psychological distress, and poorer long-term mental health trajectories, whereas men more frequently reported social role disruption and adjustment difficulties. Our preliminary findings suggest that sex and gender differences in negative mental health outcomes are nuanced, condition-specific, and outcome-dependent, highlighting the urgent need to integrate sex- and gender-sensitive mental health care into rehabilitation research and clinical practice.

Poster 12

Sex-Specific Perspective on Alcohol Use Disorder: From Epidemiology to Everyday Patient Care

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Sex is a fundamental yet systematically underutilized variable in mental health and addiction research. Although men develop alcohol use disorder (AUD) more frequently and show higher alcohol-attributable mortality, women with AUD progress faster from first use to dependence and suffer organ damage after lower cumulative alcohol exposure. These divergent trajectories underscore the critical need to integrate sex as a biological variable (SABV) across the full research pipeline — from mechanistic discovery to clinical guideline development. Our work addresses this gap on multiple fronts. In a multicenter, sex-separated longitudinal study (ReCoDe Consortium; Am J Psychiatry 2024), we identified that menstrual cycle phase and the progesterone-to-estradiol ratio are significantly associated with binge drinking in individuals with AUD. These findings are paralleled by our earlier work demonstrating that premenopausal status and higher progesterone levels are associated with lower craving in female inpatients with AUD (Prog Neuropsychopharmacol Biol Psychiatry 2021). Despite this mechanistic progress, our systematic analysis of AUD intervention studies (2014–2023) reveals that women remain substantially underrepresented in clinical AUD research. Sex still plays a subordinate role in current clinical practice guidelines for AUD. Advancing sex-sensitive care requires shared responsibility across clinicians, funders, institutional review boards, and professional societies, rigorous adoption of the Sex and Gender Equity in Research (SAGER) Guidelines, and movement beyond the oversimplified binary classification of sex (Lancet Psychiatry 2025). Our findings illustrate precisely the SABV agenda: generating mechanistic insight into sex-specific pathways and translating this knowledge into equitable, evidence-based treatment.

Poster 13

Sex-specific signatures of CYP46A1 overexpression in App knock-in mouse models of Alzheimer's Disease pathology during aging

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Altered brain cholesterol metabolism has been evidenced in aging and Alzheimer's Disease (AD). Postmortem AD brains show reduced 24(S)-hydroxycholesterol (24(S)-OH), a product of CYP46A1 activity, essential for brain cholesterol turnover. Previously, we showed that CYP46A1 overexpression induces sex-specific effects and improves memory in aging and menopause-like conditions in female mice. Here, we explored whether CYP46A1 confers sex-specific neuroprotection against AD pathology. We generated AD-like mouse models with enhanced brain cholesterol turnover. App knock-in mice carrying familial AD mutations (AppNL-F/NL-F and AppNL-G-F/NL-G-F) were each crossed with human CYP46A1-overexpressing mice (Cyp46Tg). Male and female offsprings (Cyp46TgxAppNL-F/NL-F and Cyp46TgxAppNL-G-F/NL-G-F) were analyzed at 6 (adult), 12 (middle-aged), and 20 months (aged mice). CYP46A1 overexpression affected glial, oxysterol, and lipidomic profile in a sex- and age-dependent manner. Middle-aged Cyp46TgxAppNL-F/NL-F mice of both sexes exhibited decreased hippocampal levels of Iba1. By 20 months, males showed decreased Iba1 and GFAP levels, whereas females showed reduced Iba1 immunoreactivity, indicating sex-specific glial responses over time. Lipidomic analysis revealed sex differences, including increased triglycerides in aged males. Aged females showed elevated carnitine levels, consistent with increased Cpt1c expression, involved in β-oxidation. In the AppNL-G-F/NL-G-F model, CYP46A1 overexpression restored 24(S)-OH levels and TG species in middle-aged females. Overall, CYP46A1 overexpression differentially affects glial activation and lipid metabolism across sex and age in AD-like models, with female-specific effects associated with reduced neuroinflammation and improved cholesterol and lipid homeostasis. This underscores CYP46A1 therapeutic potential, particularly for women at increased AD risk or early disease stages.

Poster 14

Proteomic profiling of three different brain regions in the Atp11bKO model of small vessel disease – a focus on sex differences

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Small vessel disease (SVD) affects cerebral microvessels, causing around 45% of vascular dementia cases. Risk factors such as hypertension have been classically recognised as drivers of the disease. However, increasing evidence underscores endothelial dysfunction in SVD. Women show more severe SVD- lesions and worse progression, but more men have severe clinical presentations than women, with increasing evidence of mechanistic sex differences in pathology and response to treatment. Despite this, studies often fail to consider sex at all, and we poorly understand the biology behind these differences. Our lab developed the Atp11bKO rat model, which shows pathological, imaging and behavioural changes of SVD without hypertension. ATP11B is a phospholipid flippase with relevance to human disease as a SNP in human ATP11B associates with SVD. To understand how loss of Atp11b alters brain tissue biology in this SVD model and how it may vary with sex, age and brain region, we performed unbiased proteomics and single-nuclei transcriptomics analysis on deep white matter, frontal cortex and cerebellum of male and female Atp11bKO rats, both at 6 weeks and 6 months. On first interrogating proteomic data, our results point to synaptic dysfunction and alterations in excitatory versus inhibitory neuronal network pathways in our rats, consistent with their dementia phenotype, with apparent sex differences at the molecular/pathway level. Studying these differences may help us understand the influence of sex differences on disease mechanisms over the life course and evaluate them in the absence of other confounders, ultimately helping us develop targeted, precision therapies.

Poster 15

The effects of intermittent fasting on neurogenesis in rats with genetic absence epilepsy in terms of sex differences

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Epilepsy affects ~50 million people worldwide, with ~30% of patients remaining drug-resistant. Adult hippocampal neurogenesis plays crucial role in cognition and is dysregulated in patients with epilepsy. Intermittent fasting (IF) has demonstrated neuroprotective effects; however, its impact on neurogenesis and gut-brain axis function in genetic absence epilepsy, particularly regarding sex differences, remains unexplored. Twenty-eight female and 28 male rats were divided into four groups: Wistar Naïve Control (WC), Wistar+IF (WIF), GAERS Epileptic Control (GC), and GAERS+IF (GIF). IF protocol (24h fasting/24h feeding) was applied for 30 days. Behavioral assessments included open-field and passive avoidance tests. Hippocampal neurogenesis was evaluated via doublecortin and calbindin immunohistochemistry and Western blot. Colon integrity was assessed using occludin immunohistochemistry, PAS staining, and histopathological scoring. Oxidative stress markers were measured by ELISA in both tissues. IF reduced seizure frequency and duration in GAERS rats when the sexes were analyzed cumulatively ($p<0.05$). GIF significantly improved passive avoidance latency compared to GC ($p<0.001$). Female rats exhibited higher locomotor activity in all groups ($p<0.05$). Doublecortin and calbindin expressions were significantly reduced in GC and restored by IF in both sexes ($p<0.05$–0.01). IF significantly increased occludin expression and goblet cell counts, while reducing histopathological damage in GAERS rats. Antioxidant capacity (GSH, SOD, CAT) was significantly elevated in GIF groups in both brain and colon tissues ($p<0.05$–0.001). IF exerts beneficial effects on epilepsy through neurogenesis enhancement and gut-brain axis modulation with limited sex-dependent differences. These findings suggest that IF is a potential noninvasive complementary therapeutic approach for epilepsy management.

Poster 16

Sex differences in stroke outcomes, treatment efficacy and mechanisms in animal models of focal cerebral ischemia: a systematic review and meta-analysis

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Ischemic stroke is a leading cause of disability, yet its pathophysiology remains incompletely understood. Preclinical models often fail to reflect key patient characteristics, such as age and sex, predominantly using young male animals. Treatments validated in these models may be ineffective or harmful for females, making it critical to understand the underlying mechanisms of sex differences. This systematic review examines sex differences in stroke injury, treatment efficacy, and underlying mechanisms.Following a pre-registered protocol (PROSPERO ID CRD42023495731), we searched 3 databases and identified 5096 unique records. The search was supplemented with references from included studies, resulting in another 7716 screened records. Ultimately, 337 studies were included in the systematic review and 245 in the meta-analysis. Multi-level random-effects meta-analysis was used to combine outcomes, and univariate meta-regression to explore heterogeneity. Data were extracted in duplicate; results from single-reviewer extraction are presented here. Females exhibit 28.5% (95% CI: -37.8, -19.2) smaller infarct volumes than males, an effect absent after ovariectomy and in aged animals. A similar pattern was observed for post-stroke neurological deficits. Mortality rates did not differ by sex. We identified 71 studies with sex-specific intervention effects, predominantly investigating inflammatory responses (39%), cell death (33%) and vascular responses (17%) as the underlying mechanisms. Male animals have larger infarcts than females, but the damage is independent of mortality. Age modulates sex differences, highlighting the role of sex hormones in stroke pathophysiology. We will further examine the underlying mechanisms of sex differences in stroke injury, repair, and treatment efficacy.

Poster 17

Investigation of the effect of cage placement on social interaction behavior in female rats exposed to postnatal stress

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Reproducibility and reduction remain significant challenges in preclinical biomedical research. While environmental factors are known to influence experimental outcomes, the impact of microenvironmental variations within animal housing—specifically cage positioning in multi-tiered rack systems—is often overlooked. Female Wistar Albino rats were subjected to a maternal separation (MS) protocol (180 min/day from PND 1 to 21) or remained as controls. Following weaning, animals were allocated to the top, middle, or bottom levels of a standard rack system. After 30 days of housing, social behavior was assessed using the Social Interaction (SI) test. Physiological and molecular markers, including serum corticosterone levels and the expression of oxytocin (OXT) and oxytocin receptor (OXTR) genes in the hippocampus, were analyzed via ELISA and RT-PCR. No statistically significant main effects of group or cage rack level were observed across behavioral, endocrine, or molecular measures ($p>0.05$). For example, social interaction time was not significantly affected by group ($F(1,4)=0.79$, $p=0.425$) or cage level ($F(4,12)=1.04$, $p=0.429$). Similarly, corticosterone, grooming behaviors, and OT/OTR expression showed no significant differences. However, moderate to large effect sizes were observed for several parameters (e.g., partial η^2 up to 0.54), indicating potential biological relevance despite limited statistical power. Although no statistically significant effects were detected, the observed effect sizes suggest that cage rack position may influence behavioral and neurobiological outcomes. These findings highlight the importance of considering housing-related variables in experimental design and underscore the need for adequately powered studies to improve reproducibility in preclinical research.

Poster 18

Bridging metabolism and pain: transcriptomic evidence for a key role of spinal oligodendrocytes

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The global rise in metabolic disorders has positioned them as major contributors to neurological dysfunction, including chronic pain, a condition that is more prevalent in females. Notably, several myelin-related pathologies also exhibit sex-specific vulnerability. While neuronal injury and inflammation are recognized contributors, they do not fully explain metabolic disease-related neurological comorbidities, highlighting a potential role for oligodendrocytes (OLs) and myelin in linking metabolic imbalance to CNS dysfunction. In rodent models, Western Diet (WD) consumption induces pain-like behaviors, as does selective depletion of OLs, which suggests a mechanistic link between metabolic state, myelin integrity and sensory processing. Single-nucleus RNA sequencing (snRNAseq) of the mouse spinal cord after three months of WD exposure. WD-fed mice displayed two distinct sensory phenotypes: mechanical sensitivity comparable to regular-diet controls and prolonged hypersensitivity. Transcriptomic analysis revealed that OL lineage cells constitute over 47% of spinal cord nuclei and are among the most diet-responsive populations, especially in female mice. WD exposure was associated with downregulation of oxidative phosphorylation-related transcripts, while pain-susceptible animals showed additional suppression of myelin genes (Mbp, Mag, Mog, Cnp, Plp1) and mRNA processing pathways. Together, these findings position spinal OLs as central integrators of metabolic and sensory signals, suggesting that OL dysfunction and myelin disruption may underlie the increased pain vulnerability associated with metabolic imbalance. Furthermore, these findings highlight the strong sex dimorphism of OL biology that could possibly underlie higher female susceptibility to chronic pain and myelin related pathologies.

Poster 19

Sex-Specific Patterns of Polypharmacy Following Traumatic Spinal Cord Injury

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Individuals with spinal cord injury (SCI) often require complex pharmacological management during early rehabilitation, leading to polypharmacy and increased risk of adverse drug events and drug–drug interactions. This study quantified medication burden and examined sex-specific patterns of polypharmacy during early SCI rehabilitation. Medications prescribed during the first 40 days post-injury in individuals with traumatic SCI were extracted and classified by anatomical therapeutic class. Polypharmacy was defined as concurrent use of more than five medications per day. Overall medication burden, prevalence and duration of polypharmacy, and sex-stratified comparisons across drug classes were performed. Among 302 participants, mean age was 50.3 years (SD 19.6) and 69.9% were male. Mean time from injury to rehabilitation admission was 6.3 days (SD 2.7), and mean rehabilitation duration was 159.8 days (SD 74.2). Patients received a mean of 9.3 medications per day during the observation period, with a maximum of 34 medications on a single day. Polypharmacy was present at 79.8% of patient-days observed. Women had a higher mean daily medication count than men (9.93 vs. 9.46) and a longer duration of polypharmacy exposure (83.3% vs. 78.3% of observed days). Sex differences in the likelihood and duration of use were observed across multiple drug classes. Polypharmacy affected approximately four in five patient-days. Women experienced consistently higher medication burden and longer exposure. These findings highlight the need for sex-aware medication review and proactive deprescribing in early SCI care, and support further research on clinical consequences.

Poster 20

Reproductive Ageing and Physical Activity in Later Life (REALL-Q) Questionnaire: Development, Validation and Analysis

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No existing questionnaire assesses the impact of menopausal, andropausal, and benign prostatic hyperplasia (BPH) symptoms on physical activity (PA). Hence, we aimed to (1) develop and (2) validate a questionnaire that directly links symptoms of menopause, andropause and BPH to PA; and (3) to investigate how symptoms of menopause, andropause and BPH impact PA. For questionnaire development (1), we adapted pre-existing menopause, andropause, and BPH questionnaires. We added questions to directly associate symptoms and PA via six symptom types. To assess reliability of the questionnaire (2) we will deploy the questionnaire twice to 120 participants (40+ years; test-re-test via intraclass correlation coefficient). A sub-sample of participants will wear an accelerometer watch (Matrix, ParmayTech, Spain; step count, PA intensity) between first and second questionnaire completion (criterion validity via Spearman's r). To assess the impact of symptoms on PA, (3) we will build multivariable regression models, adjusting for previously identified covariates. To develop the REALL-Q, we (1) systematically adapted existing questionnaires and consulted with experts to build our five-component questionnaire (biological sex; characterization of menopause; characterization of andropause, sex-specific symptoms related to PA; reproductive characteristics). Ongoing work (2&3) involves questionnaire deployment. The intent of our questionnaire is to directly link menopausal, andropausal, and BPH symptoms to PA. A sports physician, urologist, researchers, and population representatives guided the development of the final questionnaire. The findings from this questionnaire will provide information on whether, how, and to what degree, symptoms are barriers to PA, accounting for sex on a continuum.

Poster 21

Sex-Bias Immune Aging and its Interplay with X-Inactivation Escape Genes at Single-Cell Level

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The world is aging, and improving the health of the elderly is crucial. Elderly individuals are particularly susceptible to immune system failure, leading to increased vulnerability to infectious diseases. Immune responses exhibit sex-specific patterns due to a combination of hormonal and genetic factors, including the number of X chromosomes and the expression of genes escaping X-inactivation in females. However, which genes escape X-inactivation throughout life and their impact on immune cell functions remain unclear. Using single-cell multiomics methodologies, we assess whether age-related changes in cellular composition, chromatin accessibility, and transcription are sex-specific in mice. Our findings reveal a similar aging-specific remodeling of the T-cell compartment in both sexes and a pronounced sex influence on the B-cell transcriptome. Moreover, we describe a cell-type-specific landscape of X-inactivation, with escape genes contributing to female-biased expression. Notably, a subset of aged T-cells, which play a key role in aging and cancer progression, demonstrates increased transcriptional activity from the inactive X chromosome, accompanied by heightened chromatin accessibility. Our work sheds new light on the intricate interplay between sex and age, highlighting cell-type-specific escape dynamics in shaping sex-specific immunological trajectories and advantages.

Poster 22

APOE4 drives opposing neuroimmune responses in females and males with distinct implications for Alzheimer's immunotherapy outcomes

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Alzheimer's disease (AD) disproportionately affects women, particularly APOE4 carriers, with risk increasing during hormone-sensitive life stages such as menopause. Emerging evidence suggests that APOE4 alters innate immunity and meningeal lymphatic function, yet how these sex-dependent pathways shape treatment response remains poorly understood. We integrated single-cell transcriptomics, in vivo imaging of cerebrospinal fluid (CSF) drainage, lipidomics, and immune profiling in humanized APOE3 and APOE4 female and male mice. Innate immunity was pharmacologically modulated via CSF1R inhibition to define causal effects on neuroinflammation, meningeal lymphatic function, and cognition. APOE4 induced distinct sex-dependent neuroimmune states. Females exhibited heightened neuroinflammation, disrupted lipid homeostasis, and cognitive impairment, whereas males showed altered lymphatic architecture and chemokine signatures associated with relative resilience. Importantly, CSF1R-mediated innate immune suppression produced opposing effects by sex: it reduced neuroinflammation and improved cognition in females but exacerbated inflammatory profiles and accelerated cognitive decline in males. These divergent responses were associated with sex-specific leukocyte activation, differences in CSF lymphatic drainage, and distinct glial-vascular signaling programs. APOE4 establishes sex-dependent neuroimmune states that predict differential responses to immunomodulation, benefit in females and harm in males. These findings challenge "one-size-fits-all" approaches to AD therapy and suggest that immunomodulatory therapy design may require not only sex stratification but also consideration of hormone-sensitive stages, with direct implications for women at the menopausal transition.

Poster 23

EcoSplit reveals a female-specific immune–stromal program with androgen receptor sensitisation and adverse prognosis across cancers

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Sex shapes the tumor microenvironment (TME), prognosis, and response to immunotherapy: women benefit less from immune checkpoint blockade and develop more immune-related adverse events. Yet pan-cancer single-cell atlases pool sexes during decomposition, letting the male-majority signal dominate the inferred immune structure, and no framework formally tests whether an immune-stromal program in one sex lacks a counterpart in the other. We hypothesised that the female TME harbours hormone-sensitised organisation that joint factorisation cannot recover. We assembled a treatment-naive pan-cancer single-cell atlas of 1,771,229 immune and stromal cells from 737 patients across 29 cancer types and developed EcoSplit, a sex-stratified factorisation framework that tests, by permutation, whether sex-specific programs lack counterparts between sexes. Programs were profiled by composition and transcription-factor activity; signature scores were projected onto TCGA for Cox survival analysis. EcoSplit uncovered a tumor ecotype exclusive to women, recurring across seven cancer types in 10.6% of female patients and absent from any male decomposition. The ecotype is defined by co-recruitment of mast cells with stress-imprinted plasma, CD4, and CD8 T cells alongside cancer-associated fibroblasts. It shows cell-intrinsic androgen receptor sensitisation in mast cells and stress-imprinted lymphoid populations (effect size +4 to +7 standardised units, $p \leq 1.4 \times 10^{-4}$) without altered ligand exposure. In TCGA female cohorts (n=2,279, 17 cancer types), the signature predicted shorter overall survival (HR=1.27, $p=3.4 \times 10^{-6}$; age- and stage-adjusted HR=1.21, p=0.004). EcoSplit reveals a prognostic, female-specific tumor ecotype defined by androgen receptor sensitisation that male-dominated pan-cancer references cannot detect, supporting sex-stratified decomposition as a default in tumor immunology.

Poster 24

Characterizing Sex Chromosome Dosage Differences in Head and Neck Squamous Cell Carcinoma Microenvironment

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Head and neck squamous cell carcinoma (HNSCC) is a biologically heterogeneous disease with marked sex differences in incidence and prognosis. While clinical disparities are increasingly acknowledged, the molecular consequences of sex chromosome dosage alterations, such as Loss of Y chromosome (LoY) and Extreme Downregulation of Y-linked genes (EDY), remain poorly understood. Here, we investigate how these alterations influence tumor biology and reshape the tumor microenvironment (TME), with a focus on fibroblast and immune cell dynamics. Analysis of bulk RNA-seq data revealed widespread LoY and EDY events in male patients, predominantly in HPV-negative tumors, with LoY acting as a driver of EDY. Stratification into XX, XY, and XØ (EDY/LoY) groups uncovered distinct transcriptomic and cellular profiles. To enable deeper exploration, a harmonized single-cell HNSCC atlas was constructed by integrating datasets across cohorts, allowing joint analysis of gene expression, chromosomal instability, cell–cell interactions, and ongoing spatial validation efforts using multiplex protein imaging and X/Y chromosome detection. Sex chromosome dosage defined three TME profiles: female (XX) tumors exhibited increased immune infiltration and cytotoxic states, defining an immune-active phenotype; XØ tumors displayed immune-deserted features; and XY tumors were enriched in fibroblasts and exhausted immune phenotypes. Within XY tumors, inflammatory CAFs (iCAFs) showed enrichment for epithelial–mesenchymal transition and extracellular matrix pathways, consistent with a fibrotic and immunosuppressive microenvironment. Altogether, these data establish sex chromosome dosage as a determinant of tumor-stroma interactions and immune states in HNSCC. Moving beyond binary sex classifications may uncover novel mechanisms of tumor progression and inform sex-aware therapeutic strategies.

Poster 25

Interrogating Mechanisms of Sex Bias in IPO8-related Thoracic Aortic Aneurysm

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Thoracic aortic aneurysm (TAA), i.e., abnormal dilation of the thoracic aorta, can occur as an isolated condition or as part of a genetic syndrome like the recessively inherited IPO8 syndrome. Sex is a well-known determinant of TAA heterogeneity, with more frequent disease and earlier onset in men, but faster progression and worse outcomes in women once affected. Mice, including the C57BL/6N Ipo8-/- model (Van Gucht et al, 2021), recapitulate TAA sexual dimorphism and can be used to unveil sexdivergent disease mechanisms, which are currently poorly understood. First, the Ipo8-/- sexual dimorphic aortic phenotype will be assessed in an independent mouse cohort. Four groups will be studied (N=10/group): male wildtype and Ipo8/ mice as well as female wildtype and Ipo8/ mice. At 20 weeks of age, aortic root and ascending aorta diameters will be measured using transthoracic echocardiography (LAZR-X, Visualsonics). Upon sexual dimorphism confirmation, single-cell RNA-sequencing (scRNA-seq) of the aorta of male and female Ipo8/ mice will be performed to pinpoint sex-divergent mechanisms. Additionally, gonadectomy, combined with scRNA-seq, will be used to investigate hormonedependent effects on aortic growth. Confirmation of significantly larger aortic dimensions in male versus female Ipo8/ mice was obtained (p-value root = 0.010; p-value ascendens = 0.007). Confirmation of the sexdimorphic aortic phenotype in an independent cohort demonstrates its reproducibility over time. Based on this, male and female Ipo8/ mice are currently being collected for scRNA-seq. Overall, this study will advance the understanding of sex-dependent mechanisms driving TAA formation.

Poster 26

Sex Differences in Immune Response to an MVA-Based Vaccine Against Middle East Respiratory Syndrome (MERS)

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Middle East Respiratory Syndrome (MERS), caused by MERS coronavirus (MERS-CoV), remains a global health concern, and no licensed vaccine is currently available. Sex-specific differences in vaccine-induced immunity have been reported for many licensed vaccines, with women often developing stronger antibody responses than men. However, sexual dimorphism following vaccination with modified vaccinia Ankara (MVA)-based vaccines remains poorly understood. We investigated sex differences in response to the MVA-MERS-S vaccine candidate in a double-blind, placebo-controlled phase 1b clinical trial. The trial's design, as well as the results on vaccine safety and immunogenicity, were recently published by Raadsen et al. (2025). In brief, blood samples were collected longitudinally from healthy volunteers before vaccination on day zero (baseline), and up to 252 days after prime vaccination. These samples were used for a comprehensive analysis of antibody responses and for the quantification of sex hormones. Vaccination with MVA-MERS-S did not elicit a stronger immune response in females. Instead, we observed a male-biased response, characterized by higher geometric mean titres of MERS-CoV S1–specific antibodies following booster vaccination (unpublished data). This finding is consistent with a previous report by Troy et al. (2015) on the MVA-based smallpox vaccine Imvamune. Antibody titres did not correlate with sex hormone levels. Further studies using a tonsil organoid model are ongoing to investigate the observed male bias in immune response to MVA-MERS-S on a transcriptome (scRNAseq) and protein (flow cytometry) level. Our findings provide initial insights into sex-specific immune responses following MVA-MERS-S vaccination and may support future vaccine development strategies.

Poster 27

Exercise-induced cardioprotection through sex-specific remodelling in ageing murine hearts

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Ageing is an independent risk factor for cardiovascular diseases, whereas exercise can be cardioprotective. Sex differences influence age- and exercise-related cardiac remodelling, yet the underlying molecular mechanisms remain insufficiently characterised. This study aimed to identify sex-specific pathways influenced by exercise in the ageing heart. Eight-week-old female and male mice were randomly assigned to either voluntary wheel running or sedentary conditions for 18 months. Cardiac function was assessed by echocardiography. At endpoint, hearts were harvested for gravimetric and histological analyses, and single-nucleus RNA sequencing to characterise exercise-responsive transcriptional programmes across cardiac cell populations in both sexes. Even though females ran more than males, exercise improved global systolic function in both sexes and partly mitigated the age-related decline in cardiac performance, with males exhibiting a stronger hypertrophic response to training. In both sexes, exercise reduced myocardial fibrosis and cardiac inflammation, with more pronounced effects in females. Sequencing analysis revealed cardiomyocytes and fibroblasts as the cell populations with the greatest transcriptional response to exercise. In cardiomyocytes, sex-specific patterns suggested divergent molecular adaptations: genes enriched in females were associated with RNA regulation processes, whereas those differentially regulated in males were linked to extracellular matrix organisation, consistent with the greater structural remodelling observed histologically in males. In fibroblasts, exercise induced genes associated to extracellular matrix organisation in females and associated to contractile function in males. Exercise induces distinct, sex-specific remodelling mechanisms in the ageing heart, underscoring the importance of sex as a biological variable when developing strategies to harness exercise-mediated cardioprotection.

Poster 28

A brief period of cold, static preservation affects cardiac graft recovery in a rat model of donation after circulatory death (DCD) in a sex-specific manner

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Sex differences in cardiac ischemia-reperfusion injury are recognized. More recently, sex differences in cardiac recovery have been reported in a rat model of DCD, which includes exposure to warm ischemia and reperfusion. Therefore, our goal was to identify protocols to improve cardiac recovery after DCD cardiac donation in a sex-specific manner. DCD donation with a functional warm ischemic time of 22 minutes was simulated in male and female rats. After procurement, hearts were either: i) flushed with a preservation solution and put in cold static storage (CSS), ii) or topically cooled and quickly reperfused with oxygenated buffer at 25°C. Thereafter, cardiac recovery was assessed under left ventricular loading conditions. Among hearts with CSS, cardiac recovery, as measured by LV work (developed-pressure-heart rate product) was significantly greater in female vs. male hearts ($p < 0.02$). Preliminary data for hearts without CSS demonstrate improved recovery LV work in both female ($p < 0.05$) and male ($p < 0.01$) hearts compared to corresponding groups with CSS. Hearts of both sexes demonstrate improved recovery of left ventricular function when omitting CSS from the graft procurement protocol. Although higher recovery was measured in females compared to males when CSS is included, it remains to be determined whether this difference persists in the absence of CSS. These findings highlight the importance of sex differences in the development of tailored clinical protocols in heart transplantation.

Poster 29

Sex-dependent recovery of left ventricular function and corresponding gene expression in a rat model of donation after circulatory death (DCD)

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Cardiac grafts obtained with donation after circulatory death (DCD) are exposed to potentially damaging conditions, including ischemia-reperfusion injury (IRI). While sex differences have been reported in other settings of cardiac IRI, little is known in DCD. Therefore, we aimed to investigate whether sex differences induce changes in the expression of genes in response to cardiac DCD conditions, which may contribute to sexual dimorphism in graft quality. Hearts from male, female, and ovariectomized (OVX) Wistar rats underwent simulated DCD followed by 0 or 22 minutes of warm, in-situ ischemia. Afterwards, hearts were either directly collected or flushed with a cardioplegic solution followed by cold static storage and 60 minutes of warm reperfusion. Cardiac recovery was evaluated under conditions of left ventricular loading. Left ventricular tissue was used for bulk RNA-sequencing analysis. Recovery of ventricular function, measured as heart rate*developed pressure, was significantly increased in females vs. males ($p = 0.018$); OVX recovery was similar to males. Reperfusion induced inflammatory and hypoxia-responsive gene programs in all sexes. Genes with higher expression in females and positively correlated with recovery were linked to ribosomal and chromatin remodeling pathways; while those elevated in males and OVX, and negatively correlated with recovery, were associated with inflammatory and stress responses. Sex dependent gene expression differences may influence the heart's adaptation to ischemic stress during DCD-induced IRI. Sex-specific treatment of DCD hearts that accounts for differences in inflammatory and metabolic responses may improve graft quality and optimize DCD transplantation protocols for both sexes.

Poster 30

Biological Sex Influences the Physiological Response to Anesthesia in Rats

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Sex differences affect cardiovascular regulation, metabolism, and drug responses, yet little is known about sex-specific differences in anesthesia. Therefore, we aimed to determine optimal doses of injectable anesthestics using a rat model of donation after circulatory death and to investigate how biological sex and anesthetic dose interact. Young adult (10-12 weeks) male, female and ovariectomized (OVX) Wistar rats were anesthetized with IP injection. Initially, all rats received the same anesthetic dose (78 mg/kg ketamine, 7.2 mg/kg xylazine, 1.2 mg/kg acepromazine) (non-optimized protocol). In an optimized protocol, doses for males were increased (87.7 mg/kg ketamine, 8.1 mg/kg xylazine, 1.3 mg/kg acepromazine), whereas doses for females and OVX were decreased (65 mg/kg ketamine, 6 mg/kg xylazine, 1 mg/kg acepromazine). The occurrence of adverse events, hemodynamics, and blood gas parameters were compared between the two protocols. Neither protocol produced comparable anesthetic depth across sexes. Return of the pedal reflex tended to be higher in males versus females in the non-optimized protocol, and was significantly reduced with the optimized protocol ($p<0.05$ vs. non-optimized males). However, respiratory depression was more frequent in females compared to males ($p<0.05$) in both protocols. Differences in hemodynamics and blood gas parameters among sex groups remained similar between protocols. Adjusting anesthetic doses based on sex is particularly important, as a standardized dosing strategy may result in under-anesthesia in males and over-anesthesia in females. Sex is a major determinant of anesthetic depth and adverse events. This should be considered when establishing pre-clinical models.

Poster 31

Mapping the Female Brain Across the Menopause Transition: A Multi-Site Cross-Sectional Mega-Analysis

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The menopause transition, starting with perimenopause, is a critical neuroendocrine period marked by substantial fluctuations and decline in ovarian hormone production, and is associated with increased risk of cognitive decline and mood disorders. Neuroimaging studies remain limited by small samples and simplistic pre/postmenopausal comparisons, leaving perimenopause, a phase of pronounced hormonal variability and heightened neurological vulnerability, largely understudied. Large-scale approaches are needed to characterize brain changes across menopausal stages and identify biomarkers of risk and resilience for women's brain health. We present the first ENIGMA Neuroendocrinology Menopause Transition and Beyond Subgroup mega-analysis, pooling large-scale, multi-site MRI data from neurologically healthy individuals aged 35–65 years. Menopausal stages (premenopause, early/late perimenopause, early/late postmenopause) will be defined using STRAW+10 criteria where sufficient data is available, supplemented by clinical and symptom information. Brain structure derived from T1-weighted MRI data will be quantified using recon-all FreeSurfer (v7+, Desikan–Killiany atlas). We will map stage-specific structural brain trajectories across the menopause transition and test whether neuroimaging signatures can distinguish menopausal stages using multivariate classification approaches. We will further assess whether integrating clinical and symptom measures improves classification, particularly for the perimenopausal phase. This study is in the recruitment phase. We hypothesize stage-specific brain structural differences across the menopause transition, with greatest variability during perimenopause, and improved classification when combining imaging and clinical measures. This work will establish a large-scale reference framework for menopause-related neuroanatomical change, advancing our understanding of sex-specific brain aging and identifying windows of vulnerability and resilience in women's brain health.

Poster 32

Menopausal Hormone Therapy in Schizophrenia

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Research highlights sex differences in prevalence, manifestation, and treatment efficacy in schizophrenia spectrum disorder (SSD). While men are more affected before age 45, SSD incidence in women doubles after 45, corresponding to perimenopause start. It is a period of increased SSD risk, partly due to declining levels of ovarian hormones, especially estradiol. Menopausal hormone therapy (MHT) use has been associated with lower SSD relapse and first-onset risk and improved antipsychotic efficacy, yet its use dropped after 2002 due to breast cancer concerns. We aim to investigate whether perimenopausal women diagnosed with SSD are being prescribed MHT to the same extent as healthy women. Using Swedish nationwide registry data, we performed descriptive analyses of SSD diagnoses, hospitalizations, antipsychotic and MHT use, and sociodemographic characteristics. We stratified women by menopausal status using age as a proxy. Our cohort includes 1,822,056 women: n=1,229,201 in early menopause transition (MT), 45-48 years old; n= 301,747 in late MT, 49-53 years old; and n= 291,108 in early postmenopause, 54-58 years old. SSD prevalence was ~0.5% across all stages, predominantly non-severe (63–65%). Over 90% of SSD women redeemed their antipsychotic prescription. MHT redemption was low overall: ~3% in early MT and ~10% in late MT, regardless of SSD. In early postmenopause ~15% of SSD women and over 26% of healthy women took MHT. Differences in MHT redeeming patterns between healthy and SSD women, suggest that women with SSD are less often offered MHT. The overall low MHT use likely reflects post-2002 prescribing trends. Further analysis will assess statistical associations between SSD and MHT. This study has implications for managing SSD onset, relapse, and antipsychotics efficacy during menopause.

Poster 33

Guidance for sex- and gender-related data collection in chronic diseases: The Sex and Gender Data Item Set

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Despite growing recognition of the importance of sex and gender in health research, advances remain hindered by limited awareness, inconsistent terminology, and paucity of data. Addressing these gaps, we aim to provide guidance for sex and gender data collection for research on chronic diseases, along with supported evidence. The Sex and Gender Data Item Set (S&G-DIS) is being

developed using existing evidence and input from a multidisciplinary working group of clinicians, sex- and gender-health experts, epidemiologists, data owners/holders, and patient/community representatives, and informed by a pilot run at the Swiss Multiple Sclerosis Registry. Additionally, this work outlines the supporting evidence and rationale for each topic included in the S&G-DIS. We present the S&G-DIS, a 70-item survey-based data collection tool comprising sections on sex, gender identity, demographics and social determinants of health, sex hormones and related life-phases, care of sex and gender minorities, social network, healthcare access, sexual heath, and behaviours. The S&G-DIS is accompanied by supportive evidence on definitions, intersectionality, disease and treatment, sex and gender minorities, social aspects, healthcare journey, sexual health, and behaviours and attitudes, relevant to chronic disease research. The S&G-DIS, together with its supporting documentation, provides a practical framework to advance sex- and gender-informed research in chronic diseases. Currently in an advanced development stage, it offers an opportunity for scientific exchange at the SABV Symposium. Future work will focus on validation and implementation across registries and cohorts.

Poster 34

Estrous cycle-dependent modulation of inhibition in the mouse midbrain

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Female-specific physiological states including the reproductive cycle can modulate neuronal circuits and the behaviors they govern. Such flexibility in females has been observed in evolutionarily conserved instinctive behaviors, for example in defense from threat and risk assessment. The periaqueductal gray (PAG) is a key brainstem region for the initiation and execution of most instinctive behaviors, yet whether and how it participates in behavioral flexibility across the reproductive cycle remains unclear. To understand its possible role in guiding instinctive defensive behaviors across the reproductive cycle through local plasticity mechanisms, we performed ex vivo patch-clamp recordings in GABAergic and glutamatergic PAG neurons from naturally cycling female mice across estrous stages. We find significant changes in the synaptic and biophysical properties of both populations, including network changes in the receptive stages. We identified two firing-pattern-based subtypes of GABAergic neurons (phasic vs. tonic), of which only the phasic type exhibited estrous cycle-dependent differences. During the non-receptive phase, phasic GABAergic neurons displayed enhanced intrinsic excitability and reduced spontaneous excitatory synaptic input. Correspondingly, glutamatergic PAG neurons showed reduced spontaneous inhibitory input. This suggests that phasic and tonic GABAergic neurons receive input from different upstream regions, and that the estrous cycle selectively shapes the biophysical properties and synaptic drive of the phasic subpopulation. Since PAG GABAergic neurons are preferentially locally-targeting interneurons that threshold glutamatergic projection neuron activity, we postulate that reproductive state modulates behavioral output through local circuit computations. Future work will explore these changes in vivo using a combination of behavioral and in vivo recording techniques.

Poster 35

Impact of a non-invasive oestrous synchronisation protocol on sexual behaviour in Sprague-Dawley rats

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Female Sexual Dysfunction (FSD) is prevalent worldwide; however, current preclinical models often rely on invasive ovariectomy and supra-physiological hormone administration, limiting translational relevance. Our hypothesis is that a non-invasive protocol using a prostaglandin F2 analogue (cloprostenol) will effectively synchronise the oestrous cycle of female rats to study its effects on sexual motivation and behaviour, with potential implications for FSD research. Twelve-week-old intact-untrained female Sprague-Dawley rats received intramuscular- subcutaneously (SQ) injections of cloprostenol at 75, 125, or 250 µg/kg on days 0 and 3, respectively, followed by progesterone (1 mg/kg) SQ on day 4. Vaginal cytology confirmed the cycle synchronisation. Sexual motivation was assessed. Plasma/vaginal hormonal levels (oestradiol and follicle-stimulating hormone/FSH levels) were measured by enzyme-linked immunosorbent assay/ELISA. Vaginal oestradiol levels were determined in unsynchronized rats (n=28). Open-field and forced swim tests evaluated locomotion, anxiety, and depression-like behaviours. All doses synchronised rats in the proliferative/transitional phase, with hormonal levels within physiological ranges. Behavioural tests at 125 µg/kg cloprostenol showed increased proceptivity, with females exhibiting greater sexual motivation and interest, whereas higher doses were associated with decreased precopulatory behaviours. Although male rats showed increased interest in females during metoestrus or following treatment with 250 µg/kg cloprostenol. No significant differences were observed in anxiety or depression-like behaviours across the doses or oestrous phases. The non-invasive cloprostenol protocol reliably synchronised the oestrous cycle and modulates sexual motivation in female rats, providing a physiologically relevant model for investigating FSD. This approach minimises surgical interventions-high hormonal doses, thus enhancing the translational potential of future therapeutics.

Poster 36

Adolescent Dietary Restriction Alters Behavior and Disrupts the Estrous Cycle in Aging Female Wistar rats

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Dietary restriction (DR) affects reproductive and behavioral performance in an onset- and duration-dependent manner. However, the long-term effects of early-life DR remain poorly understood, especially in females. Here, we analyzed the effects of adolescent DR on reproductive and behavioral performance in female Wistar rats. Female Wistar rats exposed to 30% DR included three subgroups: early adolescent DR (EADR) from postnatal day (PND) 28 to 35, middle adolescent DR (MADR; PND35-42), and both early and middle adolescent DR (EMADR; PND28-42). The control group had ad libitum (AL) food intake during the same periods. Spatial recognition memory (SRM) was assessed using the Y-maze, anxiety-like behavior was evaluated using the light-dark box (LDB), and estrous cycle (EC) tracking was performed by vaginal smear analysis. All DR regimens delayed estrous cycling onset, most notably in EADR, with regular EC maintained up to 6 months. Disruptions in EC regularity later occurred in 70% of EADR (9 months), 60% of MADR (12 months), and 80% of EMADR rats (15 months), progressing in all groups by 18 months. Regarding behavioral performance, EMADR led to impaired SRM in 3-month-old female Wistar rats, regardless of EC phase, and decreased anxiety-like behavior compared to age-matched controls in proestrus (PE). EADR disrupted adolescent EC and led to earlier EC irregularity. The effects of EMADR on anxiety-like behavior in young adult female Wistar rats depended on EC phase and were beneficial in PE. In contrast, EMADR reduced novelty-directed spatial exploration regardless of EC phase.

Poster 37

Neurological and behavioural effects of ovarian hormone cycle suppression

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Ovarian hormone status shapes brain physiology and may contribute to female-specific vulnerability to psychiatric disorders, yet this factor remains largely overlooked in the historically male-biased field of preclinical neuroscience. Here, we investigated whether suppression of ovarian cyclicity produces measurable changes in hippocampal molecular and structural plasticity in female mice. We systematically assessed estrous cyclicity, compared hormonal profiles, and examined their impact on hippocampal function and behaviour. Our findings reveal that naturally induced cycle suppression drives significant structural changes in the ventral hippocampus and dysregulates genes critical for long-term potentiation, glutamatergic and dopaminergic signalling, likely contributing to heightened neuronal excitability. Given these findings, we next asked whether pharmacological cycle suppression via oral contraceptives (OCs) produces similar effects. This question is particularly relevant given that OCs are among the most widely prescribed medications globally, used for both contraceptive and non-contraceptive purposes, yet their impact on psychiatric outcomes remains poorly understood. To address this, we developed a mouse model of OC use. Preliminary data indicate formulation-dependent effects on anxiety- and depression-like behaviour. Ongoing work aims to elucidate the underlying molecular pathways and identify whether there are particularly sensitive periods during which pharmacological suppression poses the greatest risk for mood disorders.

Poster 38

Estimating the Effect of Combined Oral Contraception on Adolescent Mental Health

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Oral contraception is widely used and generally considered safe, yet emotional side effects are frequently cited as reasons for discontinuation or switching methods. Research on oral contraception and mental health has yielded inconsistent results, potentially due to methodological limitations such as lack of data on contraceptive history, baseline mental health, and the underrepresentation of first-time adolescent users. This study used the Target Trial Emulation framework to examine the causal effect of the combined oral contraceptive pill (COCP), ethinyl estradiol 30 µg and levonorgestrel 150 µg, between ages 13–16 years on internalizing symptoms at age 18 years. Sequential target trials were emulated using data from the population-based observational cohort Generation R combined with pharmacy dispensing records. Observational analogues of the intention-to-treat effects were estimated using linear mixed models adjusted for confounders, and observational analogues of the adherence-adjusted effects were similarly estimated excluding non-adherent participants. Across 34 pooled trials, 304 COCP initiators were matched with 1,215 controls. Among initiators, 35.5% switched to another hormonal method and 11.8% discontinued. COCP initiation showed no significant intention-to-treat effect (B= 0.03, 95% CI= –0.09; 0.15) nor adherence-adjusted effect (B= –0.10, 95% CI= –0.27; 0.08). Age at initiation, baseline symptoms, and genetic predisposition to depressive, anxiety, and bipolar disorder did not modify the effects. When modelled as a clinical trial, COCP initiation between ages 13–16 did not affect internalizing symptoms in young adulthood. However, high rates of switching and discontinuation suggest heterogeneity in individual mood responses, warranting further investigation.

Poster 39

The impact of sex and environment on the proteomic landscape of the midbrain periaqueductal gray and superior colliculus

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Defensive behaviours such as risk assessment, freezing and escape in the presence of a predator are critical for animal survival. Although stereotyped to some degree, these instinctive behaviours exhibit significant variability within and between individuals. Multiple structures across the brain orchestrate these behaviours. For example, the forebrain hypothalamic nuclei (HPN) provide motivational context, the midbrain superior colliculus (SC) – sensory information and the midbrain periaqueductal gray (PAG) – pre-motor control. Previous work has mostly focussed on behavioural variability arising from plasticity mechanisms in forebrain regions projecting to the PAG and SC, including the hypothalamus, amygdala and cortex. Here, we asked whether the midbrain SC and PAG themselves possess the molecular machinery to support plasticity. We analysed differences in the proteome in four brain regions: PAG, SC, HPN and sensory cortices (CTX) from male and female mice in different social (single- vs group-housed) and environmental context (individually ventilated vs. open-top cages) as means to induce plastic changes. This comprehensive dataset, containing over 11, 000 proteins per sample allows us to posit 1) the PAG, SC, HPN and CTX possess similar co-expression programmes related to synaptic function, 2) there are global and brain-region sex-specific proteomic differences, and 3) changes in the social and environmental context lead to both global and region-specific proteomic changes, some of which show sex-specificity. For example, the expression of inositol-1,4,5-trisphosphate-gated calcium channel, critical for calcium release from the endoplasmic reticulum during various forms of synaptic plasticity, exhibited social context modulation in females, but not males, only in the midbrain.

Poster 40

Sex- and Age-Dependent Regulation of circadian and Infradian Rhythms

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Biological rhythms extend beyond the circadian (~24 h) range to include infradian oscillations, yet how these longer rhythms are shaped by sex and aging remains poorly understood. Locomotor activity was used as a robust readout to examine rhythmic dynamics across multiple timescales. We analysed wheel-running activity in single-housed young and middle-aged male and female mice. Circadian and infradian rhythms (~5-, ~10-, and ~14-day) were quantified using Lomb–Scargle periodogram analysis. Comparisons across sex and age were performed to assess differences in rhythmicity, activity distribution, and behavioural organisation. Middle-aged mice, particularly females, exhibited more precise circadian rhythms and redistributed a greater proportion of activity into the light phase compared to young females. Infradian analysis revealed marked sex- and age-dependent differences. Young females displayed robust ~5-day rhythms that were absent in both middle-aged females and males. Notably, females exhibited an age-dependent shift from ~10-day rhythms in young animals to ~15-day rhythms in older animals, whereas males maintained relatively stable infradian organisation, with dominant rhythms consistently centred around ~10 days across age groups. Together, these findings demonstrate that infradian organisation of behaviour is shaped by both sex and age. Locomotor activity is organised across multiple timescales and is differentially modulated by sex and aging. These findings highlight the importance of considering both circadian and infradian dynamics in behavioural regulation and may have implications for understanding age- and sex-dependent vulnerability to physiological and behavioural dysfunction.

Poster 41

Sex-specific effects ketogenic diet on metabolism, behavior, and circadian activity of male and female BDNF-deficient mice

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Brain-derived neurotrophic factor (BDNF) is involved in both circadian regulation and metabolism, but role in nutritional interventions is poorly understood. Ketogenic diet (KD) gains increasing attention for a wide range of metabolic, neurological, and mental disorders, but its mechanisms remain largely elusive. Here we investigated combined effects of ketogenic diet and BDNF deficiency on mouse circadian activity, brain and peripheral metabolism, and behavior. WT and BDNF+/- mice were kept on ketogenic (KD, 90% energy from fats) or regular (RD, 13% energy from fats) diet for 2 to 4 weeks. After two weeks, body weight, fat mass, energy expenditure, and locomotion were measured in Promethion cages and EchoMRI. After four weeks, behavioral tests were performed and mice were dissected for ex vivo analysis of blood and brain samples. BDNF deficiency reduced ketogenic effect of KD, suggesting its role in ketogenesis. Body weight gain reduction was found only in both WT and BDNF males, while fat mass and calorie intake were not affected by diet or genotype. KD induced systemic inflammation and sex/genotype-specific changes in insulin, leptin, and there receptors in prefrontal cortex and ventral hippocampus along with vesicular glutamate and GABA transporters. In males, BDNF deficiency reduce total rest (time of stillness) while made it less fragmental compared to WT. KD partially restored the profile, making it closer to WT. In females, WT mice have less fragmented rest than males, while BDNF deficiency, on a contrary, made it more fragmental. KD makes the profile BDNF mice indistinguishable from WT on RD.

Poster 42

Sex-specific and shared function of PTPRN and PTPRN2 in the regulation of reproduction, growth, and melanotroph development in mice

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PTPRN and PTPRN2 are members of the protein tyrosine phosphatase receptor family but lack phosphatase activity due to mutations in two residues within their intracellular catalytic domains. These proteins are highly expressed in neuroendocrine cells and, during evolution, acquired new cellular roles within the centralized and diffuse neuroendocrine systems. Here, we analyzed sex-specific and shared roles of PTPRN and PTPRN2 in the regulation of reproduction, growth, and melanotroph development in female and male mice. This study included single knockout (Ptprn-/-, Ptprn2-/-, SKO) and double knockout (Ptprn-/-+Ptprn2-/-, DKO) mice. Animals were monitored for weight, length, puberty onset, and estrous cycle was analyzed by vaginal smear staining with 0.1% methylene-blue. Erythrocytes were counted in the Neubauer chamber. Gene expression was evaluated by qPCR, protein abundances were analyzed by Western blot method, hormones and endogen opioids levels were determined by ELISA. Immunohistochemistry was used to analyze tissue structure. Our results showed that only DKO females were infertile, and the infertility was attributed to decreased hypothalamic Kiss1 (RP3V region) and Gnrh1 expression. Melanotroph hyperplasia was detected in DKO females and males together with increased Pomc and Pax7 expression, increased levels of b-endorphins, ACTH and corticosterone. SKO and DKO females and males displayed decreased body weight, length, and expression of Gh; females showed greater fold changes. DKO and Ptprn-/- females and males had decreased numbers of erythrocytes. PTPRN and PTPRN2 have sex-specific functions in the regulation of reproduction, and shared functions in the regulation of growth and melanotroph development.

Poster 43

Sexual dimorphism in the leptin-signalling system

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The adipokine leptin, classically associated with metabolic homeostasis, also influence social behaviour through neurons expressing the long-form of leptin receptor (LepR) within the lateral hypothalamus (LH). In males, when nutritional and social stimuli are competing, LepRLH neurons prioritise social exploration towards females over food approach despite hunger pressure. Reproduction is however energetically more demanding for females, and female socio-sexual behaviour is directly affected by hormonal state. To uncover potential sex differences in the leptin-signalling system, we quantified LepR-expressing neurons along the whole antero-posterior brain axis in both sexes. Next, we studied how LepRLH neurons in females respond to and integrate nutritional and social stimuli. To address this, we combined deep-brain calcium imaging, pharmacology, opto- and chemogenetics of LepRLH neurons in females, taking into consideration their estrous cycle stage. We further mapped downstream circuitry by chemogenetically activating LepRLH neurons and quantifying c-fos expression throughout the brain. We identified sex differences in LepR-expressing neuronal populations across multiple brain nuclei. In LH, LepR neuronal responses to systemic leptin injections are sex- and estrous cycle-specific, leading to different feeding behaviour. LepRLH neurons of females also respond and promote social and sexual contact towards males, with greater responses in receptive than in unreceptive females. Activation of female's LepRLH neurons strongly inhibited the ventral premammillary nucleus, a region involved with opposite sex odours that co-expresses LepR and Esr1 in a sexually dimorphic manner. Together, our results revealed important sex dimorphism in the leptin-signalling system, providing insights into how hormonal and metabolic signals shape state-dependent behavioural choices.

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Region and testosterone-dependent transcriptomic sex differences in the brain of japanese quail

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Male and female higher vertebrates display distinct physiology and behavior as a result of genetic differences and differential exposure to hormones during development and adulthood. The genes underlying these differences are largely unknown, especially in birds. The present study investigated transcriptomic sex differences in three brain regions (medial preoptic nucleus [POM], ventromedial nucleus of the hypothalamus [VMN] and nucleus taeniae of the amygdala [TnA]) of adult male and female quail left gonadally intact or gonadectomized and treated with testosterone (GDX+T). Overall, POM showed the largest number of differentially expressed genes (DEG). As expected, some DEG turned out to be sensitive to testosterone treatment while others were insensitive, but GDX+T also uncovered DEG that were not different in intact subjects suggesting that T (or ovarian hormones) actively “repress” some otherwise sexually-dimorphic genes. Some DEG were identified in only one nucleus and tended to be more T-sensitive, particularly in the POM which, surprisingly, had female-bias from autosomes and male-bias from the Z chromosome. In contrast other DEG, most of them T-insensitive, were common to several nuclei. DEG common to POM and VMN were most abundant, being mostly male-biased and located on sex chromosomes. Most DEG common to all nuclei are only expressed in females suggesting they are located on chromosome W. Three patterns of DEG thus emerge in response to testosterone: T-sensitive, T–insensitive, and DEG normally repressed by T, each depending on neuroanatomical and chromosomal location, representing sets of candidate genes that could explain fundamental behavioral sex differences in adult birds.

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Establishing a novel rat model for mimicking human postmenopausal obesity with impaired glucose homeostasis

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Menopause predisposes women to an increased risk of obesity and diabetes. However, the contribution of menopause-related decline in estrogen exposure remains incompletely understood. We established a rodent model of postmenopausal metabolic dysfunction (MenoMet) and evaluated to which extent menopausal hormone therapy (MHT) reverses the effects of estradiol (E2) depletion. 6-month-old female rats with polygenic susceptibility for obesity were maintained on a high-energy diet and underwent Sham surgery or bilateral ovariectomy (OVX). We initially evaluated three low doses of STZ of which a 15 mg/kg dose was designated as MenoMet, resulting in weight gain and mild dysglycemia, without causing insulin-deficiency-related catabolism. MenoMet animals received SC pellets of E2 or combined E2-progesterone (P4). Oral glucose tolerance tests (OGTT) with serial measurement of glucose, insulin, and C-peptide were performed before OVX and after 1 and 8 weeks of MHT. Five weeks after MHT initiation, body weight and food intake of both E2 and E2+P4 groups returned to the levels before OVX. Pair-fed (PF) rats did not lose weight, suggesting that MHT additionally modulates energy expenditure. The E2 group and the E2 + P4 showed a ~20% reduction in glucose AUC compared to the MenoMet group. Both E2 and E2 + P4 reduced C-peptide and insulin AUC, indicative of improved insulin sensitivity. MenoMet animals showed increased fat mass, whereas MHT, but not PF reversed this effect.The MenoMet model recapitulates postmenopausal obesity and mild dysglycemia, a phenotype that is fully reversed by E2 repletion, with add-on P4 exerting neutral effects.

Poster 46

The influence of sex-hormone deprivation and black cohosh treatment on hippocampal and hypothalamic gene expression profiles in ovariectomized rats

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Menopause is associated with estrogen decline and changes in sensory and neurological function, including reduced olfactory discrimination. However, the neuro-molecular mechanisms underlying these sex-hormone-dependent changes remain insufficiently understood. We investigated whether ovariectomy alters hippocampal and hypothalamic gene expression profiles and whether treatment with isopropanolic Cimicifuga racemosa extract (iCR; black cohosh) modulates these changes. Hippocampal and hypothalamic tissue from female Sprague Dawley rats was analyzed across three conditions: intact controls, ovariectomized animals, and ovariectomized animals treated with iCR for three months. Genome-wide expression profiling was performed using rat microarrays. Differentially regulated genes were analyzed by gene set enrichment analysis, and selected olfactory receptor genes were validated by quantitative real-time PCR. iCR treatment was associated with broad transcriptional changes in both brain regions, affecting 1,957 hypothalamic and 2,119 hippocampal genes. Enrichment analyses identified biological processes related to sensory and neurological function, with a prominent overrepresentation of olfactory receptor activity among genes overlapping between ovariectomy-induced and iCR-modulated expression changes. Several olfactory receptor genes showed ovariectomy-associated regulation that was partially or fully counter-regulated by iCR. Notably, hippocampal OLR522 demonstrated significant ovariectomy-induced upregulation followed by significant downregulation after iCR treatment, consistent with compensation of sex-hormone deprivation–associated transcriptional changes.These findings suggest that estrogen deprivation affects olfactory receptor gene networks in neuroendocrine brain regions and that iCR can modulate selected components of this sex-hormone–sensitive omics signature. The data support further investigation of menopause-related sensory changes from a sex-specific neurogenomic perspective.

Poster 47

Impact of current breeding practices on the health of breeding mouse dams

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Female rodent breeders are the unspoken workhorses of animal research. Current breeding practices are designed to maximize breeding, exposing the dam to the physiological stress of concurrent pregnancy and lactation – but the effect on her welfare is unknown. In this 3R-based exploratory analysis, we investigated whether breeding experience impacts the health of the mouse dam. Two commonly used inbred mouse strains [C57BL/6J; BALB/cByJ] were used to assess behavioral, metabolic, and nutritional endpoints in postpartum dams experiencing one, two, or four consecutive cycles of pregnancy and lactation, with comparisons made to age-matched virgin females. Our findings demonstrate that maternal body weight increases with the number of reproductive cycles regardless of the mouse strain. Further, we observed a reduction in exploratory behavior with increasing reproductive cycles, as well as expected strain differences. Fecal corticosterone levels, indicative of stress, varied before, during, and after pregnancy and lactation, strain-specifically, but were not influenced by parity. Bone mineral density decreased with multiple rounds of pregnancy and lactation, strain-specific, while mother-pup interaction measures revealed robust strain differences but no parity effects. We are currently extending this work through a confirmatory study comparing retired breeders ordered from commercial breeding facilities with virgin and single-parity females to assess the cumulative physiological consequences of long-term reproductive exposure. Through this comprehensive health assessment, we aim to understand how breeding experience impacts maternal health and well-being while establishing reproductive history as an important but underrecognized biological variable in laboratory rodents, with implications for animal welfare assessment and translational biomedical research.

Poster 48

The impact of estrogen on the gut microbiome: a systematic review and meta-analysis

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Estrogens have been proposed as modulators of gut microbiome (GM) composition, yet evidence from observational studies remains inconsistent. This meta-analysis aimed to systematically summarise existing evidence on GM alterations in hypoestrogenic women – post-menopausal or premature ovarian insufficiency (POI) – compared to euestrogenic pre-menopausal controls. PubMed, SCOPUS and Embase were searched through December 2024 for studies comparing GM characteristics between hypoestrogenic and pre-menopausal women. Primary outcome was α-diversity (Shannon index). Secondary outcomes included relative abundances of Bacteroidetes, Firmicutes, and the Bacteroidetes to Firmicutes ratio. Random-effects models were used for data synthesis. Out of 1092 studies screened, 7 met the inclusion criteria (n = 45 women with POI, n = 1222 post-menopausal women, n = 463 eustrogenic controls). No significant differences were observed in α–diversity (p=0.990), Bacteroidetes (p=0.440), or Firmicutes abundance (p=0.110) between hypoestrogenic and euestrogenic groups, irrespective of POI or postmenopause. Similarly, the Bacteroidetes to Firmicutes ratio showed no significant difference between the groups (p=0.400). Study heterogeneity was high (I^2 61-99%). Current evidence does not support consistent differences in GM diversity or major bacterial phyla between hypoestrogenic and euestrogenic women. Given the substantial heterogeneity, limited control of confounding factors, and variability in methodological quality, these findings should be interpreted with caution. High-quality, well-controlled studies are needed to better define the relationship between estrogen status and the GM.

Poster 49

Establishment and characterization of patient derived endometriosis organoids for high throughput screening

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Organoids – three dimensional cultures derived from patient tissue – provide a model system that preserves disease-specific features. For endometriosis, where novel treatment strategies are urgently needed, organoids offer a platform that can increase the understanding of disease mechanisms and enable the discovery of more effective diagnostic and therapeutic approaches. However, adaption of culture and handling protocols to enable high-throughput screening is necessary to achieve sufficient throughput and reproducibility from handling precious patient-derived material. This can provide a physiologically relevant and scalable system suitable for systematic drug response profiling. Endometriotic lesions from patients were collected and processed for organoid culturing. Multiple enzymatic dissociation protocols were tested to optimize cell yield and viability, including combination of collagenases and DNase at different incubation times. Organoids were embedded in extracellular matrix and maintained under different media formulations to support growth. Image-based screening methods for read-outs of morphology, proliferation and viability were established for extracted tissues and cultivated organoids, and optimal conditions were selected for future high-throughput drug screening. Here we show that a combination of collagenase IV and V together with DNaseI gave the highest yield of living cells during processing. Through testing of different media options and formulations, we found a setup suitable for downstream applications, including phenotypic characterization and drug response studies. Patient-derived organoids represent a promising platform for modelling endometriosis. The optimized protocols enable reproducible organoid generation and provide a foundation for high-throughput screening with potential to advance into personalized treatment strategies for endometriosis patients.

Poster 50

Mediterranean Phytochemicals as Emerging Therapeutic Strategies against Endometriosis

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Endometriosis is an estrogen-dependent chronic inflammatory disease. Surgery and long-term treatments with NSAIDs or oral contraceptives show limited efficacy and adverse effects. Increasing evidence involves endocrine disruptors (EDs) in endometriosis onset and progression, highlighting the need for safer and more effective approaches. A stepwise approach was designed to investigate the therapeutic potential of Mediterranean plant extracts (PEs): phytochemical standardization and characterization of five PEs and in vitro screening with human endometrial cell lines and comparison with conventional NSAIDs. The three best-performing PEs were selected for in vivo toxicokinetic (TK) and organotropism studies. The most promising PE selected from the TK study will be tested in vivo to evaluate ED-induced endometriosis-like lesions. In parallel, a human observational study enrolls 60 patients with endometriosis; urine and blood samples for ED quantification and miRNome analysis, biopsies to establish primary cell cultures are collected to assess ED accumulation and PE effects. The extracts included Olea europea (OE), Verbascum thapsus (VT), Citrus sinensis (CS), Citrus limon, Serenoa repens. OE, VT and CS were selected for the TK study based on their polyphenolic content and in vitro anti-oxidant/inflammatory activities, including the reduction of PGE_2 and LTB_4 levels without affecting cell viability. From the TK study, VT emerged as the most promising, showing the highest distribution in the uterus and ovaries. The human study is ongoing. Mediterranean PEs represent promising candidates for complementary and preventive strategies in endometriosis, supporting future translational and clinical studies within the Italian National Health System.

Poster 51

Gender-affirming hormone therapy initiated in early puberty affects the hepatic and whole body metabolic response to a dietary challenge in a mouse model of adolescent gender transition

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Specifically for transgender adolescents, it may include gonadotropin-releasing hormone analogues (GnRHa) to suppress puberty, followed by testosterone (T) or estradiol (E2). As sex hormones influence various metabolic tissues, this approach might have metabolic consequences, particularly given this population's sedentary lifestyle and unhealthy dietary habits. We used a mouse model mimicking the clinical trajectory of transgender adolescents to explore the effects of hormonal therapy on hepatic and whole-body metabolic response to a dietary challenge. Prepubertal 4-week-old female and male mice were treated with the GnRHa degarelix (DGX) to suppress puberty, followed by the administration of T to females and E2 to males from 8 weeks of age. Animals were fed a western diet for 12 weeks, starting at 16 weeks of age. Their metabolic phenotype was compared to vehicle-treated mice of both sexes. Compared to control males, DGX+E2 increased fat mass resulting in a female profile, and induced expression of inflammation and fibrosis markers in liver. Compared to control females, DGX+T increased body weight towards control male levels but with a higher proportion of fat mass. Moreover, DGX+T induced an unfavorable glucolipid profile compared to control females (high insulin, triglycerides and cholesterol), accompanied by more pronounced hepatic steatosis. Using a mouse model of adolescent gender transition within a western dietary context, we show that gender-affirming therapy initiated in early puberty results in changes in adiposity, glucolipid profile and hepatic phenotype.

Poster 52

Uncovering the Effects of Adolescent Gender Transition on Skeletal Muscle Using Mouse Models

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Sex is a major determinant of muscular variability, with pronounced differences between males and females in muscle composition, mass and strength. Sex hormones, emerging during puberty, drive these sex differences and affect muscle health throughout life. Gender-affirming hormone therapy represents a unique context of sex hormone modulation, providing a powerful model to assess their role in skeletal muscle. In transgender adolescents, specifically, puberty suppression (PS) may precede the desired gender transition, which is induced by the administration of gender-affirming hormones (GAH). Considering the importance of musculoskeletal robustness and physical fitness for life-long health, it is concerning that PS was recently found to impair muscle mass development. It remains unknown whether GAH administration is effective at mitigating this deficit, if adolescent gender transition also has effects on muscle function and fitness, and whether muscle health in later life is affected. The aim of this study is therefore to investigate the effects of adolescent gender transition on skeletal muscle in depth. Using preclinical mouse models mimicking the hormone strategy in trans adolescents, effects on muscle function and composition will be assessed in vivo (muscle mass, grip strength, endurance capacity) and ex vivo (contractility, histology, biochemical assays). Cellular and molecular mechanisms will be investigated by single-nucleus transcriptomics on mouse muscle tissue and in vitro treatment of primary cells. Finally, we will study the effects of PS followed by GAH on muscle's regenerative capacity and adaptive response to atrophy, using the aforementioned mouse models.

Poster 53

Feminization of the male liver transcriptome drives adaptive and functional remodeling in a weight cycling mouse model of MASLD

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Metabolic dysfunction-associated steatotic liver disease (MASLD) shows marked sexual dimorphism, with men developing more severe disease. However, the molecular basis of this difference remains poorly understood. We established a preclinical MASLD model incorporating weight cycling, a clinically relevant feature that often accompanies lifestyle-based disease management, to investigate sex-dependent mechanisms. Adult C57BL/6J mice of both sexes underwent repeated cycles of Western diet (WD) feeding and chow diet (CD) recovery. Control groups were maintained on CD or exposed to a single WD challenge. Metabolic phenotyping, liver histology, micro-computed tomography, and transcriptomic analyses were performed. Differential expression and pathway analyses identified sex-specific signatures. Repeated WD exposure induced more severe hepatic steatosis in males than females, accompanied by higher serum ALT and a more severe upregulation of steatotic, inflammatory and fibrotic genes despite similar glucose intolerance. Transcriptomic analyses revealed a collapse of liver-identity networks in males, with downregulation of the transcriptional repressor Bcl6 and marked feminization of the hepatic transcriptome. This shift was associated with increased lipid catabolism, suggesting an adaptive response to metabolic stress, but also with altered pharmacogene expression. Human liver transcriptomic data indicate a similar feminization pattern in men with increasing MASLD severity. In a weight-cycling MASLD mouse model, repeated metabolic stress induces feminization of the male liver transcriptome through Bcl6 repression. This adaptive reprogramming may improve lipid handling but alters pharmacogene expression, with potential consequences for drug metabolism. These findings highlight hepatic feminization as a key process in MASLD and support sex-specific approaches in disease management.

Poster 54

Unraveling sex differences in the hepatic response to androgens

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Androgens, that primarily act through the androgen receptor (AR), have anti-steatosic effects in male liver, while promoting steatosis in female liver. This project aims to understand how one transcription factor, the AR, can exert opposing actions on the same tissue depending on the sex. To unravel the AR contribution to sex-dependent hepatic androgen action, female and male mice were injected degarelix to suppress gonadal hormones, treated for 2 weeks with vehicle, testosterone, or dihydrotestosterone, a non-aromatizable androgen to distinguish androgenic from estrogenic effects, while being fed with western diet. Biochemical, histological, and molecular readouts were used to quantify hepatic steatosis. Ongoing experiments include AR blockade with the AR antagonist enzalutamide. To investigate the molecular determinants, integrative ATAC-seq, transcriptomics, and proteomics will be performed. Functional validation will be conducted via pharmacological or siRNA-mediated perturbation in vivo. Degarelix reduced body weight in males, mainly through loss of lean mass. T reduced body weight in females, primarily via decreased fat mass. T reduced hepatic steatosis in both sexes, whereas DHT had no significant effect. Notably, DHT increased LDL-C in females, while in males both T and DHT elevated total cholesterol levels. The lack of DHT effect on hepatic steatosis suggests a role for estrogen signaling in mediating T-induced hepatic responses. These findings indicate that androgen effects on hepatic metabolism are sex-dependent and may involve crosstalk with estrogen signaling. Ongoing studies will elucidate the molecular basis of AR-driven sexual dimorphism, advancing precision strategies for androgen-related liver metabolic diseases.

Poster 55

Sex Hormones Shape Drug-Induced Liver Cell Phenotypes

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Approximately 90% of drug candidates fail during clinical trials, with ~30% of failures attributed to toxicity. Many drugs show different side effect profiles between sexes: men tend to experience more kidney toxicity, while women are overrepresented for liver damage. In the 1990s, 8 out of 10 drugs were withdrawn due to adverse reactions in women —largely because they had never been tested on women. Still today, little effort is devoted to implementing sex and hormone differences in pre-clinical drug safety testing, which rarely, if ever, consider sex and hormonal status. Here, we investigate how sex hormones modulate liver cell drug responses using high-content imaging combined with advanced image analysis. We profile morphological and subcellular phenotypes induced by drugs known to cause liver toxicity and assess the impact of estrogen pre-treatment. We find that most drugs yield distinct phenotypes at concentrations that are orders of magnitude lower than what is needed to induce toxicity with conventional viability assays. Estrogen pre-treatment modulates these phenotypes at subtoxic concentrations. For tetracycline-antibiotics, the degree of estrogen modulation recapitulates sexual dimorphism known form real-world adverse event profiles. Our results demonstrate that sex hormones can substantially alter cellular drug responses in liver cells and may contribute to sexual dimorphism in drug-induced liver injury. Our approach enables systematic incorporation of sex and hormonal status into preclinical drug safety assessment, providing an opportunity for drug developers to identify sex-specific liabilities before entering clinical trials.

Poster 56

Sex Disparities in Human Lung Cancer Cell Line Availability and Use: A Call for Attention

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Modern medicine has been historically androcentric. While the inclusion of women in clinical trials has improved, integrating sex as a biological variable (SABV) in preclinical animal research remains incomplete. At the cellular level, the situation is even more critical. Despite evidence that every cell has a sex, implications of sex in cellular research remain largely overlooked. In this context, investigating the current state of sex representation in cell line-based research appears necessary. Focusing on lung cancer – a prevalent disease with documented sex differences – we mapped the sex distribution of human lung cancer cell lines of EuropePMC publications. Of 1,490 human lung cancer cell lines identified, 48% were male-derived, 16% female-derived, and 36% of undetermined sex. This disproportion intensified in publications: of 200,131 retrieved articles, 87% cited male cell lines, 12% female, and 1% undetermined sex. Among the 23 most-cited cell lines, 18 were male-derived and only 5 female-derived. A marked male predominance exists in both the availability and use of lung cancer cell lines. These findings suggest that preclinical research may be conducted predominantly on male-derived cells, raising concerns about the generalizability of findings to female biology – a question still scientifically unresolved. This is particularly concerning given documented clinical sex differences in lung cancer, from disease presentation to treatment response. Clarifying the implications of SABV in lung cancer cellular research stands as a scientific priority to ensure rigor and translational relevance.

Poster 57

Sex differences in a mouse model of chronic kidney disease

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Chronic kidney disease (CKD) exhibits marked sex differences, with higher prevalence in women but faster progression in men. The underlying mechanisms are however unclear, highlighting the need for more sex-inclusive research. Here, we used 5/6th nephrectomy (NX) to model CKD in mice of both sexes, followed by an in-depth phenotypic characterization focused on sex differences. NX was applied to 16-week-old male and female mice to induce CKD. For both sexes, SHAM-operated controls were included. Blood and urine biomarkers, including creatinine and blood urea nitrogen (BUN), were analyzed at baseline, three weeks post-surgery (intermediate timepoint) and six weeks post-surgery (end point), along with water/food intake and urine production. At endpoint, kidneys were harvested. Bone health was evaluated through micro-computed tomography and three-point bending tests, as CKD is associated with disturbances in mineral metabolism leading to increased fracture risk. Polyuria and polydipsia were observed in NX groups of both sexes, with females affected earlier and more severely. Over time, increased BUN and serum creatinine levels confirmed decreased kidney function after NX in a sex-dependent way (females>males). At endpoint, bone porosity was increased by NX along with a reduction in bone strength in females but not in males. Histological evaluation of the kidneys to assess disease severity is ongoing. Altogether, these preliminary results suggest that both kidney and extra-renal effects of NX induction differ between sexes and underscore the importance of advancing our understanding of sexual dimorphism in CKD progression and manifestations.

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Baseline fetuin-A shapes sex-dependent responses in acute kidney injury

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Fetuin-A is a circulating mineral chaperone that buffers calcium-phosphate debris released during tissue injury. Because female mice have higher endogenous fetuin-A than males, we asked whether baseline fetuin-A shapes responses to ischemia-reperfusion injury (IRI) as a model for acute kidney injury. Unilateral renal IRI was induced in young adult male and female mice by clamping the left renal pedicle for 20 min at 37°C. Human plasma-derived fetuin-A or PBS was administered either prophylactically (before IRI) or therapeutically (after surgery). Blood, urine, and kidneys were collected 24 h later to assess fetuin-A levels, injury, and inflammatory markers. Baseline circulating fetuin-A fell within minutes after surgery in both sexes. Males showed greater injury and inflammatory activation after IRI, whereas females were partially protected. Prophylactic fetuin-A supplementation increased renal fetuin-A availability and reduced early injury and inflammation in both sexes, although the magnitude of benefit differed by sex. In contrast, post-IRI supplementation had little effect on tubular injury markers but significantly reduced inflammatory mediators, with stronger effects in males. Endogenous fetuin-A is a sex-dependent modifier of renal IRI and treatment response. Higher baseline fetuin-A may contribute to protection in females, whereas lower levels in males are associated with greater injury burden and responsiveness to exogenous fetuin-A. Incorporating sex and baseline fetuin-A status may improve the design of fetuin-A-based treatment strategies for acute kidney injury.

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Cardiometabolic Disease Burden in Women with Spinal Cord Injury: The Role of Menopausal Status

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Women with spinal cord injury (SCI) are at increased risk of cardiometabolic disorders, but differences by menopausal status remain poorly characterized. This study describes the cardiometabolic disease burden and preventive use of cardiometabolic medication in women undergoing first inpatient rehabilitation after SCI and examines differences by menopausal status. Women with SCI and no history of cardiovascular disease admitted for first inpatient rehabilitation were classified as pre- or postmenopausal. Comorbidities, injury characteristics, other clinical variables, and preventive use of cardiometabolic medications were assessed. Changes in medication use during rehabilitation and associated factors were analyzed using mixed-effects logistic regression. Among 181 women (mean age 53.35 ± 19.78 years; 60% postmenopausal), postmenopausal women had a higher prevalence of hypertension and of diabetes at admission to rehabilitation. There were no significant differences in preventive cardiometabolic medication use at baseline by menopausal status, yet, during rehabilitation, the odds of receiving beta-blockers, cardiac drugs, and RAAS inhibitors were significantly higher in postmenopausal women. Injury characteristics, prevalent diabetes and hypertension were also associated with medication use during rehabilitation. Postmenopausal women with SCI present with a higher cardiometabolic risk burden at rehabilitation admission but do not differ in baseline preventive treatment, suggesting potential gaps in early risk recognition. The observed increased use of beta-blockers, cardiac drugs, and RAAS inhibitors during rehabilitation in postmenopausal women indicates evolving clinical management over time. These findings highlight the importance of integrating menopausal status into early cardiometabolic risk stratification and optimizing preventive treatment initiation in women with SCI.

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Male mice rupture patellar tendon struts more often than females with failure possibly attenuated by running

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Tendon injury and recovery rates differ between males and females, yet rehabilitation strategies do not account for sex. The biological and behavioral factors underlying these differences remain poorly defined. C57BL/6 mice (16-22 weeks) underwent central-third patellar tendon resection with the contralateral leg serving as intra-animal sham control. Tendons were harvested for bulk RNA sequencing (day 3) and mechanical analysis (day 14), and hindlimbs were imaged under micro-CT (day 14). A subset of mice was placed into cages with voluntary running wheels following surgery and activity levels were monitored for two weeks. Proper healing was defined by visually intact tendon struts, while improper (ruptured) healing was marked by large, tough, inflexible tissue masses. Males exhibited markedly higher rupture rates two weeks post-surgery (20/25) compared to females (3/58). Transcriptomic analysis revealed a pro-vascularization, pro-innervation signature in males, whereas females demonstrated an inflammatory wound healing signature. Males had greater quadriceps cross-sectional area and femur length, but similar knee moment arms relative to females. Males ran greater distances at early timepoints post-surgery, and housing with voluntary running wheels modestly reduced male rupture rates (20/25 to 3/7). Sex differences in tendon healing are substantial, with males exhibiting higher rupture rates, distinct transcriptomic signatures, and differential activity patterns post-surgery. These findings highlight the importance of incorporating sex as a biological variable in tendon injury studies and indicate the potential need for sex-based rehabilitation protocols to improve healing outcomes.

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Sex as a variable in mitochondrial diseases

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Mitochondria regulate immune responses, but it remains unclear how mild mitochondrial dysfunction affects host defence and whether these effects differ by sex. We investigated sex-dependent immune phenotypes in a preclinical model of mild mitochondrial dysfunction. Investigation into their immune responses from both sexes will explain not only how mitochondria are contributing to the immune system beyond energy supply, but also how sex play the role as a variable in mitochondrial diseases. Male and female mutant and control mice underwent baseline phenotyping, viral challenge, vaccination and re-challenge. Clinical status, body weight and humoral responses were assessed longitudinally. Baseline immune composition was broadly similar across genotypes, although mutant mice were lighter than controls. Following infection, female mutant mice maintained better health and showed comparable viral control compared to female controls, whereas genotype-related differences were smaller in males. After vaccination and re-challenge, protective responses were preserved across sexes and genotypes. Antibody titres were generally comparable between genotypes, with higher titres in females than in males. Mild mitochondrial dysfunction was associated with sex-dependent differences in infection responses without loss of vaccine responsiveness. These findings support explicit consideration of sex as a biological variable in studies of mitochondrial disease and immune function.

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Changes in saliva due to social stress in pigs: the influence of sex

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Social mixing is a relevant welfare challenge in pigs as regrouping cause aggressive interactions and can induce acute physiological responses involving stress, inflammation, oxidative stress and tissue damage. Although sex hormones are not classical stress biomarkers, estradiol and testosterone can modulate stress-related pathways, including hypothalamic-pituitary-adrenal axis activity. This preliminary study explored whether sex hormones are associated with different salivary biomarker correlation patterns depending on sex and the social context. Pigs in the final transition period were allocated to control groups, composed of familiar animals, or mixing groups, composed of unfamiliar animals. Within each condition (control and mixed), animals were grouped as males (n=9), females (n=7) or mixed-sex groups with males and females (n=9, 5 females and 4 males). Saliva samples were collected before and 3 hours, 1, 3 and 7 days after the mixing. Correlation heatmaps were generated between estrogen or testosterone and a profile of salivary biomarkers that evaluated stress, inflammation, oxidative status, tissue damage and neuroendocrine response. Females showed the most pronounced changes at 3 h post-mixing. At this time in control females, estrogen concentrations were negatively correlated with most salivary biomarkers, whereas in mixed females the correlations were predominantly positive. Testosterone showed a different pattern, with the most evident positive associations appearing later, mainly at days 1, 3 and 7, and especially in mixed males and mixed-sex groups. These preliminary results suggest that social mixing induces a dynamic reorganization of sex hormone–salivary biomarker correlation patterns in pigs. The findings support considering sex as a biological variable not only in biomarker concentrations, but also in the interpretation of biomarker associations during social stress.

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Structural vascular alterations in intra-uterine growth restricted piglets: cross-sectional area of umbilical cord, aorta and pulmonary artery

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Intrauterine growth restriction (IUGR) is associated with increased perinatal mortality and long-term cardiovascular risk, potentially involving sex-specific vascular adaptations. This study investigates sex differences in fetal vascular development in IUGR and normal birth weight (NBW) piglets. Umbilical cords (NBW: ♂=146; ♀=134; IUGR: ♂=146; ♀=134) were collected immediately after birth from a commercial pig farm. A subset of animals was used for aortic and pulmonary artery analysis (NBW ♂=21; ♀=20; IUGR ♂=21; IUGR ♀=20). IUGR was defined as birth weight < mean litter weight −1 SD with IUGR phenotype, while NBW piglets fell within ±1 SD. Paraformaldehyde fixated, paraffin-embedded tissue sections were stained with hematoxylin and eosin. Cross-sectional area (CSA) was determined and normalized to body weight (relative CSA). Linear mixed models assessed effects of IUGR and sex. Complete umbilical cord analysis showed reduced absolute CSA of umbilical vein and artery in IUGR piglets ($p<0.0001$ for both), with no sex differences (vein $p=0.608$; artery $p=0.343$). In contrast, the relative CSA of both vessels was increased in IUGR piglets compared to NBW piglets ($p<0.0001$) , again without any significant sex-related differences (vein $p=0.302$; artery $p=0.420$). Preliminary analyses of aorta and pulmonary artery revealed reduced absolute CSA in IUGR ($p<0.0001$ for both) and increased relative CSA (aorta $p=0.013$; pulmonary artery $p=0.002$). No sex differences were observed (aorta absolute $p=0.310$, relative $p=0.664$; pulmonary artery absolute $p=0.184$, relative $p=0.417$). In conclusion, IUGR is associated with pronounced vascular remodeling across fetal circulations. No sex-specific differences were detected, suggesting limited sexual dimorphism in these structural vascular adaptations within the current dataset.

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Chair of EU-SABV COST Action (CA24168)

Editor

Dr. Ivana Jaric

Design and layout

Milos Jaric

www.sabvsymposium.org

SABV SYMPOSIUM 2026

23-24 June • Zurich, Switzerland

www.sabvsymposium.org