Chronobiology: from the Cell to Medicine and Society

7th Conference of the Canadian Society for Chronobiology
Centre hospitalier de l'Université de Montréal (CHUM)
Montreal, Canada

May 25-27, 2025

CSC 2025

Canadian Society for Chronobiology
Société canadienne de chronobiologie

SCC 2025

Full Scientific Program

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WELCOMING WORDS

Dear Participants,

It is a great honor to welcome you to Montreal for the Conference Chronobiology: from the Cell to Medicine and Society, the 7th Conference of the Canadian Society for Chronobiology (CSC)!

The Program Committee and the Trainee Program Committee are excited about the scientific content of the conference that represents the important diversity of biological rhythm research in Canada and the numerous applications it has notably for health and disease. Hosting the Conference within the *Centre hospitalier de l'Université de Montréal* (CHUM) is a great indication of the recognition of the impact of chronobiology research for human health in particular. These impacts are going to be well highlighted in the two public conferences as well as throughout the scientific program of the Conference, and during the Mrosovsky lecture offered this year by Amita Sehgal from the University of Pennsylvania. Therefore, the members of Program Committees hope that you are equally excited about the content of the program, and about this opportunity to assemble members of the CSC and colleagues from abroad.

The 2025 version of the Conference is of particular importance for training the next generation of scientists and clinical staff at many levels. Indeed, trainees were given major roles in the organization of the Trainee Day content and of the overall program, have been invited to contribute to every aspect of the main scientific program, and were supported with travel awards. We invite you to attend with enthusiasm the Datablitz sessions in particular, during which selected trainees will showcase their research in a vibrant manner. Presentation prizes will also be awarded to trainees, and to help them show their skills, we encourage you to attend the sessions of oral presentations and posters and to interact with them during the time devoted to questions/discussion.

The organization of the Conference has benefited from collaborations between the CSC and other key international societies such as the Society for Research on Biological Rhythms (SRBR), an important financial and communication partner. Other partners have also contributed with an essential support, and these include the *Réseau québécois de recherche sur le sommeil* (Réseau Sommeil) and the Canadian Sleep Research Consortium that will notably ensure a long-term impact of the translational content via video recording and national broadcasting. Please take the time to visit the kiosks of our multiple partners/sponsors during the lunches and breaks since their contribution truly deserves your attention!

Of course, each of you is an important part of the success of the conference and we are warmly thanking every one of you for your presence and the rich scientific discussions to come! We truly wish you a fantastic Conference!

Valérie, on behalf of the Program Committee

Valérie Mongrain, Ph.D.
Chair, Program Committee of the 7th Conference of the CSC

ACKNOWLEDGEMENTS

Program Committee

Valérie Mongrain, Université de Montréal and *Centre de recherche du* CHUM (Chair)
Petronela Ancuta, Université de Montréal and *Centre de recherche du* CHUM (Co-chair)
Diane B. Boivin, McGill University and Douglas Mental Health University Institute (Co-chair)
Éric Paquet, Université Laval
Kazue Semba, Dalhousie University
Ruifeng Cao, Rutgers University (USA)
Roelof Hut, University of Groningen (The Netherlands)

Trainee Program Committee

Tanya Leduc, Université de Montréal and *Centre de recherche du* CHUM (Chair)
Katelyn Horsley, University of Calgary
Jonathan Dias, Université de Montréal and *Centre de recherche du* CHUM
Cassandra Goldfarb, Concordia University

Other people who importantly contributed to the organization

Rebecca Robillard, University of Ottawa
Élodie Kodjo, *Centre de recherche du* CHUM
Mario Legault, *Centre de recherche du* CHUM
Ève Beaulieu, *Centre de recherche du* CHUM
Benoît Delignat-Lavaud, *Centre de recherche du* CHUM
Bruno Geoffroy, *Centre de recherche du* CHUM
Simon Gauthier, CHUM
Stéphanie Valois, Department of Neuroscience, Université de Montréal
Nancy Crête, Department of Neuroscience, Université de Montréal
Isaak Mainguy (DJ for the banquet)

Abstract Evaluation Committee

Roelof Hut, University of Groningen (Chair)
Petronela Ancuta, Université de Montréal and *Centre de recherche du* CHUM
Neus Ballester Roig, Kurume University (Japan)
Nicolas Cermakian, McGill University and Douglas Mental Health University Institute
Nicole Gervais, University of Groningen
Ilia Karatsoreos, University of Massachusetts Amherst
Brianne Kent, Simon Fraser University
Tami Martino, University of Guelph
Ralph Mistlberger, Simon Fraser University
Éric Paquet, Université Laval

Judges of presentations

Judges of oral and poster presentations who have generously agreed to contribute and to allow trainees to benefit from presentation awards (Ruifeng Cao [Chair], Micheal Antle, Sara Bernardez Noya, Alexandre Caron, Hai-Ying Mary Cheng, Robert Dallmann, Benoît Delignat-Lavaud, Phillip Karpowicz, Achim Kramer, Zheng Kuang, Patricia Lakin-Thomas, Giacomo Maddaloni, Annie Vallières, Laura van Rosmalen, Mark Viggars).

Funding and support

This conference was supported by a grant from the Canadian Institutes of Health Research, and funding from the Réseau Sommeil, the CSC, the SRBR, the Canadian Sleep Research Consortium, the Réseau SIDA/MI, the Department of Neuroscience of the Université de Montréal, the Faculty of Medicine of the Université de Montréal, the Canada Research Chair in Sleep Molecular Physiology, the *Centre de recherche du* CHUM (CRCHUM), the Center for Cardiovascular Investigation of the University of Guelph, and the *Faculté de médecine dentaire* of the Université Laval. We are also grateful to the following companies their generous support: Eisai, FourWaves, Génome Québec, Tecniplast, Vector Builder, and Wisent.

Please thank the generous sponsors of this event (by visiting their exhibit table if applicable):

IMPORTANT INFORMATION

For those traveling from and to the USA, please consult your institution for advice prior to traveling notably regarding the protection of your confidential information.

Duration of presentations and guidelines for presenters in symposia and slide sessions

Symposium speakers should prepare a presentation of a maximum of 20 minutes, and speakers of slide sessions a presentation of a maximum of 10 minutes (both of which will be followed by a 5-minute period of questions/discussion). Please strictly respect the allocated time.

Speakers should prepare for their presentation by arriving 20 minutes before the beginning of the session in which the presentation is scheduled to upload the slides on the computer or verify that a personal computer can adequately connect to the AV system. It is highly recommended to have a backup of the slide set (e.g., two USB keys or a personal computer and a USB key).

Datablitz

Datablitz speakers should prepare a presentation of a maximum of 2 minutes and a single slide with no animation. The slide (pdf format) should be sent via email to eve.beaulieu.chum@ssss.gouv.qc.ca before the end of the day on May 19, 2025. Slides will be assembled and shown on the presentation screen as part of the same file. Presenters are asked to arrive 10 minutes before the beginning of datablitz sessions to meet the chair of the session and to find a seat near the presentation podium. All presenters of datablitz sessions are also assigned to poster sessions (on the same day), and should thus also prepare a poster.

Posters

Posters should be of a maximum of 4 feet of height by 4 feet of width in size (122 by 122 cm). Posters P1 to P19 are assigned to Day 2 [May 26] and P20 to P39 to Day 3 [May 27]. Posters should be installed on the assigned poster boards during the morning coffee break or lunches, and should be removed from boards no later than 20h00 (8 PM) on May 26 and no later than 18h15 (6:15 PM) on May 27.

Trainees who would like to be considered for a presentation prize are invited to prepare a presentation of their poster of a maximum of 4 minutes. Judges will be assigned to posters that are presented by trainees and will evaluate the presentations and posters during poster sessions. Trainees are thus invited to stay close to their posters during the poster sessions (see also below).

Meals

All meals will be served in the Foyer of the 1st floor of building A (1050 St-Denis Street, Montreal), except for banquet for registered people taking place at Auberge Saint-Gabriel (426 St-Gabriel Street, Montreal). Lunches are offered to all registered participants. Special requirements will be covered by individually prepared lunch boxes notably comprising vegetarian options. Please pick boxes corresponding to your dietary requirements.

For the opening reception of May 25, drink coupons will be distributed together with name tags at the registration kiosk. These coupons will allow for the distribution of alcohol-free beverages and beverages with alcohol. Please feel comfortable sharing your coupons with others if you are not planning to use them.

Presentation prize

Prizes will be offered to the top-ranked trainees giving an oral presentation or presenting a poster.

Poster presenters (trainees) are asked to stay near their posters for the full poster session they are assigned in order for them to avoid missing the visit of the judges. We are particularly happy to share that the following presentation prizes will notably be offered: Réseau Sommeil Award, Canadian Sleep Research Consortium Award, Award of the Department of Neuroscience of the Université de Montréal, Eisai Award, Wisent Award.

Internet access

The following Wi-Fi network can be used to access internet from the Conference facilities:
CHUM-Public

Social media

If posting something about the 2025 Canadian Chronobiology Conference (CSC 2025) on social media, please use the following hashtag: #CSC2025SCC

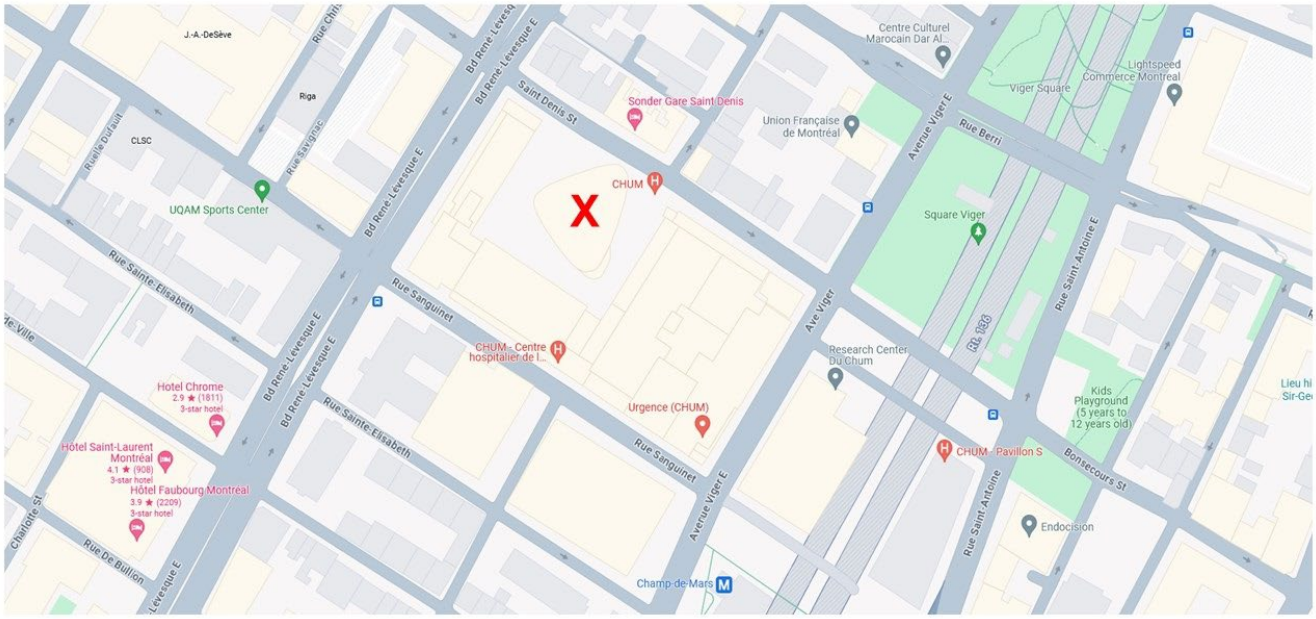
Room for parents with children

Parents with needs for young children are invited to use the room A01.9209B that will be made available at all time from the beginning of the main scientific program on the afternoon of May 25.



MAPS AND FACLITIES

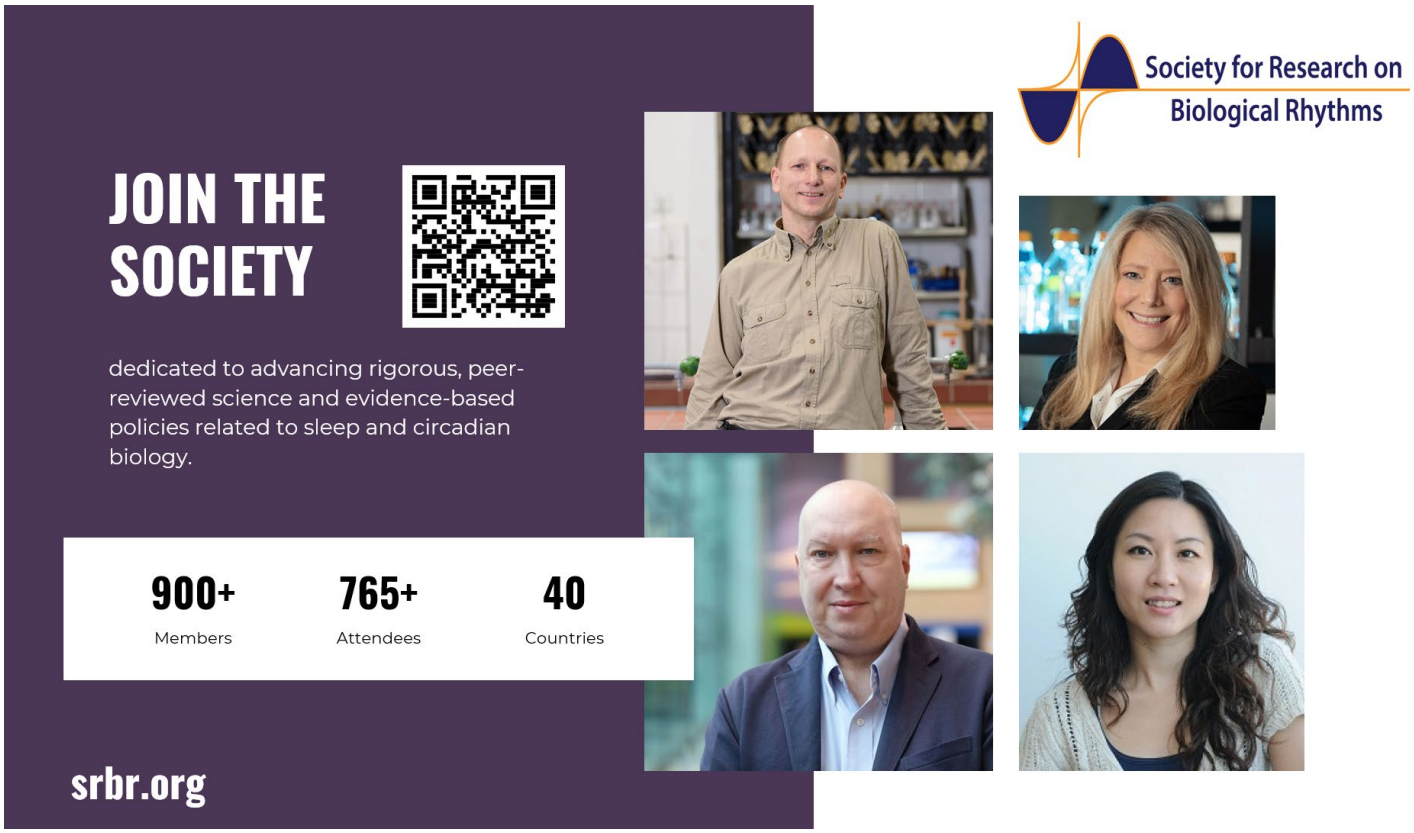
All activities will take place at the CHUM building A located at 1050 St-Denis Street, Montreal (QC). The following maps can help you finding the building. The nearest subway station is Champ-de-Mars.





The main auditorium of the conference is the Amphithéâtre Pierre-Péladeau that can be accessed via the 1st floor (door A01.9220) or the 2nd floor. Please use the 2nd-floor entry when accessing after the beginning of a session. The second main conference room is the room A02.9209AB of the 2nd floor that can be reached via the stairs or the elevators.

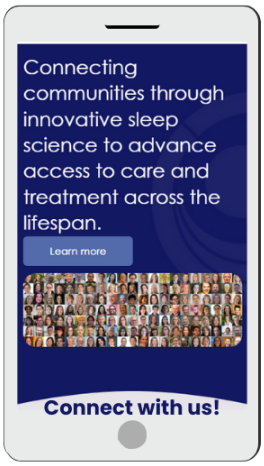
Lunches and coffee breaks will take place in the Foyer of the 1st floor, where the exhibitor tables will be located as well, and poster sessions will take place in the Foyer of the 2nd floor (accessible via the stairs or the elevators). Please feel comfortable asking questions to our devoted administrative and logistic staff who will be happy to guide you (Élodie Kodjo, Mario Legault and Ève Beaulieu).



Canadian Sleep Research Consortium
Consortium canadien de recherche sur le sommeil

The Canadian Sleep Research Consortium is as a national hub of sleep scientists and clinicians advancing research and interventions to optimize sleep health throughout the lifespan.

By fostering new partnerships between academia, government, industry and community-based organizations, we aim to catalyze the translation of sleep sciences and technology into practice and health promotion initiatives for diverse communities.



CIHR IRSC

researchsleep.ca
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Focus Areas

Knowledge Mobilization and Training
Indigenous Peoples Health
Health Disparities and Equity/Diversity/ Inclusion
Technology and Data Management


Insomnia & Mental Health


Sleep Across the Lifespan


Sleep Health Equity



SCHEDULE IN A NUTSHELL

MAY 25, 2025

08:15-09:10	Trainee Day workshops 1 and 2 (Amphithéâtre Pierre-Péladeau and room A02.9209AB)
09:15-10:25	Trainee Day symposium 1 (Amphithéâtre Pierre-Péladeau)
10:25-10:50	Coffee break and networking (room A01.9209AB)
10:50-11:35	Trainee Day workshops 3 and 4 (Amphithéâtre Pierre-Péladeau and room A02.9209AB)
11:40-12:50	Trainee Day symposium 2 (Amphithéâtre Pierre-Péladeau)
12:50-13:50	Trainee Day looping lunch (lunch provided; Foyer of the 1st floor)
13:50-15:30	Trainee Day outdoor active team building (meeting point = Foyer of the 1st floor)
15:00-17:30	Public lectures (first in French and second in English; Amphithéâtre Pierre-Péladeau)
17:40-19:30	Opening word + symposia 1 and 2 (Amphithéâtre Pierre-Péladeau and room A02.9209AB)
19:30-21:00	Opening reception with food (Foyer of the 1st floor)

MAY 26, 2025

08:45-10:30	Symposia 3 and 4 (Amphithéâtre Pierre-Péladeau and room A02.9209AB)
10:30-11:15	Group picture and coffee break (Foyer of the 1st floor)
11:15-12:15	Slide sessions 1 and 2 (Amphithéâtre Pierre-Péladeau and room A02.9209AB)
12:15-13:20	Lunch boxes and visit of sponsors (Foyer of the 1st floor)
13:20-14:30	Walk to the Old Port of Montreal (meeting point = Foyer of the 1st floor)
14:40-15:10	Datablitz 1 (Amphithéâtre Pierre-Péladeau)
15:10-15:55	General meeting of CSC members (Amphithéâtre Pierre-Péladeau)
15:55-17:25	Poster session 1 and visit of sponsors (Foyers of the 1st and 2nd floors)
17:30-19:15	Symposia 5 and 6 (Amphithéâtre Pierre-Péladeau and room A02.9209AB)
19:30	Dinner on your own (not provided)

MAY 27, 2025

09:00-10:45	Symposia 7 and 8 (Amphithéâtre Pierre-Péladeau and room A02.9209AB)
10:45-11:15	Coffee break and visit of sponsors (Foyer of the 1st floor)
11:15-12:45	Slide sessions 3 and 4 (Amphithéâtre Pierre-Péladeau and room A02.9209AB)
12:45-14:00	Lunch boxes and visit of sponsors (Foyer of the 1st floor)
14:15-14:45	Datablitz 2 (Amphithéâtre Pierre-Péladeau)
14:45-16:15	Poster session 2 and visit of sponsors (Foyers of the 1st and 2nd floors)
16:30-17:45	Mrosovsky lecture (Amphithéâtre Pierre-Péladeau)
18:15-22:00	Banquet, awards and closing words (Auberge Saint-Gabriel)

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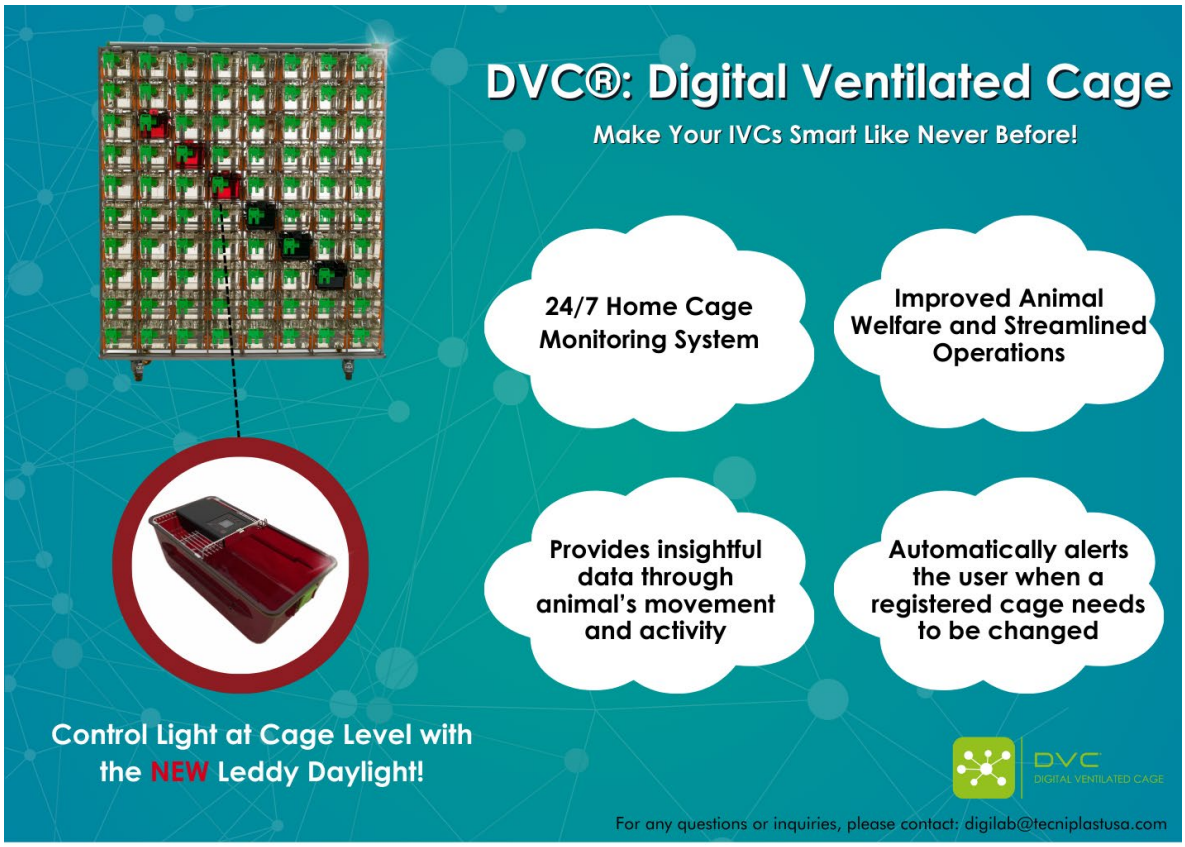

TECNIPLAST

DETAILED SCHEDULE

DAY 1	May 25, 2025
08:15-08:25	*Amphithéâtre Pierre-Péladeau* Trainee Day opening word
08:25-09:10	*Amphithéâtre Pierre-Péladeau* Trainee Day workshop 1: **Giving the perfect scientific talk** Chair Katelyn Horsley, University of Calgary, Canada Speaker **Michael Antle**, University of Calgary, Canada *Room A02.9209AB* Trainee Day workshop 2: **Post-doc search - how and when** Chair Tanya Leduc, Université de Montréal, Canada Speakers **Maria Neus Ballester Roig**, Kurume University, Japan **Tara Delorme**, University of Massachusetts, USA **Sarah Ferraro**, Harvard Medical School, USA
09:15-10:25	*Amphithéâtre Pierre-Péladeau* Trainee Day symposium 1: **Translational and applied chronobiology** Chair Zainab Taleb, University of Windsor, Canada Speakers **Éric Paquet**, Université Laval, Canada ''Pan-cancer analysis of circadian and cell cycle interactions at the subtype level using RhythMate'' **Vanya Khanna**, University of Guelph, Canada ''Circadian-regulated autophagy and BECLIN-1: a sex-specific protective mechanism in heart attack-induced ischemia-reperfusion injury'' **Christophe Moderie**, McGill University and Stanford University ''Preliminary evidence of altered 24-hour cortisol secretion in premenstrual dysphoric disorder'' **Amanda Szubinski**, Concordia University, Canada ''Chronobiology of metabolic dysfunction: the interplay of androgen receptors with circadian rhythms in the novel AR19-Q mouse model''
10:25-10:50	*Room A01.9209AB* Coffee break and networking
10:50-11:35	*Amphithéâtre Pierre-Péladeau* Trainee Day workshop 3: **Secrets of the publication process** Chair Maria Neus Ballester Roig, Kurume University, Japan Speakers **Charles Bourque**, McGill University, Canada **Nicolas Cermakian**, McGill University, Canada

10:50-11:35	*Room A02.9209AB* Trainee Day workshop 4: **A variety of career avenues** Chair Mahgol Darvishmolla, Concordia University, Canada Speakers **Erika Bélanger-Nelson**, Pfizer Canada **Jean-François Schmouth**, CRCHUM, Canada **Marc-André Raymond**, CSL Vifor, Canada
11:40-12:50	*Amphithéâtre Pierre-Péladeau* Trainee Day symposium 2: **Mathematical and modeling approaches to the analysis of circadian data** Chair Benoît Delignat-Lavaud, CRCHUM, Canada Speakers **Paul Franken**, University of Lausanne, Switzerland ''Not all that is rhythmic is circadian: modelling the contribution of sleep-wake state to the daily changes in gene expression'' **Turner Silverthorne**, University of Toronto, Canada ''Less is more: insights from simple mathematical models of the circadian clock'' **Jamison Burchett**, University of Rochester, USA ''MYC and epithelial to mesenchymal transition independently predict circadian disruption in lung adenocarcinoma'' **Adam Stinchcombe**, University of Toronto, Canada ''A mathematical model for the role of dopamine-D2 self-regulation in the production of ultradian rhythms''
12:50-13:50	*Foyer of the 1st floor* Trainee Day looping lunch (lunch provided)
13:50-15:30	*Foyer of the 1st floor = meeting point* Trainee Day outdoor active team building This activity concludes the Trainee Day program.
	Amphithéâtre Pierre-Péladeau Public lectures sponsored by the RÉSEAU SOMMEIL and the CANADIAN SLEEP RESEARCH CONSORTIUM Réseau sommeil — Canadian Sleep Research Consortium / Consortium canadien de recherche sur le sommeil
15:00-16:10	**Public lecture-French: Annie Vallières**, Université Laval, Canada **Diane B. Boivin**, McGill University, Canada ''Mieux vivre avec des horaires atypiques''
16:20-17:30	**Public lecture-English: Roelof Hut**, University of Groningen, The Netherlands ''Why daylight saving time should be abolished''

17:40-17:45	*Amphithéâtre Pierre-Péladeau* Opening word by **Mrs. Carole Jabet** Scientific director, FRQ Health sector
17:45-19:30	*Amphithéâtre Pierre-Péladeau* Symposium 1: **Brain rhythms and clocks shaping mental health** Chairs Ruifeng Cao, Rutgers University, USA Allison Brager, US Army, USA Speakers **Ciaran Murphy-Royal**, Université de Montréal, Canada ''Astrocytes drive the effects of stress on diurnal activity'' **Rebecca Robillard**, University of Ottawa, Canada ''Rhythms and mental health: from internal desynchrony to community behaviors'' **Micheal Antle**, University of Calgary, Canada ''Waking up your rhythm: an arousal input to the circadian clock'' **Colleen A. McClung**, University of Pittsburgh, USA ''Molecular rhythm disruptions in major psychiatric disorders and how they contribute to disease'' *Room A02.9209AB* Symposium 2: **Individual differences in biological rhythms** Chairs Kazue Semba, Dalhousie University, Canada Julie Carrier, Université de Montréal, Canada Speakers **Nicole Gervais**, University of Groningen, The Netherlands ''Translational and sex-based perspectives on sleep regulation of memory in healthy and pathological aging'' **Le Zhou**, McGill University, Canada ''On night owls and early birds: insights from a multimodal population study'' **Jessica Mong**, University of Maryland, USA ''Sex differences in sleep: impact of biological sex and sex steroids'' **Christophe Moderie**, McGill University, Canada *******Travel Award granted ''From clocks to care: integrating circadian considerations in women's health''
19:30-21:00	*Foyer of the 1st floor* Opening reception (with food and drinks)

DAY 2	May 26, 2025
08:45-10:30	*Amphithéâtre Pierre-Péladeau* Symposium 3: **Shiftwork and body health** Chairs Diane B. Boivin, McGill University, Canada Keith C. Summa, Northwestern University, USA Speakers **Annie Vallières**, Université Laval, Canada ''Combining behavioral and circadian approaches to improve sleep and mental health in shift workers'' **Kenneth Wright Jr.**, University of Colorado Boulder, USA ''Clinical practice recommendations for the treatment of shift work disorder'' **Garth Swanson**, Rush University, USA ''It's about time: circadian misalignment in ulcerative colitis'' **Ilia Karatsoreos**, University of Massachusetts Amherst, USA ''Understanding the brain-body consequences of disrupted biological timing'' *Room A02.9209AB* Symposium 4: **Rhythms of the immune system going right or wrong** (sponsored by the RÉSEAU SIDA/MI) Chairs Petronela Ancuta, Université de Montréal, Canada Martin Olivier, McGill University, Canada Speakers **Sara Bernardez Noya**, University of Pennsylvania, USA ***SRBR Travel Award granted ''Bridging metabolic and sleep aspects of sickness'' **Zheng Kuang**, Carnegie Mellon University, USA ''Surveilling the gut: a diurnal rhythm in the sentinel tuft cells'' **Nicolas Cermakian**, McGill University, Canada ''Circadian clocks in immune cells and in parasites'' **Laura A. Solt**, The Scripps Research Institute, USA ''Regulation of TH17-mediated inflammation by circadian clock proteins''
10:30-11:15	*Foyer of the 1st floor* Group picture and coffee break
11:15-12:15	*Amphithéâtre Pierre-Péladeau* Slide session 1: **Physiological functions** (see full abstracts after the detailed schedule) Chair Nicole Gervais, University of Groningen, The Netherlands Speaker O1 **Gregory Pearson**, University of Massachusetts Amherst, USA ''Diurnal rhythms of neuroimmune processes prime the olfactory bulb's response to an intranasal challenge'' Speaker O2 **Allison Yang**, University of Calgary, Canada ***Travel Award granted ''Examining the relationship between mild circadian disruption and spatial navigation using mouse models''

	Speaker O3 **Sarah Ferraro**, Harvard Medical School, USA *******Travel Award granted ''Prion-like properties of CLOCK mediate circadian resilience'' Speaker O4 **Lewis Depaauw-Holt**, Université de Montréal, Canada ''Astrocytes drive sexually dimorphic effects of stress on orexin neurons and running wheel behaviour''
11:15-12:15	*Room A02.9209AB* Slide session 2: **Pathologies and methods** (see full abstracts after the detailed schedule) Chair Aarti Jagannath, University of Oxford, UK Speaker O5 **Tanya Leduc**, Université de Montréal, Canada ''Overexpression and rescue of Nlgn2 splice isoforms in mice: effects on behavior and vigilance states'' Speaker O6 **Danae Penichet**, McGill University, Canada ''Non-additive effects of prenatal infections and circadian disruption on behaviour and hippocampal cell-type specific gene expression'' Speaker O7 **Ben Rogers**, McGill University, Canada ''Clocking in on ataxia: Per2 dysregulation in the cerebellum of spinocerebellar ataxia type 6 (SCA6) mice'' Speaker O8 **Turner Silverthorne**, University of Toronto, Canada *******Travel Award granted ''How to find optimal measurement schedules for biological rhythm discovery using PowerCHORD''
12:15-13:20	*Foyer of the 1st floor* Lunch (lunch boxes provided) and visit of sponsors
13:20-14:30	*Foyer of the 1st floor = meeting point* Healthy discovery walk to Montreal Old Port
14:40-15:10	*Amphithéâtre Pierre-Péladeau* Datablitz 1: **Pathologies** (see full abstracts after the detailed schedule) Chair Roelof Hut, University of Groningen, The Netherlands Speaker P1 **Niruththaan Rameshkumar**, University of Guelph, Canada *******CCVI Distinguished Talk ''Loss of REV-ERBα enhances reperfusion recovery following myocardial ischemia and reperfusion'' Speaker P2 **Amirhossein Jahani**, Université de Montréal, Canada ''Impaired nocturnal slow-wave activity decay precedes epileptic seizures'' Speaker P3 **Tara Delorme**, University of Massachusetts, USA *******Travel Award granted ''Assessing day-night disparities in neuronal DNA damage responses among those with opioid use disorder''

	Speaker P4 **Vanya Khanna**, University of Guelph, Canada ***CCVI Distinguished Talk ''Circadian-regulated autophagy and BECLIN-1: a sex-specific protective mechanism in heart attack-induced ischemia-reperfusion injury'' Speaker P5 **Mallory Metcalfe**, University of Guelph, Canada ***CCVI Distinguished Talk ''Circadian mechanisms and sex-specific regulation in heart attack recovery: CLOCK's role in myocardial ischemia-reperfusion injury'' Speaker P6 **Jamison Burchett**, University of Rochester, USA ''MYC and epithelial to mesenchymal transition independently predict circadian disruption in lung adenocarcinoma'' Speaker P7 **Amanda Szubinski**, Concordia University, Canada ''Chronobiology of metabolic dysfunction: the interplay of androgen receptors with circadian rhythms in the novel AR19-Q mouse model'' Speaker P8 **Bridget Ward**, McGill University, Canada ''Emergence of infradian rhythms and their relevance for cyclicity in bipolar disorder'' Speaker P9 **Stephanie U**, Simon Fraser University, Canada ***Travel Award granted ''A protocol for studying the role of circadian rhythms in the resilience to dementia'' Speaker P10 **Chloé Léveillé**, University of Ottawa, Canada ''Investigating circadian patterns and seasonal variations in disruptive behaviours in mental health care''
15:10-15:55	*Amphithéâtre Pierre-Péladeau* General meeting of CSC members (attendance of CSC members needed)
15:55-17:25	*Foyer of the 2nd floor* Poster session 1 (with small bites) and visit of sponsors (see full abstracts after the detailed schedule) P1 to P10 – **see Datablitz 1 for presenters and titles** P11 **Nicolas Lemmetti**, Université de Montréal, Canada ''The absence of Neuroligin-2 differentially modulates wake/sleep architecture, spectral and multifractal activities in male and female mice'' P12 **Jenna Geary**, University of Calgary, Canada ''Chronic circadian disruption alters cardiac function and glucose regulation in mice'' P13 **Sarra Beji**, Université Laval, Canada ''Effect of a cranberry proanthocyanidin-rich extract on metabolic health and circadian rhythm'' P14 **Huirong Luo**, McGill University, Canada ''Coping with sleep disturbances and fatigue: the influence of gender, age and shift types among healthcare workers during the COVID-19'' P15 **Rachna Patel**, University of Windsor, Canada ''Time-restricted feeding effects on colorectal tumorigenesis in the Apcmin model''

	P16 **Anzala Murtaz**, McGill University, Canada ''Mild traumatic injury in the late night causes a circadian shift'' P17 **Isaac Alejandro Vidal Paredes**, Université de Montréal, Canada ''Inhibition of mitochondrial fragmentation in endothelial cells promotes blood-retinal barrier integrity and neuroprotection in experimental glaucoma'' P18 **Heberto Quintero**, Centre de recherche du CHUM, Canada ''Metabolomic profiling unveils retinal energetic stress in early glaucoma'' P19 **Petronela Ancuta**, Université de Montréal, Canada ''The circadian clock transcriptional repressor REV-ERBα/ß as a new pharmacologic target in HIV-1 cure interventions''
17:30-19:15	*Amphithéâtre Pierre-Péladeau* Symposium 5: **Precision medicine, chronotherapy and new technologies to infer individual rhythms** Chairs Éric Paquet, Université Laval, Canada Andrée-Ann Baril, Université de Montréal, Canada Speakers **Arielle Elkrief**, Université de Montréal, Canada ''The gut miocrobiome as a modulator of the response to cancer immunotherapy'' **Robert Dallmann**, Warwick Medical School, UK ''Using TimeTeller to estimate circadian clock phase and function in cells, tumours and people'' **Achim Kramer**, Charité Universitätsmedizin Berlin, Germany ''Circadian phase: from molecules to men'' **John Hogenesch**, Cincinnati Children's, USA ''Building circadian medicine'' *Room A02.9209AB* Symposium 6: **Peripheral oscillators regulating physiological functions** Chairs Tami Martino, University of Guelph, Canada Charles Bourque, McGill University, Canada Speakers **Mark Viggars**, University of Florida, USA *******Travel Award granted ''Endurance exercise initiates de novo circadian gene programs in skeletal muscle across the lifespan'' **Phillip Karpowicz**, University of Windsor, Canada ''Circadian rhythms regulate regeneration in the colon'' **Laura van Rosmalen**, Salk Institute, USA *******Travel Award granted ''Energy balance drives diurnal and nocturnal brain and peripheral rhythms'' **Stéphane Dissel**, University of Missouri - Kansas City, USA ''Sleep regulation, beyond the brain''
	Dinner (not provided)

DAY 3	May 27, 2025
9:00-10:45	*Amphithéâtre Pierre-Péladeau* Symposium 7: **Updates on the circadian regulation of sleep** (sponsored by the RÉSEAU SOMMEIL) Chairs Nadia Gosselin, Université de Montréal, Canada Adrien Peyrache, McGill University, Canada Speakers **Christina Schmidt**, Université de Liège, Belgium ''Association between circadian sleep regulation and the aging brain'' **Ralph Mistlberger**, Simon Fraser University, Canada ''Sleep and circadian regulation: nonphotic factors'' **Aarti Jagannath**, University of Oxford, UK ''A multiomic approach to identifying the substrates of sleep and circadian regulation'' **Paul Franken**, University of Lausanne, Switzerland ''Circadian homeostasis and sleep-wake driven clocks'' *Room A02.9209AB* Symposium 8: **Mechanisms underlying biological oscillations** Chairs Florian Storch, McGill University, Canada Joel Levine, University of Toronto Mississauga, Canada Speakers **Giacomo Maddaloni**, Harvard Medical School, USA *******SRBR Travel Award granted ''Adaptation to photoperiod via dynamic serotonin- glutamate neurotransmitter segregation'' **Patricia Lakin-Thomas**, York University, Canada ''Is the TOR (Target of Rapamycin) pathway an oscillator in *Neurospora*?'' **Hai-Ying Mary Cheng**, University of Toronto, Canada ''The many roads that lead to SCN clock entrainment'' **David Morse**, Université de Montréal, Canada ''Translating clock output into daily rhythms''
10:45-11:15	*Foyer of the 1st floor* Coffee break, networking and visit of sponsors
11:15-12:45	*Amphithéâtre Pierre-Péladeau* Slide session 3: **Physiological functions, pathologies and health care** (see full abstracts after the detailed schedule) Chairs Isaac Alejandro Vidal Paredes, Université de Montréal, Canada Speaker O9 **Maeve Scotland**, University of Calgary, Canada *******Travel Award granted ''Identifying arousal inputs to the intergeniculate leaflet in hamsters'' Speaker O10 **Brennan Baca**, University of Massachusetts Amherst, USA ''Endocannabinoids: a link between circadian disruption and metabolic dysfunction''

	Speaker O11 **Huirong Luo**, McGill University, Canada ''Impact of gender and work schedules on sleep and fatigue of frontline healthcare workers during COVID-19'' Speaker O12 **Zainab Taleb**, University of Windsor, Canada ***Travel Award granted ''Colons lost in time: delayed regeneration in mice lacking an epithelial clock'' Speaker O13 **Petronela Ancuta**, Université de Montréal, Canada ''Daily variations in integrated HIV-DNA load, residual viral transcription and genome-wide transcriptional profiles in CD4+ T-cells of people with HIV-1 receiving antiretroviral therapy'' Speaker O14 **Noah Fryou**, University of Pennsylvania, USA ''Torpor, inflammation, recovery sleep & alpha2-adrenergic agonist hypnosis''
11:15-12:45	*Room A02.9209AB* Slide session 4: **Core mechanisms of rhythmicity and pathologies** (see full abstracts after the detailed schedule) Chair Tanya Leduc, Université de Montréal, Canada Speaker O15 **Nicole Gilette**, Harvard Medical School, USA ***Travel Award granted ''Structural and functional insights on the interactions of the clock protein BMAL1 with CaMKIIα and its role in regulating circadian synaptic function'' Speaker O16 **Sebastián Boy Waxman**, McGill University, Canada ''Looking for temperature-driven and circadian rhythms in parasite Leishmania major'' Speaker O17 **Adriano Vettese**, York University, Canada ''Investigating connections between target of rapamycin (TOR) activity and circadian rhythmicity in the fungus *Neurospora crassa*'' Speaker O18 **Maria Neus Ballester Roig**, Kurume University, Japan ***SRBR Travel Award granted ''The frequency and power of sleep slow wave activity is shaped by potassium channels'' Society for Research on Biological Rhythms Speaker O19 **Adam Stinchcombe**, University of Toronto, Canada ''A mathematical model for the role of dopamine-D2 self-regulation in the production of ultradian rhythms'' Speaker O20 **Brian Altman**, University of Rochester, USA ''BMAL1 and circadian rhythms support robust innate immune signaling in lung cancer''
12:45-14:00	*Foyer of the 1st floor* Lunch (lunch boxes provided) and visit of sponsors
14:15-14:45	*Amphithéâtre Pierre-Péladeau* Datablitz 2: **Physiological functions, core mechanisms of rhythmicity, ecology and environment** (see full abstracts after the detailed schedule) Chair Cassandra C-Areal, Université de Sherbrooke, Canada

	Speaker P20 **Scanny Chancelle Nzie**, Université de Montréal, Canada ''Wake/sleep architecture and electrocorticographic activity following the inactivation of cofilin in male and female mice'' Speaker P21 **Christiane Meyer**, Concordia University, Canada ***CCVI Distinguished Poster ''Behavioral and physiological effects of cardiomyocytes-specific *Bmal1* knockout in male mice'' Speaker P22 **Christophe Moderie**, McGill University, Stanford University ''Preliminary evidence of altered 24-hour cortisol secretion in premenstrual dysphoric disorder'' Speaker P23 **Mahgol Darvishmolla**, Concordia University, Canada ''Sex-specific effect of Bmal1 deletion in the dorsomedial striatum on alcohol consumption in mice'' Speaker P24 **Amelia Mesich**, University of Toronto, Canada ''The genetics of temporal activity patterns in cichlid fish'' Speaker P25 **Jinhui Hu**, McGill University, Canada ***Travel Award granted ''Selective dopamine transporter knock out in the adult ventral tegmental area leads to circadian period lengthening and emergence of infradian locomotor components'' Speaker P26 **Alice Ayres**, Simon Fraser University, Canada ***Travel Award granted ''Going wild: circadian rhythms of lab rats living in social groups outdoors'' Speaker P27 **Leanne van der Merwe**, McGill University, Canada ''Impact of osteocyte-specific Bmal1 deletion on bone mass, microstructure, and strength'' Speaker P28 **Sepehr Abdolahi**, Université Laval, Canada ''Investigating transcriptional dynamics of circadian and cell cycle interactions via dual synchronization and RNA velocity'' Speaker P29 **Ayasha Abdalla-Wyse**, University of Toronto, Canada ''Decoding the evolution and genetics of sleep architecture across cichlid fish''
14:45-16:15	*Foyer of the 2nd floor* Poster session 2 (with coffee) and visit of sponsors (see full abstracts after the detailed schedule) P20 to P29 – **see Datablitz 2 for presenters and titles** P30 **Mary Hudson**, Simon Fraser University, Canada ''Complex interactions between food and light-entrainable activity rhythms revealed by LD cycle shifts'' P31 **Andree Stevens**, Concordia University, Canada ''Circadian regulation of core body temperature in an androgen receptor mutant mouse model of metabolic syndrome'' P32 **Rojin Jalal Jalali**, York University, Canada ''The role of the TOR pathway in circadian rhythmicity in *Neurospora crassa*''

	P33 **Katelyn Horsley**, University of Calgary, Canada ''Chemogenetic activation of orexin cells induces non-photic-like phase shifts in mice'' P34 **Ann Zhang**, University of Toronto, Canada ''Temporal patterns in social interaction as a motivated behaviour'' P35 **Amanda Zacharias**, Queen's University, Canada ''Site- and cell-type-specific miRNA and mRNA genes and networks across the CNS'' P36 **Julia Maja**, University of Toronto, Canada ''Decoding the genomics of circadian and circannual rhythms in teleost fishes'' P37 **Mark Viggars**, University of Florida, USA ''Exercise modifies systemic core clock expression and promotes de-novo transcriptional programmes'' P38 **Benoit Delignat-Lavaud**, CRCHUM, Canada ''The role of the cell adhesion protein NLGN1 in modulating the responses of the circadian clock to light'' P39 **Minjeong Shin**, University of Alberta, Canada ''PKA instructs Drosophila Clock protein in regulating circadian transcription, mediating transcriptional synchrony in the circadian neuronal network''
16:30-17:45	*Amphithéâtre Pierre-Péladeau* **Mrosovsky lecture: Amita Sehgal**, University of Pennsylvania, USA (sponsored by the RÉSEAU SOMMEIL) ''Regulating brain lipid metabolism by time-of-day influences''
18:15-22:00	*Auberge Saint-Gabriel* 426 St-Gabriel St., Montreal, QC, H2Y 2Z9 (900 m walk from the CHUM; aubergesaint-gabriel.com/en/about-us/) **Banquet, awards and closing words**

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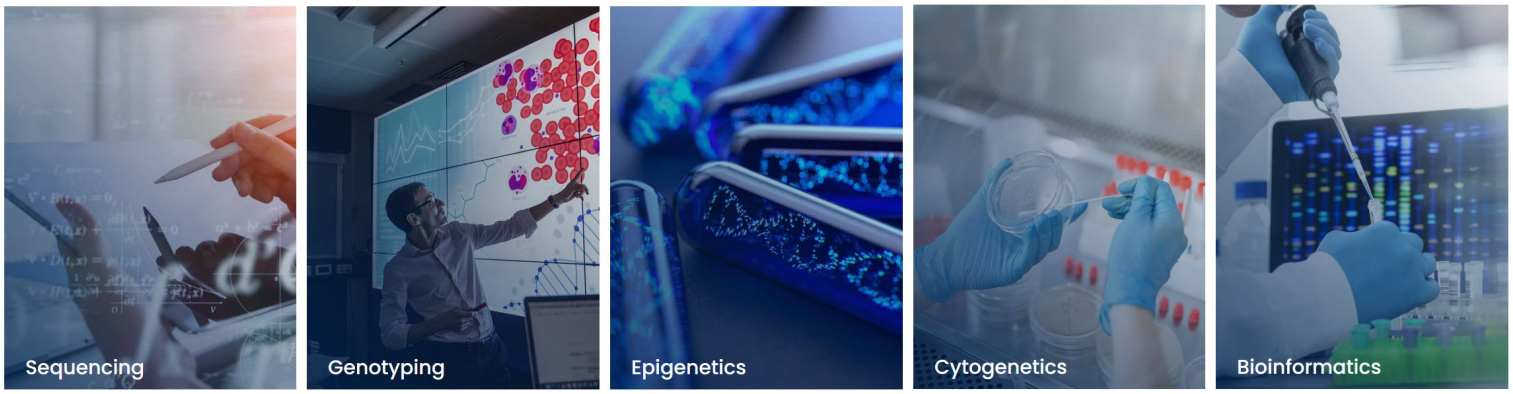

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ABSTRACTS of oral presentations and posters

Oral presentations: pages 25 to 44

Posters (including Datablitz): pages 45 to 83

O1

Diurnal rhythms of neuroimmune processes prime the olfactory bulb's response to an intranasal challenge

Gregory L. Pearson, Brennan Baca, Jiexin Wang, Patricia Reis, Stephanie Gottwals, Nathan Santos, Giancarlo Denaroso, Saïd Akli, Ilia Karatsoreos

- Department of Psychological and Brain Sciences, University of Massachusetts Amherst, USA

The interaction of circadian and immune processes in brain homeostasis is an important new area of research. To investigate the heterogeneity of daily neuroimmune transcriptional rhythms across brain regions, we collected mouse olfactory bulbs and somatosensory cortices over 8 times of day and extracted RNA. Using Nanostring and DiffCircaPipeline, we detected 55 rhythmic transcripts shared between brain regions, 49 distinct to the somatosensory cortex, and 106 distinct to the olfactory bulb. These data suggested that while daily changes in neuroimmune processes are likely important throughout the brain, time of day may play a larger role in the olfactory bulb. Using Metascape, we found that rhythmic olfactory bulb transcripts that peaked around dusk were associated with immune processes. This suggests the olfactory bulb is primed to mount greater neuroimmune responses at some times of day than others. To test this, we intranasally challenged mice with poly(I:C) (a virus-like immune stimulus) or vehicle at ZT0 (dawn) or ZT12 (dusk), collected olfactory bulbs at 0-, 3-, 12-, and 24-hours post-inoculation, and found that time of inoculation produced distinct olfactory bulb transcriptional responses. This indicates the olfactory bulb is primed to differentially respond to an intranasal challenge in a time-of-day-dependent manner. To test if microglia also show differential responses, we intranasally challenged mice with poly(I:C) or vehicle at ZT0 or ZT12, isolated olfactory bulb microglia 24-hours post-inoculation, and used imaging flow cytometry. We detected two distinct microglia populations defined by the presence of intrinsically fluorescent puncta. This distinction was functionally relevant, as intranasal poly(I:C) at ZT12 produced a greater change in the proportion of these populations than at ZT0. We conclude that neuroimmune rhythms prime the olfactory bulb to differentially respond to intranasal poly(I:C) in a time-of-day-dependent manner, and that microglia may contribute to these responses.

O2

Examining the relationship between mild circadian disruption and spatial navigation using mouse models

Allison Yang, Jenna Gearey, Katelyn Horsely, Melinda Wang, Michael C. Antle

- Department of Psychology, University of Calgary, Canada
- Hotchkiss Brain Institute, University of Calgary, Canada

Circadian disruption contributes to cognitive deficits, including impaired spatial navigation. Spatial learning and memory is a hippocampal-dependent process essential for learning to navigate novel environments. Previous research suggests extreme alterations to sleep cycles significantly decreases spatial learning and memory, however these manipulations do not reflect typical circadian misalignments experienced by humans, such as in cases of sleep phase disorders or social jet lag. To model effects of subtle circadian misalignment, we maintained C57BL/6J mice on either a short T22.75 LD cycle or a standard 24-hour LD cycle from gestation to observe effects of chronic mild circadian disruption on spatial learning and memory. The Morris Water Maze (MWM) task was used to measure behavioural outcomes. Mice completed five training days with a hidden platform, followed by a single probe trial where the platform was removed. Both short-cycle mice and standard cycle = mice exhibited comparable learning effects over the course of the training days evidenced by similar latency reduction. During training, short-cycle mice spent more time in the centre of the pool compared to controls, demonstrating reduced thigmotaxis. During the probe trial, short cycle mice spent significantly more time in the adjacent quadrant compared to controls. While mice from the standard cycle spent more time in the target quadrant during the probe trial, this difference was not significant. Additionally, we are investigating the effects of mild circadian disruption on hippocampal hippocampal neurogenesis using bromodeoxyuridine (BrdU) immunohistochemistry. Preliminary behavioural findings suggest minimal negative impacts on spatial learning and memory as a result of mild chronic circadian disruption. Further immunohistochemical analysis will provide additional insight into its neural impact.

O3

Prion-like properties of CLOCK mediate circadian resilience

Sarah Ferraro, Elizabeth Mahoney, Yana Honcharuk, Hannah Blume, Lyric Gonzalez, Tamar Paserman, Sarah Visconti, Wakako Okuda, Kevin Zhang, Jonathan O. Lipton

- Boston Children's Hospital, Boston, USA, Harvard Medical School, Boston, USA

Circadian dysfunction strongly contributes to cardiovascular, metabolic, and neuropsychiatric disorders, suggesting that the circadian timekeeper plays a critical role in the maintenance of cellular homeostasis. While circadian clocks anticipate physiological need, they also buffer unpredictable environmental perturbation, pointing to compensation as a central feature of the circadian system. We have found that the core circadian protein CLOCK forms reversible rhythmic condensates in the cytoplasm that are responsive to stress. We have mapped this behavior to the large, evolutionarily conserved C-terminal intrinsically disordered region (IDR), which encloses the coiled-coil domain required for timekeeping. This domain is also essential for CLOCK's condensation. On the other hand, an abutting prion-like domain is required for the resolution of these structures and is essential for the recovery of circadian timekeeping after stress. Thus, we have identified a biochemical and biophysical mechanism intrinsic to a core circadian regulator that senses and compensates for environmental perturbation. Remarkably, these functions of CLOCK are similar to many disease-associated neurodegenerative proteins like huntingtin. We propose that loss of prion-like resilience is a key mediator for the loss of circadian function that accompanies physiological aging and neurodegenerative disease.

O4

Astrocytes drive sexually dimorphic effects of stress on orexin neurons and running wheel behavior

Lewis Depaauw-Holt, S. Hamane, B. Rogers, Anthony Bosson, Ciaran Murphy-Royal

- Université de Montréal, Canada
- Centre de recherche du CHUM, Canada

Astrocytes are integral to the regulation of neural circuits, where they modulate synaptic inputs and local circuit dynamics. By coordinating communication within and between brain circuits, astrocytes ensure the proper functioning of neuronal networks. Astrocytes in the SCN are active in shaping circadian timekeeping and themselves demonstrate a 24hr molecular clock. The lateral hypothalamus (LH), home to wake promoting orexin neurons, is a key hub for integrating circadian signals and external cues to fine tune behavioural processes. Astrocytes interact with orexin neurons to regulate sleep-wake cycles, through time-of-day specific shuttling of metabolic substrates. Stress-induced elevations in glucocorticoids are known to impair the metabolic support role of astrocytes. Here, we tested whether stress alters LH astrocytes to influence orexin neuron mediated running wheel behaviour. We employed an early life stress (ELS) paradigm from P10-P17 (limited bedding with 4 hours maternal separation per day). After ELS we observed increased wheel running in males and decreased running wheel activity in females. ELS significantly altered astrocyte morphology in the LH. To implicate astrocytes in LH mediated running wheel behaviour we injected mice with an AAV2/5-Gfap-HM3D(Gq)-mCherry to induce calcium fluctuations in LH astrocytes. Gq-coupled calcium signaling in astrocytes impaired running wheel behaviour in both male and female mice. To investigate the contribution of stress induced glucocorticoid signaling in observed behavioural phenotypes we conducted ELS in and Nr3c1fl/fl line and injected AAV2/5-Gfap-Cre to delete glucocorticoid receptors (GR) in LH astrocytes. Conditional deletion of astrocyte GR in the lateral hypothalamus significantly ameliorated the synaptic and behavioral deficits caused by ELS, in both sexes. Our data suggest that ELS perturbs hypothalamic circuits and behaviour through astrocyte glucocorticoid signaling in a sex-specific manner. These disruptions underlie stress-induced behavioral dysfunction and emphasize the need to consider sex as a biological variable in understanding astrocyte-mediated mechanisms of stress.

O5

Overexpression and rescue of Nlgn2 splice isoforms in mice: effects on behavior and vigilance states

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- Centre d'études avancées en médecine du sommeil, CIUSSS-NIM, Canada
- Centre de recherche du Centre hospitalier de l'Université de Montréal, Canada
- Département de biochimie, Université de Montréal, Canada

Neurodevelopmental disorders (NDDs) often present with sleep disturbances which potentiate symptomatology. Synaptic adhesion molecules (SAMs) such as Neuroligins (NLGNs) modulate vigilance states through their regulation of neurotransmission, and NLGN mutations were found in patients with NDD. Clarifying how NLGNs shape sleep-wake duration and quality could thus have tangible outcomes in the treatment of NDDs. NLGN2 mainly regulates inhibitory transmission, yet exists in two isoforms that are differentially expressed between glutamatergic and GABAergic synapses. Nlgn2 knockout (KO) mice exhibit anxiety-like behavior and abnormal social interactions, and spend more time awake, with massive changes in electrocorticographic (ECoG) activity. However, it remains unclear whether adult modulation of Nlgn2 expression can affect behavior and sleep phenotypes, for which the differential roles of each NLGN2 variants is still unknown.

Adult Nlgn2 KO mice and wild-type (WT) littermates were injected in the motor and visual cortices with a virus encoding either of the NLGN2 variants, or the green fluorescent protein (GFP) as a control. Mice underwent ECoG electrode implantation, and signal was recorded for 24h of baseline, 6h of sleep deprivation, and 18h of recovery. Anxiety and social behaviors were explored using the open field, elevated plus maze, and 3-chamber tests. Nesting capacity was also evaluated.

Preliminary data suggests that manipulating NLGN2 expression in adult mice reverses the increased time spent awake and some of the changes in ECoG activity observed in KOs. Moreover, Nlgn2 rescue restores the impaired preference for social novelty seen in KOs, but not the abnormal nesting behavior. The differential isoform effects however remain to be clarified. Additionally, gene expression analyses indicate altered expression of chloride channels and other SAMs under NLGN2 manipulations.

Overall, this work will increase the understanding of the mechanisms by which NLGN2 shapes behavior and vigilance states, and potentially uncover a druggable target for sleep-wake modulation in NDDs.

O6

Non-additive effects of prenatal infections and circadian disruption on behaviour and hippocampal cell-type specific gene expression

Danae Penichet, Tie Yuan Zhang, Tara C. Delorme, Ahmed A. Bouteldja, Albert Pelinovsky, Nick O'Toole, Lalit K. Srivastava, Patricia P. Silveira, Nicolas Cermakian

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- Integrated Program in Neuroscience, McGill University, Canada
- Department of Psychiatry, McGill University, Canada

Introduction: While prenatal infections are a well-established risk factor for neurodevelopmental disorders, it is poorly understood how environmental factors, such as circadian disruption, during early life can modify this risk. We characterized behavioural phenotypes and cell-type-specific molecular changes associated with exposure to prenatal infections and early-life circadian disruption. Methods: To recapitulate the risk conveyed by a viral infection in the first trimester of pregnancy, pregnant C56BL/6 mice were injected with either saline (control) or viral mimetic poly (I:C) on embryonic day 9.5. After weaning, offspring were housed either under 12-hour:12-hour light-dark (LD) cycles or under chronic jet lag (CJL), consisting of a 6-hour phase advance every other day for four weeks. After two additional weeks of LD, mice either underwent behavioural testing or were sacrificed for dorsal-hippocampal single-nucleus RNA sequencing (snRNAseq). Results: Male mice were more affected by prenatal infection exposure, which led to a novelty-induced anxiety phenotype (increased open-field activity levels over time($p<0.001$) and acoustic startle response($p=0.0002$); decreased elevated plus-maze open-arm entries ($p=0.0036$)). Interestingly, CJL increased the social novelty preference of mice exposed to prenatal infections. In contrast, females were most affected by CJL, which significantly decreased their open-field activity over time($p=0.0080$) and time in the open arms($p=0.0158$). Single-cell differential gene expression analyses of male dentate gyrus neurons revealed a non-additive effect of the two factors, whereby CJL seemed to shield against gene expression changes caused by the infection model alone. Pathway enrichment analysis revealed that prenatal infections mostly affect intracellular pathways, while CJL affects synapse and membrane channel activity. Interestingly, when both factors are present, only membrane channel activity pathways are disrupted. Conclusion: Our results show sexual dimorphisms where male and female mice display altered behaviours after prenatal infection- and CJL-exposure, respectively. Yet, snRNAseq reveals independent and counter-acting molecular changes by prenatal infections and CJL.

O7

Clocking in on ataxia: Per2 dysregulation in the cerebellum of spinocerebellar ataxia type 6 (SCA6) mice

Ben Rogers, Anna Cook, Maia List, Alanna Watt

- McGill University, Canada

Spinocerebellar ataxia type 6 (SCA6) is an autosomal-dominant neurodegenerative disorder that leads to the progressive loss of motor coordination and cerebellar dysfunction. While the hallmark of SCA6 is motor, sleep disturbances are increasingly recognized as a prevalent occurrence in patients. Sleep disturbances significantly impact quality of life and well-being of these patients. However, the relationship between sleep disorders and the underlying pathological mechanisms driving ataxia in SCA6 remains unclear. Interestingly, recent studies have identified that the clock genes are rhythmically in the cerebellum throughout the light-dark cycle. This prompted us to examine the expression of clock genes in the cerebellum of male and female SCA6 and litter-matched wild-type (WT) mice. We observed a reduction in the expression of Per2 in the cerebellum at ZT10 without any significant changes in other clock genes. Expression was largely limited to cerebellar Purkinje cells, the principal cells of the cerebellum that are affected in SCA6. Furthermore, SCA6 mice demonstrate impaired running wheel activity during the transition from the light to dark phase at ZT10. We believe that by understanding the dysregulation of clock genes in the cerebellum of SCA6, we will gain valuable insights into non-motor dysfunction and may also identify novel therapeutic strategies to address both motor and non-motor symptoms in SCA6, that may also have implications for other forms of ataxia.

O8

How to find optimal measurement schedules for biological rhythm discovery using PowerCHORD

Turner Silverthorne, M. Carlucci, A. Petronis, Adam Stinchcombe

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- The Krembil Family Epigenetics Laboratory, The Campbell Family Mental Health Research Institute, Centre for Addiction and Mental Health, Canada
- Institute of Biotechnology, Life Sciences Center, Vilnius University, Lithuania

Despite tremendous improvements to omic technologies over the last several decades, there remain fundamental challenges that limit the detection of novel biological rhythms. One such challenge is the range of timescales encountered in chronobiology. Especially if rhythmic activity is under-characterised, meaningful signals may be overlooked as random noise simply because samples are collected too rapidly or slowly relative to the duration of the underlying cycle. Here, we show that cycles of unknown periodicity can be more reliably detected using irregularly spaced measurement schedules. We derive an optimization problem for maximizing the statistical power of the cosinor model across a range of periods and acrophases. Solving this problem numerically using our PowerCHORD library reveals several experimental contexts in which irregularly spaced measurements offer significant improvements over the standard practice of equispaced sample collection. By sharing the benefits and limitations of PowerCHORD optimization, we hope it will join the vast array of tools available to chronobiologists.

O9

Identifying arousal inputs to the intergeniculate leaflet in hamsters

Maeve Scotland, Katelyn G. Horsley, Chantelle McCance, Michael C. Antle

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- Hotchkiss Brain Institute, Cumming School of Medicine, University of Calgary, Canada
- Department of Physiology and Pharmacology, Cumming School of Medicine, University of Calgary, Canada

While light plays a major role in entraining circadian rhythms, non-photic cues can also reset our circadian clock. Arousal and exercise can produce large phase advances when they occur in the mid-subjective day. These phase shifts are mediated through the innervation of the SCN by Neuropeptide Y neurons from the intergeniculate leaflet (IGL). However, the mechanism by which the IGL is recruited during these manipulations is unknown. It is hypothesized that this non-photic pathway to the circadian clock is activated by an arousal input. In this study, we examined what arousal inputs might participate in the activation of the IGL during a non-photic manipulation. To investigate this, male and female Syrian hamsters were surgically implanted with unilateral cannulas aimed at the IGL. The acetylcholine (ACh) agonist carbachol, the glutamate agonist NMDA, and orexin (an important arousal neuropeptide that densely innervates the IGL) were injected into the IGL at CT6. We found that when orexin was applied to the IGL, it produced small and inconsistent phase shifts that, overall, did not significantly differ from the vehicle control. Conversely, carbachol and NMDA both caused non-photic-like phase shifts when independently injected into the IGL. However, a cocktail containing both carbachol and NMDA inhibited each other's phase-shifting effects. Interestingly, a cocktail that included orexin, carbachol, and NMDA reversed this inhibition and yielded the largest phase shifts of all. This suggests that the IGL is likely activated by numerous convergent arousal inputs during a phase-shifting non-photic manipulation. Funding sources: Natural Sciences and Engineering Research Council of Canada (NSERC).

O10

Endocannabinoids: a link between circadian disruption and metabolic dysfunction

Brennan A. Baca, Giancarlo E. Denaroso, Said Akli, Gregory L. Pearson, Walker Sorensen, Jiexin Wang, Catherine Hume, Matthew N. Hill, Ilia N. Karatsoreos

- Dept. of Psychological and Brain Sciences, University of Massachusetts Amherst, USA
- Dept. of Cell Biology and Anatomy, University of Calgary, Canada

Circadian rhythm disruption is a significant risk factor for cardiometabolic diseases such as obesity and diabetes. We have shown that exposure to a shortened environmental period (T20; 10h Light, 10h Dark) leads to weight gain, increased adiposity, and elevated plasma insulin and leptin. Endocannabinoids, lipid derived signaling molecules, are both metabolically relevant and circadian regulated. Therefore, we studied their role in the development of T20-induced metabolic disorder. Our data show that exposure to T20 alters plasma endocannabinoids in a manner consistent with that seen in overweight humans. We next show that male, but not female mice gain excessive weight following just 5-weeks of T20, despite no change in gross feeding. To test the necessity of the endocannabinoid system in observing this phenotype, we exposed global cannabinoid type 1 receptor (G-CB1r) WT and KO mice to T20 and control conditions while monitoring behavior. We found that G-CB1r KO males were protected against T20-induced weight gain, despite exhibiting similar behavior disruptions as WT males. We provide evidence suggesting that T20-induced weight gain may be the result of a decoupling between feeding and macronutrient oxidation preference, as measured by indirect calorimetry. Given the lack of behavioral difference between G-CB1r WT and KO males, we posited endocannabinoid mediated T20-induced weight gain may be peripherally mediated. Furthermore, because the liver is both endocannabinoid competent and a major site of macronutrient oxidation, which we show to be disrupted under T20, we asked if liver-specific (L)-CB1r signaling specifically was necessary for T20-induced weight gain. We show that while L-CB1r KO males are not protected against T20-induced weight gain, they are spared from elevated levels of insulin, glucagon, leptin, and plasma triglycerides, suggesting that hepatic CB1r is responsible for part, but not all, of the T20-induced metabolic phenotype.

O11

Impact of gender and work schedules on sleep and fatigue of frontline healthcare workers during COVID-19

Huirong Luo, Philippe Boudreau, Rafael Pérez Medina Carballo, Manuela Ferrari, Michel Perreault, Niamh Power, Stéphanie Grenier, Patricia Debergue, Wendy Hori, Diane B. Boivin

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- National Research Council of Canada, Canada
- Beth Israel Deaconess Medical Center, Clinical Research Center, USA

Introduction: Sleep and fatigue are critical components of health, especially among shift workers. Gender-specific vulnerabilities are understudied. This study investigates the interplay between gender and work schedules in influencing sleep and fatigue. Methods: A survey was conducted from June to August 2021 using questionnaires targeting healthcare workers (HCWs) in Montreal. Participants included HCWs such as nurses, respiratory therapists, perfusionists, and healthcare aides. The survey collected data on demographics, work schedules, COVID contacts, sleep and fatigue complaints. Ordinal regression models examined the independent and interactive effects of gender, work schedules, and covariates on sleep and fatigue. Results: Participants (n=575, 42.5 ± 11.4 years old; 84.7% women reported working regular day (54.6%), evening (15.0%), night (11.0%), or rotating shifts (11.3%). Compared to men, women reported more severe sleep problems (OR = 1.52, p = 0.048), sleep worries (OR = 1.69, p = 0.017), and fatigue complaints (OR = 2.18, p < 0.001), despite fewer work hours (-2.8 hours per week, p < 0.001). Adjusting for work hours, gender, age, and COVID contacts, work schedules significantly influenced sleep and fatigue outcomes. Night shift workers reported more sleep worries compared to evening shift workers (OR = 2.13, p = 0.019). Rotating shift workers had more fatigue complaints compared to night (OR = 2.31, p = 0.012) and evening shift workers (OR = 2.62, p = 0.002). There was no interaction between gender and work schedule on outcomes. Conclusion: Women HCWs consistently reported worse outcomes despite working fewer hours. More sleep and fatigue complaints were observed with rotating and night shifts. These findings highlight the need to integrate chronobiological perspectives into workplace policies to address shift work challenges and support women's health. Support: This study was supported by funding from the National Research Council of Canada. HL was supported by the China Scholarship Council.

O12

Colons lost in time: delayed regeneration in mice lacking an epithelial clock

Zainab Taleb, Ryan Wan, Mehr Fatmah, Vania Carmona-Alcocer, Phillip Karpowicz

- University of Windsor, Department of Biomedical Sciences, Canada

Circadian disruption has been linked to an increased risk of colitis. We, and others, have previously established that mice lacking clock genes, such as Bmal1, exhibit severe colitis. In order to assess a tissue-specific role of the clock, we tested the regenerative effects of Bmal1 specific to intestinal epithelial tissue using EpiCtrl (Vil+/+;Bmal1flox/flox) and EpiΔBmal1 (VilCre/+;Bmal1flox/flox) mice. Dextran Sulfate Sodium (DSS) was applied to induce acute colitis and mice were allowed to recovery following the removal of DSS. We hypothesized that the absence of a functional circadian clock disrupts colitis recovery. Prior to colitis, EpiΔBmal1 mice show signs of a weakened intestinal barrier. Following induction of colitis, EpiCtrl and EpiΔBmal1 mice exhibit no differences in disease severity or tissue histopathology. However, during recovery EpiΔBmal1 mice show increased disease activity that is sex-specific. A histological analysis further revealed that EpiΔBmal1 conditional mutants show an inability to resolve colonic ulcers during the recovery phase. Overall, EpiCtrl mice are able to recapitulate their intestinal architecture 2 weeks after colitis is induced while EpiΔBmal1 mice remain in a damaged state with an increased presence of hyperplastic crypts which remain stuck in a state of healing. We also notice disrupted expression of cMyc under homeostatic conditions as well as IL1ß, Nlrp3, and Nlrp6 inflammasomes during recovery in EpiΔBmal1. Together, this data suggests that mice lacking Bmal1 in intestinal epithelial cells have deficits in key pathways involved in barrier protection and regeneration in order to recover from colitis, resulting in inefficient regeneration. Our results support a critical role for Bmal1 in intestinal epithelial cells during post-colitis regeneration and recovery.

O13

Daily variations in integrated HIV-DNA load, residual viral transcription and genome-wide transcriptional profiles in CD4+ T-cells of people with HIV-1 receiving antiretroviral therapy

Augustine Fert, Debashree Chatterjee, Tomas Raul Wiche Salinas, Delphine Planas, Amelie Cattin, Laurence Raymond Marchand, Etiene Moreira Gabriel, Christ-Dominique Ngassaki-Yoka, Yuwei Zhang, Josee Girouard, Abdelali Filali-Mouhim, Nicolas Cermakian, Daniel E. Kaufmann, Jean-Pierre Routy, Petronela Ancuta

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Background: Biological functions exhibit circadian rhythms to align with day/night environmental changes. The circadian clock master regulators CLOCK/BMAL1 bind on E-boxes in the promoters of clock-regulated genes, including HIV-1. Circadian variations in residual viral transcription were reported in people with HIV-1 (PWH) receiving antiretroviral therapy (ART). Here, we investigated variations in CD4+ T-cell counts/phenotype and transcriptional profiles of in relationship with daily variations in residual HIV-1 transcription during ART.

Methods: Eleven male ART-treated PWH were admitted at the CHUM Unit for Innovative Therapies for 36 hours. Blood was collected every 4 hours, before food intake, for 24 hours. Plasma levels of cortisol/melatonin and markers of intestinal permeability were measured by ELISA. Flow cytometry allowed the quantification/characterization of leukocytes. CD4+ T cells were sorted for cell associated integrated HIV DNA and Gag HIV-RNA quantification by nested PCR/RT-PCR and Illumina RNA-Sequencing. The impact of time on immunological/virological parameters was investigated using Cosinor and linear mixed models.

Results: Peaks in melatonin and cortisol levels were observed at 4:00 and 8:00, respectively. CD4+ T-cell counts were at nadir levels in the morning, but significantly increased at 20:00, when cells expressed the highest levels of the HIV-1 co-receptors CCR5/CXCR4 and a Th17, gut-homing, follicular helper and effector memory phenotype. Although integrated HIV DNA levels per million CD4+ T-cells were stable, the proviral load normalized per cell number/blood volume reached the highest abundance at 20:00. The HIV-RNA/DNA ratio (surrogate marker of HIV transcription) peaked at 4:00. Robust changes in differential gene expression were observed at 20:00 and 4:00, including transcripts encoding for regulators of T-cell functions and viral transcription.

Conclusions: Altogether, our results demonstrate the abundance of CD4+ T-cells carrying proviral HIV-DNA in the blood at 20:00, with a peak in residual HIV-1 transcription at 4:00, and reveal a unique transcriptional signature associated with these immunological/virological variations in ART-treated PWH.

O14

Torpor, inflammation, recovery sleep & alpha2-adrenergic agonist hypnosis

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The adrenergic alpha-2 agonist dexmedetomidine (Dex) produces sedation and hypnosis through its action at the alpha-2a adrenergic receptor and downstream activation of neural assemblies associated with NREM sleep. Dex's action at these same receptors alters thermoregulation, resulting in significant decreases in temperature. This pairing of large drops in temperature with hypnosis is paralleled in other physiologic processes: illness/inflammatory-related sleep and torpor. Mice with cell-specific knockout of the alpha-2a adrenergic receptor in subcortical glutamatergic neurons have grossly normal sleep structure but show profound resistance to hypnotic and thermoregulatory effects of dexmedetomidine compared with floxed alpha-2a adrenergic receptor controls. These same cell-specific knockouts show normal torpor-related temperature changes in response to caloric restriction. Mice were given IP Dex and evaluated for behavioral sedation and temperature changes over 1 hour, with a separate cohort evaluated for EEG-related changes in response to Dex. Cell-specific knockout and floxed-control mice with implanted EEG headpieces underwent continuous recording for sleep scoring over 3 days. The same mice were injected with 1 mg/kg LPS to induce an inflammatory response and inflammatory-related sleep response analyzed. Our results find that a2a KO mice are resistant to the sedative-hypnotic and temperature regulating effects of Dex, though their regular sleep architecture is not affected. There does not appear to be a common pathway for the interrogated processes via adrenergic alpha-2a receptors on subcortical glutamatergic neurons. Funding Acknowledgment: National Institutes of General Medicine Science R35GM142712; and Department of Anesthesiology at the University of Pennsylvania

O15

Structural and functional insights on the interactions of the clock protein BMAL1 with CaMKIIα and its role in regulating circadian synaptic function

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Every 24 hours, animals undergo massive, predictable behavioral plasticity in synchrony with light cycles. In mammals, circadian behavioral rhythms are regulated by an endogenous molecular clock comprised of a transcription-translation feedback loop, however, their synaptic basis remains unclear. We found that the core clock protein, BMAL1, rhythmically localizes to synapses, dependent on its phosphorylation at S42 (pBMAL1 S42) (Barone et al., 2023). A phospho-incompetent mouse model, BMAL1 S42A, loses rhythmic BMAL1 in synapses and also displays a loss of circadian variation of long-term potentiation, a CaMKIIα-dependent function. Preliminary data also demonstrates a pBMAL1 S42-dependent rhythm in the synaptic vesicle pool, possibly through the rhythmic regulation of the CaMKIIα-substrate, Synapsin1 (Barone, unpublished). The synaptic BMAL1 interactome is enriched with pre-synaptic vesicle associated proteins (including Synapsin1) as well as with CaMKIIα. In vitro, BMAL1 potentiates the autophosphorylation of CaMKIIα at T286, suggesting that the biochemical basis for aberrant synaptic rhythms in BMAL1 S42A is mis-regulation of CaMKIIα by BMAL1.To probe the molecular interface of BMAL1/ CaMKIIα interactions we developed a co-immunoprecipitation assay from HEK293T cells and tested for the requirement of key phosphorylation sites and functional domains. We found that the central structured region of BMAL1 is sufficient for interactions while flanking disordered regions are insufficient. Moreover, BMAL1 binds to a novel site in the CaMKIIα kinase domain distinct from the substrate binding pocket. To assess the structural and functional consequences of BMAL1/ CaMKIIα-interactions we employ a FRET/FLIM based CaMKIIα sensor as well as biochemical assays. We find that BMAL1 promotes an open conformation CaMKIIα, which potentiates its interactions with substrates, like Synapsin1.Our data supports a model for rhythmic synaptic function regulation by BMAL1 through its interactions with CaMKIIα. Rhythmic localization of BMAL1 to synapses may gate biochemical tuning of CaMKIIα on circadian timescales giving rise to rhythmic synaptic function.

O16

Looking for temperature-driven and circadian rhythms in parasite Leishmania major

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Most organisms present 24h rhythms. Some of these rhythms are controlled by endogenous clocks, while some others are driven by acute responses to the environment. In parasitic infections, these daily rhythms play an important part in host-pathogen interactions. This is the case with Leishmania spp., a protozoan parasite transmitted by a sandfly, responsible for the development of the deadly disease leishmaniasis. Leishmania can adapt its functions and morphology to the host's body temperature, but it is unclear if it also responds to daily temperature cycles in the sandfly. Additionally, Leishmania infection is regulated by the host's circadian clock, but whether the parasite itself exhibits circadian rhythms remains unknown. To investigate driven and endogenous rhythmic oscillations in Leishmania major, promastigotes were subjected to daily temperature cycles of 25°C to 30°C, which is within the temperature range that their sandfly vectors normally live in. Then, some cultures remained temperature cycling (AT) and some were released into constant conditions (TT). Parasites were sampled every 4h over 48h for RNA sequencing, and transcripts were analyzed for rhythmic expression. In AT, 10.7% of the measured transcripts (924) exhibited rhythmic expression of around 24h, and permutation analyses showed that this was significant with an FDR<0.1. Follow-up qPCR experiments for some of the differentially expressed genes showed that these are acutely responding to temperature changes. Pathway analysis of the temperature-responsive transcripts highlighted functions related to morphological changes, redox homeostasis, and metabolism. In contrast, under TT, only 3.2% (248) of transcripts showed 24h rhythms, a non-significant number according to our permutation analyses. Our findings suggest Leishmania major responds rhythmically to environmental temperature cycles, but these do not entrain a transcriptional circadian clock. Understanding Leishmania rhythms may set a basis for targeting the parasite through environmental or therapeutic interventions. Funding: CIHR, Douglas Foundation. Students supported by CONAHCYT, FRQS, CGS-M.

O17

Investigating connections between target of rapamycin (TOR) activity and circadian rhythmicity in the fungus Neurospora crassa

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Circadian (24-hour) rhythmicity is driven by a biological clock present in nearly all eukaryotic cells, which enables cells to adapt to and anticipate daily changes in their environment. It has been proposed that the TTFL (transcription translation feedback loop) is required for operation of this biological clock. This model however fails, as rhythmicity can still be seen even when this TTFL is non-functional. This suggests the involvement of another oscillator important for generating rhythmicity. My hypothesis is that a pathway called TOR (Target of Rapamycin) can function as a circadian oscillator. I am testing my hypothesis in the filamentous fungus, Neurospora crassa, by manipulation of the feedback mechanisms within TOR. By adding pulse treatments of amino acids such as arginine or sugars like glucose, an activation of TOR activity should result and consequently, shift the timing of the clock. By adding inhibitors of TOR such as Torin, the opposite effect should be seen on both TOR activity and clock timing. If a change in the phase occurs simultaneously with a change in TOR activity, the importance of TOR is suggested. These TOR modulators are added to Neurospora exposed to different hours of total darkness (different circadian phases). To assay TOR activity, I measure the phosphorylation of a TOR output S6 ribosomal protein by western blotting using a novel method developed in our lab. Circadian rhythmicity is assayed by observing the rhythm of fungal growth and sporulation (conidiation) on solid agar. My project will allow for the further understanding of mechanisms responsible for circadian rhythms in Neurospora crassa, as well as other organisms that have similar pathways including humans. My research is funded by NSERC.

O18

The frequency and power of sleep slow wave activity is shaped by potassium channels

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Slow neuronal synchronies in the cerebral cortex—slow wave activity (SWA); <4Hz—are the hallmark of deep restorative sleep and a metric of sleep need. Recent research suggests that slower (<1Hz) and faster (1-4Hz) frequencies of SWA mediate distinct cognitive benefits, but the mechanisms governing this oscillatory speed remains unknown. We hypothesize that voltage-gated potassium channels (KV) and voltage-gated potassium/sodium channels (KNV), which neuronal excitability and bursting, also regulate sleep and the frequency of sleep brain oscillations.

To test so, we conducted three approaches: (1) KV or KNV knockout (KO) mice were recorded with the respiration-based snappy sleep stager (SSS) and/or via the electroencephalogram (EEG); (2) neuron-specific gain/loss-of-function KV/KNV constructs were injected in adult mice via viral vectors (AAV) and EEG was recorded; (3) the implication of KV/KNV for the hypnotic and SWA-inducing drug effects was studied in mice KO or mutants for KV/KNV.

Analyzing sleep phenotypes in 42 knockout mice lacking Kv channels revealed that mice knock-out (KO) for the heart-related slowly-activating potassium channels Kcnq1 and Kcne1 exhibited reduced sleep time by 2.5 to 3 hours and slowed-down SWA frequency. In contrast, Kcnq2KO mice showed reduced SWA power but did not modify the peak frequency. Downregulation of either Hcn1 or Hcn2 channels in excitatory neurons slowed SWA frequency by ~1 Hz and increased SWA power by 10-30%. Notably, Hcn2 was required for the typical homeostatic responses of SWA power following sleep deprivation. Moreover, dexmedetomidine, a sedative acute antidepressant agonist for alpha-2 adrenergic receptors, required Hcn2 to enhance sleep and SWA.

These findings highlight critical roles of potassium channels in tuning SWA frequency and mediating homeostasis- and drug-induced neuronal synchronies, providing insights into molecular mechanisms of sleep quality.

O19

A mathematical model for the role of dopamine-D2 self-regulation in the production of ultradian rhythms

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Ultradian behavioural rhythms are highly-flexible oscillations in goal-directed behaviour with periods shorter than a day. They remain mysterious in both their biochemical mechanisms and their functional significance, but are generally believed to be a reflection of neural dynamics. We propose that D2 autoreceptor-dependent dopamine self-regulation in the midbrain-striatal synapses gives rise to ultradian rhythmicity. We express this hypothesis in an ordinary differential equation based mathematical model in a dual-negative feedback-loop structure. Numerical integration and bifurcation analysis shows that the oscillations have a flexible and parameter-sensitive period in agreement with experimental observation. The model also demonstrates the masking-entraining effects of circadian (approximately 24 hour) regulation on ultradian rhythms and the rapid-resetting effect of transient excitation. This reveals the crucial role of circadian-ultradian interaction in consolidating behavioural activity and coordinating the motivation to engage in recurring, albeit not highly predictable events, such as social interactions.

O20

BMAL1 and circadian rhythms support robust innate immune signaling in lung cancer

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Disruption of the molecular circadian clock is indicative of poor prognosis in non-small cell lung cancers (NSCLCs), but direct evidence for a causal link between circadian clock deregulation and malignancy is missing. One potential reason for poor outcomes in NSCLC is an immunologically cold tumor, which evades immune cell-mediate killing when developing. It was previously shown in the lung that the internal circadian clock of lung epithelial cells (the cells that give rise to NSCLC) have rhythmic innate immune activity. We found that BMAL1, a central regulator of the molecular clock, is downregulated in human NSCLCs, and that low BMAL1 is an indicator of poor prognosis. In addition, deletion of BMAL1 in a mouse model of NSCLC accelerates cancer progression. However, how BMAL1 restrains tumorigenesis remains unclear. We discovered that human lung tumors with lower BMAL1 have decreased transcriptional signatures of innate immune activity. This effect is cancer cell-autonomous, as lung epithelial cells lacking BMAL1 bear the same signature of depressed immune signaling. To test the role of BMAL1 and circadian rhythms in the tumor immune microenvironment, we deleted BMAL1 in a mouse model of NSCLC with an intact immune system. In the absence of BMAL1, cancer cells had an impaired response to inflammatory stimuli and formed tumors more rapidly in vivo. We performed single cell RNA-sequencing on tumors ± BMAL1, and found that the tumor-infiltrating neutrophils and macrophages (innate immune cells) in BMAL1 KO tumors were less inflammatory, and instead expressed an angiogenesis signature (bringing in new blood vessels to the tumor), which is pro-tumorigenic. Together, these data suggest that oscillatory signals from cancer cells with intact molecular clocks support a robust (and potentially circadian) anti-tumor immune environment in lung cancer, and when cancer cells are arrythmic, this may result in an immunologic environment that instead promotes tumor growth.

P1

Loss of REV-ERBα enhances reperfusion recovery following myocardial ischemia and reperfusion

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Heart attacks are characterized by the blockage of blood flow to the heart muscle, leading to myocardial damage and necrosis. Contemporary reperfusion therapy, termed myocardial ischemia and reperfusion (mI/R), removes this blockage and restores blood flow. However, during this process, the heart muscle sustains damage, which can ultimately progress to heart failure, for which there is no cure. Our goal is to explore ways to reduce mI/R damage and prevent heart failure. Here, we focus on the role of the circadian gene REV-ERBα in the heart's recovery from mI/R. While REV-ERBα is implicated in cardiac repair, its exact mechanism in the heart remains unknown. To test this, mI/R was induced using the ex vivo Langendorff procedure. This involved perfusing isolated mouse hearts with a Krebs-Henseleit solution, pacing the hearts at 420 beats/min, and inserting a balloon to measure Left Ventricular Developed Pressure (LVDP) as a percentage of baseline (%BL). We first compared wild-type (REV-ERBα+/+) and homozygous (REV-ERBα-/-) male mice under both mI/R and non-ischemic conditions. Our results indicate that male REV-ERBα-/- exhibit enhanced mI/R recovery compared to male REV-ERBα+/+ controls, by 30 minutes post-reperfusion. Next, we analyzed sex differences. Our results show that female REV-ERBα+/+ mice (75.32% ± 3.60%) have similar recovery to their REV-ERBα-/- counterparts (76.22% ± 5.36%). In contrast, male REV-ERBα+/+ mice (71.94% ± 7.82%) displayed lower recovery compared to REV-ERBα-/- (92.78% ± 3.29%). Together, our results suggest that in the absence of REV-ERBα, male mice exhibit enhanced mI/R recovery, whereas females showed no difference in recovery. We plan on using Affymetrix RNA microarrays and Genespring bioinformatics to identify the genes and pathways downstream of REV-ERBα that influence cardiac repair, in a sex and genotype manner. Identifying these pathways could lead to new approaches that improve cardiac repair and recovery from mI/R in vivo.

P2

Impaired nocturnal slow-wave activity decay precedes epileptic seizures

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(DKN, VM, and EBA are equally contributing principal investigators)

Introduction: Impaired sleep, widely recognized as an epileptic seizure trigger, has seldom been investigated at the microarchitecture scale in people with epilepsy (PWE). Sleep homeostasis describes the brain's energy stability as synaptic reorganization occurs during slow-wave sleep. Our hypothesis is that impaired sleep homeostasis may increase daytime seizures likelihood. Our goal is to investigate the relationship between the exponential decay of slow-wave activity (SWA) on scalp electroencephalography (EEG) and seizure occurrence the following day. Methods: PWE were recruited from the Centre hospitalier de l'Université de Montréal (CHUM) epilepsy monitoring unit between April 2019 and July 2022. Nights followed by a seizure in the 24h following wake were classified as "pre-seizure", and those without as "non-pre-seizure". We excluded the first night, and nights with sleep deprivation or nocturnal seizures. SWA (1-5 Hz) was extracted from continuous EEG recordings. Sleep cycles were identified by the intersection of SWA signals with local minima. Cycle peaks and area under the curve (SWA-AUC) were used to fit exponential decay functions $a \cdot e - b \cdot t + c$, where a, b and c may be interpreted as the initial SWA value, slope of SWA decay, and residual SWA by the night's end, respectively. Exponential decay parameters were statistically compared between pre-seizure and non-pre-seizure nights. Results: A total of 189 nights from 32 patients were analyzed, including 52 pre-seizure and 137 non-pre-seizure nights. In SWA-AUC analysis, parameters a and b were significantly lower in pre-seizure nights ($p<0.05$). No significant difference was found in peak analysis. Conclusions: Our results suggest that impaired nocturnal SWA decay precedes epileptic seizures. SWA may serve as a potential noninvasive biomarker for seizure forecasting, which may improve seizure forecasting models. More research is necessary in larger cohorts to explore the underlying mechanisms. Funding: Epilepsy Canada Foundation, CIHR, NSERC, Canada Research Chair in Sleep Molecular Physiology and FRQS.

P3

Assessing day-night disparities in neuronal DNA damage responses among those with opioid use disorder

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The genome is constantly subjected to environmental and internal mutagens, leading to diverse forms of DNA damage in human tissues, including the brain. Accumulated neuronal DNA damage was traditionally associated with aging/neurodegenerative diseases. Findings from our laboratory indicate a potential connection between opioid use disorder (OUD) and higher neuronal mutation rates. Here, we measured classic markers of DNA damage and repair: 8-oxoguanine (8-oxoG) and 8-oxoGDNA glycosylase (OGG1) in the postmortem human striatum. 60-70% of patients meet the criteria for sleep/circadian disorders, and altered sleep schedules affect oxidative DNA damage, so we also examined 8oxoG and OGG1 immunofluorescence across time of day. Postmortem dorsal striatum tissue punches (n=6 subjects per sex per unaffected and OUD) were processed for immunofluorescence targeting 8-oxoG and OGG1. A cosine regression analysis was conducted to access rhythmicity of the expression levels of DNA damage markers across the day, plotted using time of death. Our data indicates increased average nuclear 8oxoG and OGG1 intensity in OUD neurons compared to neurons from unaffected matched controls (Mann Whitney, 8oxoG $p < 0.001$ and OGG1 $p < 0.001$). Nuclear 8oxoG intensity did not differ by neuron area for OUD, but higher 8oxoG intensity was associated with smaller neurons in controls (linear regression slope, $p=0.025$). Preliminary data revealed no significant rhythm in OUD or controls ($p > 0.05$). When comparing day versus night expression in mean nuclear 8oxoG and OGG1, no significant 2-way interactions (time of death x treatment) or main effects were observed ($p > 0.05$). By describing the cellular levels of DNA damage in OUD striatal neurons, and how they may vary in the day versus night, we can leverage these data to gain insights into molecular alterations in human striatum associated with opioid addiction.

P4

Circadian-regulated autophagy and BECLIN-1: a sex-specific protective mechanism in heart attack - induced ischemia-reperfusion injury

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A heart attack occurs when blood flow in the coronary arteries is reduced or blocked, which causes damage to the heart tissue. Restoring blood flow can paradoxically cause further injury, known as myocardial ischemia-reperfusion (mI/R) injury. Autophagy, a process partially regulated by circadian mechanisms, plays a protective role in mI/R injury. BECLIN 1, a key regulator of autophagy, is essential for autophagosome formation and maintaining the balance between protective and excessive autophagy during mI/R. However, its precise role in cardiac protection post-mI/R is unclear. To investigate this, we used the ex vivo Langedorff technique to induce mI/R injury in excised hearts from BECLIN 1 knockout (Bcl2AAA) and wild-type (WT) mice. Hearts were perfused with Krebs-Henseleit buffer, subjected to 20 minutes of ischemia by halting perfusion and then reperfused for 30 minutes. Left ventricular developmental pressure (LVDP) was measured using a pressure transducer to assess cardiac function. Our results indicate BECLIN 1 is protective in female hearts, as female Bcl2AAA showed significantly reduced recovery with % LVDP of baseline 62.18% ± 2.47 % compared to WT female hearts (81.28% ± 9.21%). However, sex-specific differences were not observed in males, as LVDP recovery was similar between male Bcl2AAA (66.23% ± 3.89 %) and female Bcl2AAA (62.18% ± 2.47 %) hearts, as well as between male WT (63.12% ± 3.08%) and male Bcl2AAA (66.23 ± 3.89 %). These data suggest that BECLIN 1's cardioprotective role is sex-specific. Next, we will perform microarray and bioinformatics analyses to identify the genes and molecular mechanisms underlying BECLIN 1's protective effect in female hearts during mI/R. These findings will enhance our understanding of circadian-controlled recovery mechanisms and contribute to the development of circadian-based therapies to improve post-MI outcomes

P5

Circadian mechanisms and sex-specific regulation in heart attack recovery: CLOCK's role in myocardial ischemia-reperfusion injury

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Cardiovascular disease is the leading cause of death in Western societies, with heart attack (myocardial infarction, MI) being a major contributor. MI occurs when coronary blood flow is restricted, leading to hypoxic injury in cardiac tissue. Following treatment, restoring blood flow can cause further damage, known as myocardial ischemia-reperfusion (mI/R) injury. CLOCK is a core circadian regulator, and has been shown to influence cardiomyocyte survival during ischemic stress, but its role in mI/R recovery remains unclear. This study investigates CLOCK's role in mI/R recovery using an ex vivo Langendorff heart perfusion model. Murine hearts were perfused with Krebs-Henseleit buffer and subjected to 20 minutes of ischemia followed by reperfusion, with recovery assessed by measuring isovolumetric left ventricular developed pressure (LVDP) as a % of baseline. To evaluate the importance of CLOCK in mI/R recovery, we assessed homozygous ClockΔ19/Δ19, heterozygous ClockΔ19/+, and wild-type Clock+/+ hearts. We found a genotype-dependent effect, with male ClockΔ19/Δ19 hearts exhibiting the poorest recovery (11.39% ± 0.99%), while ClockΔ19/+ (45.20% ± 6.44%) and Clock+/+ (39.58% ± 3.88%) displayed intermediate recovery. There was also a sex-dependent effect, with females exhibiting better LVDP recovery than males. Female ClockΔ19/Δ19 (30.29% ± 17.92%) had reduced recovery compared to female ClockΔ19/+ (55.33% ± 24.67%) and Clock+/+ (63.11% ± 24.67%) hearts. These findings suggest that CLOCK plays a critical role in mI/R recovery and that sex-specific factors may influence the efficacy of circadian-based therapies to improve post-MI outcomes. Future studies with microarrays and bioinformatics analyses will identify the genes and pathways regulated by CLOCK in this process.

P6

MYC and epithelial to mesenchymal transition independently predict circadian disruption in lung adenocarcinoma

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The molecular clock is disrupted in some cancers, and its disruption can promote tumorigenesis in mouse models. However, there is no method to determine which specific patient tumors are disrupted. To address this, we utilized Clock Correlation Distance (CCD) to determine how gene expression of select circadian and cancer-related genes in lung adenocarcinoma (LUAD) correlates with circadian status in patient tumors. Comparisons were made by sorting samples into quartiles based on the expression levels of genes of interest. We analyzed circadian genes BMAL1 and NR1D1, whose variations we found correlated to survival in non-small cell lung cancer, and MYC, an oncogene amplified or translocated in ~30% of human cancers, which is known to disrupt the clock. Individual circadian genes' expression were not reliable markers for circadian disruption; however, MYC expression did show a significant correlation to disruption, as both the highest and lowest MYC levels in LUAD correlated with disruption. High MYC levels correlating to disruption was predicted, however low expression was not. To determine the cause of this disruption, enrichment analysis was used to compare the low MYC group to the least disrupted samples. We found that Epithelial to Mesenchymal Transition (EMT) and TGF- β signaling were differentially enriched in the more disrupted tumors. We then used Gene Set Variation Analysis to score enrichment for each sample, and compared enrichment quartiles using CCD. We found that lower enrichment in both pathways (i.e., tumors were more epithelial) correlated with circadian disruption. To verify this in vitro, we exposed epithelial LUAD cells to TGF-β to induce EMT. TGF-β treatment caused a significant increase in the amplitude of BMAL1: Luciferase oscillations in these cells. The identification of markers of disruption such as EMT and MYC could play an important role in stratifying which specific lung tumors harbor circadian rhythm disruption.

P7

Chronobiology of metabolic dysfunction: the interplay of androgen receptors with circadian rhythms in the novel AR19-Q mouse model

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Background: Metabolic Syndrome (MetS) is a major global health concern, affecting approximately 25% of the population and significantly increasing the risk of diabetes, cardiovascular disease, and stroke. Androgen receptors (ARs) which are ligand-dependent nuclear transcription factors play a critical role in metabolic homeostasis. Disruptions in AR signaling have been implicated in MetS, particularly through interactions with circadian clock genes that regulate metabolic processes. However, the sex-specific effects of these disruptions remain poorly understood. Methods: Using a humanized androgen receptor mouse model (AR-19Q), we investigated the impact of AR signaling on metabolic and circadian functions in male and female mice. We assessed daily fluctuations in blood glucose levels and clearance, liver mitochondrial respirometry, and the expression of key clock proteins in metabolic tissues. Additionally, locomotor activity was evaluated using running wheels and motion detectors, providing insight into daily rhythms and potential behavioral alterations. Results: AR-19Q male mice developed non-alcoholic fatty liver disease and MetS-like phenotypes, exhibiting impaired glucose clearance specifically during the end of the light phase. Notably, Per1 expression was constitutively upregulated in the liver, suggesting a link between circadian misalignment and metabolic dysregulation. Because central clock function was only mildly affected in both sexes, the tissue-specific circadian alterations appeared to drive the observed metabolic disturbances, with more pronounced effects in males. Notably, in male mutant mice, three months of voluntary wheel running improved blood glucose uptake and prevented the development of MetS phenotypes. Conclusion: These findings highlight an important link between AR-dependent circadian regulation and metabolic health and provide insights into sex-specific vulnerabilities to the development of MetS. The AR-19Q model offers a valuable platform for exploring the molecular mechanisms of metabolic dysfunction and potential sex-specific chronotherapeutic interventions.

P8

Emergence of infradian rhythms and their relevance for cyclicity in bipolar disorder

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The circadian clock does not fully explain the phenomena of sleep-wake rhythms extending beyond the 24hr period. We have previously found evidence that a second dopamine-based oscillator is independently generating sleep-wake rhythms and is capable of producing cycles with a period of 48hrs and beyond. Intriguingly, these infradian (>24hr) rhythms in sleep-wake have also been described in cases of bipolar disorder (BD) where patients experience mania every other day with intervening depression, associated with short and long sleep respectively. BD's rhythmicity and links to the dopamine system closely echo sleep-wake patterns generated by the dopaminergic oscillator (DO) in mice, suggesting a link. We characterized the emergence of infradian locomotor rhythms generated by this oscillator using chronic methamphetamine treatment in drinking water as means of infradian rhythm induction. We found the onset time of infradian rhythms (>27hr) following exposure to Meth to be indistinguishable between male and female mice. Similarly, male and female mice did not display overt differences in the dominant period observed at 9 weeks post Meth treatment onset. By quantifying activity at the mean peak phase of circadian activity (α), we also found that mice exhibiting an infradian component with a period shorter than 48hr show 'beat cycling' with respect to daily locomotor activity. These regular fluctuations in activity during circadian α are the result of discordant frequencies between the circadian clock and the DO.These results are in agreement with clinical research indicating that BD affects both women and men nearly 1:1. Furthermore, the observation of 'beat cycling' suggests the interactions between the circadian clock and the DO may be responsible for BD cycling with a period greater than 48hr. Together, these results provide support for infradian rhythmic mice as a model for bipolar cycling and advance our understanding of the basis of BD cyclicity.Funding: NSERC-CGSM

P9

A protocol for studying the role of circadian rhythms in the resilience to dementia

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Introduction: Alzheimer's disease (AD) is a neurological disorder marked by cognitive decline, with progression varying across individuals despite similar neuropathologies. Understanding the mechanisms that contribute to cognitive resilience in AD is critical. Circadian rhythms changes are associated with AD, including altered daily behavioural patterns (such as 'sundowning'), reduced robustness of daily rest-activity cycles, and loss of suprachiasmatic nucleus (SCN) neurons. However, circadian disruption remains an understudied risk factor of AD. This study aims to outline a protocol for investigating how circadian rhythms influence cognitive resilience in AD.

Methods: Fifty participants (aged 50+) will be recruited to undergo circadian rhythm assessments using serially collected samples of saliva and urine. Samples will be collected every three hours for 48-hours to measure markers of endogenous circadian rhythms driven by central SCN oscillators (urinary aMT6s, urinary and salivary cortisol). To analyze circadian rhythm amplitude and acrophase, cosinor analysis will be applied to the 48-hour melatonin and cortisol rhythms. Participants will also wear wrist actigraphy and complete sleep diaries for 14 days. Cognitive function will be assessed using a battery of cognitive tests designed to assess the earliest cognitive changes in dementia. Participants will have their cognitive functioning assessed both at baseline and after two years to evaluate cognitive decline.

Anticipated results: We anticipate low-amplitude and phase-delayed circadian rhythms will be associated with poorer cognitive functioning at baseline and increased cognitive decline over the 2-year period.

Implications: This research aims to deepen our understanding of circadian dynamics in the resilience to dementia. The findings may inform future efforts to explore modulation of circadian rhythms as a therapeutic target for AD, enhance early detection strategies, inform personalized interventions, and contribute to healthcare policies that support brain health and aging resilience. Funding: The study is funded by the Alzheimer Society Research Program.

P10

Investigating circadian patterns and seasonal variations in disruptive behaviours in mental health care

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Objective: Evidence suggests that circadian rhythms influence certain aspects of emotions and behaviours. However, little is known about whether behavioural problems follow a diurnal pattern in individuals at risk for both circadian and emotional dysregulation. This study examines whether disruptive behaviours among individuals receiving mental health care at a tertiary psychiatric facility exhibit circadian variation.

Methods: Data on "code white" alerts, emergency notifications of disruptive behaviour, were obtained from the hospital's occupational safety team for the years 2017-2023. The total number of code white alerts for each one-hour time bin across all days was calculated. A Fourier series model was applied in MATLAB to fit the data and extract parameters for the average number of code white events per hour, considering both the overall dataset and seasonal variations.

Results: Visual inspection revealed a sinusoidal pattern in hourly code white counts, with an acrophase occurring between 2 PM and 3 PM and a nadir between 3 AM and 4 AM. Curve fitting confirmed this pattern ($R^2 = 0.94$). Seasonal analysis indicated an earlier acrophase in summer and winter (1 PM to 2 PM) compared to spring and autumn (2 PM to 3 PM). Summer also demonstrated the highest mesor and amplitude.

Conclusion: These preliminary findings suggest a circadian modulation in the frequency of disruptive behaviour among individuals receiving mental health care. While further research is needed to explore the underlying mechanisms, this phenomenon may be related to reduced alertness and energy levels in the afternoon, which can impair emotional regulation and decision-making. Understanding the impact of circadian factors on disruptive behaviours could inform strategies to enhance self-regulation and guide healthcare teams in preventing and responding to behavioural emergencies more effectively.

P11

The absence of Neuroligin-2 differentially modulates wake/sleep architecture, spectral and multifractal activities in male and female mice

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Neuroligin-2 (NLGN2) is a synaptic adhesion molecule shaping GABAergic neurotransmission and for which mutations have been linked to neurodevelopmental disorders. The loss of NLGN2 in male mice was shown to increase the time spent in wakefulness, decrease the time spent in slow wave sleep (SWS), and to alter electrocorticographic (ECoG) activity. However, whether the lack of NLGN2 impacts wake/sleep states in female mice remains to be established. We aimed to compare sexes for the impact of the absence of NLGN2 on the wake/sleep architecture, and spectral and multifractal ECoG activities. Nlgn2 knockout (KO) mice and wild-type (WT) littermates were implanted with ECoG electrodes, and ECoG signals were recorded for 24 hours under undisturbed conditions. Nlgn2 KO animals of both sexes spent more time awake and less time in SWS and paradoxical sleep (PS), with KO males spending less time in PS during both the light and dark periods compared to WT males (difference only during the dark in females). Moreover, Nlgn2 KO animals displayed longer wakefulness and shorter SWS and PS episodes, and KO males (but not females) showed more wake and SWS episodes during the light period, suggesting an instability of vigilance states in KO animals. For the multifractal analysis, the most prominent Hurst exponent (Hm) was significantly increased in Nlgn2 KO animals during all three states. Also, Hm was less dispersed (less multifractal) in wakefulness during the light period in Nlgn2 KO animals, and less dispersed only in female KO during PS. Finally, Nlgn2 KO animals of both sexes showed spectral activity differences when compared to WT, notably a slower peak frequency during PS. This study highlights that the effects of lacking NLGN2 on wake/sleep phenotypes slightly differ between sexes in a manner that depends on time-of-day, and could help understanding sleep disturbances in neurodevelopmental disorders.

P12

Chronic circadian disruption alters cardiac function and glucose regulation in mice

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Cardiometabolic disease is a leading causes of death worldwide. One factor that may contribute to the risk, onset, and severity of symptoms is disrupted circadian rhythms. Our study uses two strains of mice to further elucidate this relationship: healthy controls, and a mouse model of insulin resistance with short freerunning periods (~22.75hrs) and enlarged hearts, raised in either a 24-hour or 22.75-hour LD cycle. Through glucose and insulin tolerance tests, routine electrocardiograms from 1-4 months old, and histology, we reveal worse cardiometabolic health outcomes for mice gestated and housed in a mismatched LD cycle compared to those in an LD cycle that matches their endogenous rhythm. This was characterized by heightened blood glucose levels following a glucose or insulin bolus, altered electrophysiological parameters of the cardiac waveform, and increased cardiomyocyte size. Circadian disruption due to work/social schedules or circadian-related disorders in people is often confounded with other unhealthy lifestyles. The present study demonstrates that circadian disruption on its own can lead to adverse health states.

P13

Effect of a cranberry proanthocyanidin-rich extract on metabolic health and circadian rhythm

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Background: Environmental cues play a fundamental role in maintaining energy homeostasis by regulating internal biological clocks that generate circadian rhythms. While light is the most well-known zeitgeber, other factors such as ambient temperature and diet also significantly influence these rhythms. The combined effects of these non-photic zeitgebers, along with the potential of chronobiotic substances to realign disrupted clocks and improve metabolic function, remain incompletely understood.

Aims: This study aimed to investigate the synergistic effects of diet, ambient temperature, and a cranberry proanthocyanidin-rich extract (CPRE) with a chronobiotic potential on the intrinsic clocks of metabolic tissues.

Material and methods: Male C3H/HeJ mice were fed a high-fat diet (HFD) for 12 weeks. During the final 4 weeks, they were exposed to either 10˚C or 30˚C and received a daily gavage of CPRE (0.2 mg/g) at zeitgeber time 2 (ZT2). Tissues were collected at ZT4-8-12-16-20-24. Food intake, body weight, body composition, blood glucose, insulin and triglyceride levels were measured. The expressions of metabolic genes and core circadian clock genes were analyzed in key metabolic organs.

Results: Regardless of temperature, CPRE improved glycemia during both the light and dark phases without significantly affecting food intake. CPRE also enhanced the expression of glycolysis-related genes in the liver. HFD disrupted the rhythmic expression of metabolic and clock genes, attenuating the chronobiotic effects of CPRE, which only partially restored rhythmicity.

Conclusion and perspectives: CPRE significantly improved glycemia in obese mice by enhancing liver glycolysis. However, these metabolic benefits occurred independently of a synchronization of the circadian clock.

P14

Coping with sleep disturbances and fatigue: the influence of gender, age and shift types among healthcare workers during the COVID-19

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Background
Healthcare workers (HCWs) face sleep disturbances and fatigue from demanding workloads seeking various coping strategies. This study examines factors affecting coping strategies selection during COVID-19.

Methods
A survey (June-August 2021) was conducted among Montreal frontline HCWs to collect data on demographics and coping strategies for sleep disturbances and fatigue. Logistic regression examined the impact of gender, age, and shift types on coping strategy selection.

Results
Among 520 participants (42.6 ± 11.1 years), 83.8% were women. Shift types included daytime (59.8%), evening (16.2%), night (11.7%), and rotating (12.3%) shifts. Common coping strategies were physical activity (45.8%), social support (36.0%), self-help/spiritual activities (33.7%), leisure (33.3%), and stimulants (24.4%). Fewer HCWs reported tobacco, alcohol or cannabis use (13.3%), medications (10.2%), medical support (10.2%), or psychotherapeutic support (8.1%). Women were more likely to seek social support (OR = 2.01, p = 0.013) and take medications (OR = 3.43, p = 0.043) than men. Older age correlated with reduced likelihood of seeking social support (OR = 0.84 per +10 years, p = 0.038) and stimulants use (OR = 0.72 per +10 years, p < 0.001). Compared to evening shift workers, those on daytime shifts (OR = 2.04, p = 0.014) and rotating shifts (OR = 2.51, p = 0.013) were more likely to seek social support. Rotating shift workers had lower odds of substances use than daytime (OR = 0.08, p = 0.014) and night shift workers (OR = 0.09, p = 0.027).

Conclusion
Gender, age, and shift types influenced HCWs' reported coping strategies to mitigate fatigue and sleep problems during COVID-19. These findings highlight the need for personalized coping resources for HCWs.

P15

Time-restricted feeding effects on colorectal tumorigenesis in the Apcmin model

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Circadian rhythms regulate daily physiology and impact cancer through many avenues such as regulating stress responses, anti-tumour immunity, metabolism, cell differentiation, apoptosis, and stem cell maintenance. Circadian rhythms also impact the gastrointestinal tract: many protein coding genes have circadian transcriptional rhythms regulated by the clock, and disruptions in clock activity can affect gastrointestinal regeneration. Loss of circadian rhythms, through Bmal1 loss-of-function, or environmental clock disruption has been shown to increase intestinal tumorigenesis via dysregulation of intestinal stem cell pathways. A form of nutrition called Time-Restricted Feeding (TRF), where food availability is restricted to peak activity, can boost and synchronize circadian rhythms and decrease tumour growth of lung cancer xenografts; however, whether TRF impacts the initiation of tumours is unknown. Apcmin mice develop tumours in the small intestine that are accelerated by circadian disruption. Pilot experiments performed in our lab suggest that TRF can reduce tumorigenesis in Apcmin mice, however, whether circadian rescue is a factor in this reduced tumorigenesis, is unknown. To determine how TRF reduces tumour number and regulates proliferative capacity and affects circadian/daily transcriptional rhythms in Apcmin mice, TRF will be performed and small intestine tissue will be analyzed. Intestinal tumour number will determine how TRF affects tumour initiation and size, and histopathology will determine further changes in tumour and cell proliferation and size, apoptosis, translational activity, and other processes, between TRF and non-TRF mice. Further RNA sequencing of the intestine will reveal how TRF affects daily transcriptional rhythms over the entire circadian cycle. Together these tests will characterize the cell and molecular biology underlying the effects of TRF on intestinal tumorigenesis. Funding is provided by Canadian Institute for Health Research, Worldwide Cancer Research, and the Cancer Research Society.

P16

Mild traumatic injury in the late night causes a circadian shift

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Traumatic brain injury (TBI) is a bump, blow, or jolt to the head that disrupts the proper functioning of the brain (CDC). Some common causes of TBI include falls, motor vehicle accidents, assaults, and sports injuries. Mild TBI (mTBI) (Glasgow coma scale 13-15) makes up 70-90% of all reported TBI cases and affects ~42 million people worldwide annually. Although moderate to severe TBI is diagnosed by CT scans, mTBI often goes undetected. Aside from the more recognized side effects of mTBI such as cognitive impairment and headaches, 1/3 of mTBI patients have dysautonomias and circadian rhythm disruptions. A circadian rhythm is ~24 hours and maintained by a master clock in the suprachiasmatic nucleus (SCN) which relays to and synchronizes peripheral clocks and is vital to the maintenance of many physiological cycles. Using the lateral head impact model of mTBI we found that 1. mTBI at ZT 19 (late night) induces phase advances in locomotor activity and wake-associated physiological temperature-rise onset via data collected from implanted recording devices. 2. mTBI in the late night advances the firing onset of SCN vasopressinergic (SCNVP) cells via electrophysiology. Immunohistochemistry also shows increased c-Fos activation in SCNVP cells after mTBI. In conclusion, this project establishes that mTBI causes a circadian phase shift, which may be associated with the activation of SCNVP cells.

P17

Inhibition of mitochondrial fragmentation in endothelial cells promotes blood-retinal barrier integrity and neuroprotection in experimental glaucoma

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Vascular endothelial cell (EC) dysfunction and loss of blood-retinal barrier (BRB) integrity during glaucomatous neurodegeneration is poorly understood. Here, we tested the hypotheses that: i) BRB dysfunction occurs in the early stages of glaucomatous damage, and ii) restoring EC mitochondrial function protects barrier integrity and promotes retinal ganglion cell (RGC) survival. Ocular hypertension (OHT) was induced by intracameral injection of magnetic microbeads in Endo-MitoEGFP mice, a strain with labeled mitochondria selectively in ECs. Fluorescein angiography was used to image in vivo retinal vascular leakage. BRB permeability was examined across the entire retina after retro-orbital administration of fluorescent tracers. Confocal imaging and Imaris software were used for 3D reconstruction and analysis of mitochondrial complexes. Reactive oxygen species (ROS) in retinal ECs were assessed with MitoSOX. The expression of tight junctions and mitochondrial fission proteins was quantified by immunoblotting. Mitochondrial fragmentation was inhibited with Mdivi1, a specific Dynamin-related protein 1 (Drp1) inhibitor. RGC density was stereologically quantified in RBPMS-stained retinas. Fundus angiography revealed progressive fluorescein leakage post-OHT induction, which persisted over time. Histological imaging showed a significant increase in tracer leakage (550 Da) in OHT-exposed retinas versus sham controls. We observed marked mitochondrial fragmentation in ECs in glaucomatous retinas concomitant with elevated Drp1 levels. Mitochondria fragmentation correlated with increased ROS production in ECs. The expression of the tight junction claudin 5 (Cldn5) in ECs was reduced during OHT. Mdivi1-mediated Drp1 inhibition restored mitochondrial integrity, reduced ROS levels, preserved Cldn5 expression, enhanced BRB function, and promoted RGC survival in glaucoma. Our data demonstrate marked mitochondrial fragmentation in ECs and early BRB integrity disruption caused by OHT-induced stress. Inhibition of the fission protein Drp1 prevented mitochondrial fragmentation, mitigated vascular leakage, and promoted RGC survival. These findings suggest that strategies that restore mitochondrial function are beneficial to preserve BRB integrity and counter neurodegeneration in glaucoma.

P18

Metabolomic profiling unveils retinal energetic stress in early glaucoma

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Metabolic dysfunction plays a pivotal role in the pathophysiology of glaucoma, contributing to retinal ganglion cell (RGC) death and subsequent vision loss. This study aimed to investigate whether, prior to neurodegeneration, ocular hypertension (OHT), a major glaucoma risk factor, disrupts retinal metabolism, leading to bioenergetic deficits, with a focus on central carbon metabolism. OHT was induced by intracameral injection of magnetic microbeads in mice. Retinas were collected two weeks post-injection, a timepoint with established OHT but undetectable RGC loss. Retinas from sham and OHT groups were randomized, blinded, and subjected to metabolomic testing. Liquid chromatography coupled with mass spectrometry (LC-MS) quantified concentration levels of glycolysis, tricarboxylic acid cycle (TAC), and pentose-phosphate pathway metabolites. Metabolomic analysis unveiled a substantial decrease in glycerol-3-phosphate and lactate levels in glaucomatous retinas, indicating disturbed glycolysis and TAC. Moreover, OHT-induced damage significantly reduced energy carriers, including ATP, ADP, GTP, GDP, and NAPDH. Notably, OHT led to a negative shift in ATP/AMP and ADP/AMP ratios, suggesting diminished oxidative phosphorylation (OXPHOS) activity and limited energy availability. These findings align with our previous work demonstrating AMP-activated protein kinase (AMPK) hyperactivation and mitochondrial dysfunction in early glaucoma. Our study identifies potential targets within key metabolic pathways for retinal neuroprotection, presenting novel avenues for further research.

P19

The circadian clock transcriptional repressor REV-ERBα/ß as a new pharmacologic target in HIV-1 cure interventions

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Background: Th17-polarized CD4+ T-cells are enriched in viral reservoirs (VR) in people with HIV-1 (PWH) receiving antiretroviral therapy (ART). Th17 cells express HIV permissiveness factors, including the circadian clock components/regulators BMAL1 (transcriptional activator binding to E-boxes in the HIV-LTR), RORC2 (regulator of Th17 polarization and HIV transcription) and REV-ERB¤/¤ (transcriptional repressors of BMAL1/RORC2). Thus, we hypothesized that REV-ERB¤/¤ inhibit HIV-1 by modulating BMAL1/RORC2 expression/activities.

Methods: Memory CD4+ T-cells of HIV-uninfected individuals were exposed to HIV-1 in vitro. Early/late reverse transcripts, and integrated HIV-DNA were quantified by nested real-time PCR. HIV-1 replication was quantified by FACS and ELISA. A viral outgrowth assay (VOA) was performed using memory CD4+ T-cells of ART-treated PWH. RNA-Sequencing was performed using the Illumina technology. Differential gene expression was validated by real-time RT-PCR and western blotting.

Results: REV-ERB¤ was predominant in CD4+ T-cells. TCR-mediated activation in memory CD4+ T-cells led to REV-ERB¤/¤ downregulation and RORC2 upregulation. SR9011 decreased RORC2 and IL-17A but not BMAL1 mRNA expression, and reduced HIV-1 replication/outgrowth in T-cells of ART-treated PWH. Counterintuitively, SR8278 also reduced HIV replication/outgrowth, in part by decreasing the expression of the HIV-1 co-receptor CCR5. In a single-round infection model, both SR9011 agonist and SR8278 antagonist increased HIV-DNA levels and intracellular expression of HIV-p24, but decreased viral release. These effects coincided with an increased SAMHD1 phosphorylation and BST2 expression, consistent with an increased reverse transcription but restricted viral release, respectively. Finally, RNA-Seq performed in TCR-activated CD4+ T-cells from ART-treated PLWH revealed an increased APOBEC3G expression in the presence of SR8278, indicative of an impaired virulence of progeny virions.

Conclusions: Altogether, our results provide evidence that REV-ERB differentially modulate specific steps of the HIV-1 replication cycle and support the use of pharmacological REV-ERB blockade as a novel strategy to revert HIV latency while limiting viral propagation in HIV-1 cure interventions.

P20

Wake/sleep architecture and electrocorticographic activity following the inactivation of cofilin in male and female mice

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Sleep is essential for cerebral homeostasis and neuronal plasticity. Sleep loss impairs plasticity and increases the intensity of subsequent sleep, as marked by an increase in slow wave activity on the electrocorticogram (ECoG). Cofilin, a protein involved in structural plasticity, was shown to be altered by sleep deprivation (SD), but its role in shaping ECoG activity during wake/sleep states remains to be explored. The aim of this study is to determine the involvement of cofilin in the regulation of ECoG activity in mice under both undisturbed and SD conditions, and to determine whether an effect depends on sex. The hypothesis is that cofilin inactivation will modify the quality of the ECoG during normal and recovery sleep.

To test this, adult male and female C57BL/6J mice were injected with an adeno-associated virus expressing an inactive cofilin (mutation of serine 3 to aspartic acid: AAV9-CaMKIIα-cofilinS3D-HA) or a control AAV (AAV9-CaMKIIα-eGFP) in the motor and visual cortices. ECoG electrodes were implanted during the same procedure. The ECoG signal was recorded for 48 hours without intervention, then during 6 hours of SD, and finally 42 hours of recovery. Preliminary results in both sexes indicate that cofilin inactivation did not alter the time spent in wakefulness, slow wave sleep or paradoxical sleep over the 24-hour baseline. The number of episodes and the mean episode duration of all three states also remained unchanged between experimental groups. For the motor cortex, spectral power during wakefulness tended to be higher under cofilin inactivation in comparison to controls for frequencies between 1 and 50 Hz but was unchanged by the manipulation for slow wave sleep and paradoxical sleep. The responses to SD will next be analyzed. This project will help to define the impact of cofilin inactivation on sleep quality under normal conditions and during recovery from sleep loss.

P21

Behavioral and physiological effects of cardiomyocytes-specific *Bmal1* knockout in male mice

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Cardiovascular disorders are a leading cause of mortality, often accompanied by mood disorders such as depression and anxiety, which adversely affect the quality of life and cardiovascular outcomes. This study investigates the role of Bmal1, a critical gene in maintaining cardiac function, in the context of both cardiac physiology and associated behavioral changes. We generated a cardiomyocyte-specific Bmal1 knockout (KO) mouse model using Cre-lox technology to selectively remove Bmal1 from heart muscle cells as validated with gene expression analysis, without affecting circadian clocks within extracardiac tissues. At 10-12 weeks of age, mice received an intravenous tail vein injection of cardiotropic viral vectors (AAV9-cTNT-Cre) to induce Bmal1 deletion. Following cardiac function was assessed over time, and behavioral consequences were evaluated through standardized tests. Our results indicate that Bmal1 KO mice demonstrated a progressive decline in cardiac function, highlighted by significant reductions in fractional shortening and ejection fraction. Behavioral assessments revealed anxiety-like symptoms, as evidenced by altered performance in the sucrose preference and novelty-suppressed feeding tests. Notably, no significant differences were observed in motor function, as measured by the Rota Rod test. These results indicate that cardiomyocyte-specific Bmal1 deletion significantly impacts both cardiac health and behavioral stability in adult male mice. The study underscores the pivotal role of Bmal1 in the interplay between cardiovascular disorders and mood disorders, contributing crucial insights into the molecular mechanisms underlying their comorbidity. This research may pave the way for novel therapeutic strategies targeting Bmal1 to improve outcomes in patients suffering from simultaneous cardiovascular and mood disorders.

P22

Preliminary evidence of altered 24-hour cortisol secretion in premenstrual dysphoric disorder

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Introduction
Premenstrual Dysphoric Disorder (PMDD) is a menstrual cycle–related mood disorder often characterized by insomnia during the luteal phase (LP). Both mood disorders and sleep disturbances have been linked to abnormal cortisol secretion, and there is evidence for menstrual cycle modulation of cortisol. We hypothesize that cortisol dysregulation prior to and during sleep contributes to sleep disruptions in PMDD.

Methods
Seven women (32.0 ± 5.7 years) with PMDD-related LP insomnia completed a constant posture protocol in both follicular (FP) and luteal phases (LP). During each 24-hour protocol (with an 8-hour sleep period), hourly blood samples were collected via an indwelling catheter and assayed for cortisol (radioimmunoassay). Hourly data points were aligned to time since lights on (TSLOn) and aggregated into 2-hour bins per participant, then averaged by menstrual phase. Mixed-model ANOVA assessed the effect of menstrual phase (FP vs. LP). One participant's FP data and four participants' LP data were incomplete, limiting sample size in each condition.

Results
Analyses showed a strong effect of time-of-day bin on cortisol ($p < 0.0001$). Including the menstrual phase (FP vs. LP) significantly improved the model fit ($p = 0.014$), and a time × menstrual phase interaction ($p = 0.025$) indicated that the 24-hour cortisol profile differed between menstrual phases. These results suggest altered LP cortisol rhythms compared with FP. Missing data in several participants likely reduced power to detect further differences.

Conclusions
Preliminary findings suggest that PMDD may involve altered 24-hour cortisol patterns during the luteal phase. Larger studies, with fewer missing data, are needed to clarify the role of phase-dependent cortisol changes in PMDD's insomnia and mood symptoms.

P23

Sex-specific effect of Bmal1 deletion in the dorsomedial striatum on alcohol consumption in mice

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Circadian clock genes play a central role in the regulation of behavior, including reward related processes, affective states, and motor functioning. Specifically, recent work has revealed a sexspecific effect of Bmal1 deletion in the striatum on voluntary alcohol consumption in mice: augmentation in males and suppression in females. Interestingly, Bmal1 deletion in the nucleus accumbens augmented alcohol consumption in both males and females, but the specific effect of Bmal1 deletion in other striatal subregions has not been determined. Thus, in the present study we ablated Bmal1 from neurons of the dorsomedial striatum (DMS) and dorsolateral striatum (DLS) of male and female mice and assessed voluntary alcohol consumption using an intermittent two-bottle choice test. The results revealed that Bmal1 deletion in the DMS decreases alcohol intake and preference in females but not in males and that deletion in the DLS had no effect in either males or females. Our result demonstrates a female-specific effect of Bmal1 deletion in the DMS on alcohol consumption. Thus, we studied alcohol consumption in ovariectomized females with Bmal1 deletion in DMS to assess the association between female hormone secretion and Bmal1 function in DMS. No difference in alcohol consumption and preference between ovariectomized Bmal1 ablated mice and the control group was found, whichm suggests that Bmal1 exerts its function in DMS only in the presence of female hormones. Overall, this work demonstrates a sex-specific and region-specific effect of Bmal1 on alcohol consumption. Future experiments should explore the mechanism driving the interaction between Bmal1 and female hormones in the DMS on motor coordination and drinking behavior.

P24

The genetics of temporal activity patterns in cichlid fish

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Temporal activity patterns reflect the repeated daily timing of various behaviours and physiological states driven by circadian rhythms and homeostatic pressure. A given species may be most active during the night (nocturnal), during the day (diurnal), at twilight (crepuscular) or at irregular intervals (arrhythmic). The molecular and evolutionary mechanisms driving differences in temporal activity patterns are poorly understood. To address this, we use the model clade of Lake Tanganyika cichlids, which demonstrate a wide variety of activity patterns and have abundant genomic information, to quantify this behaviour and investigate its genetic basis. We screened the temporal activity patterns of 60 cichlid species in a standardized lab setting. From this we identified two principal components of cichlid activity patterns, their day-night preference and their crepuscular preference. A phylogenetically corrected genome-wide association of these components of temporal activity patterns revealed unique variants highly associated with day-night preference and with crepuscular preference respectively. These preferences have a parabolic relationship with each other where species with a strong day or night preference tend to be non-crepuscular and crepuscular species tend to have a weak day-night preference, suggesting that crepuscularity may play a facilitative role in evolutionary transitions between diurnal and nocturnal activity. To further investigate the role of crepuscularity, a crepuscular (Neolamprologus brichardi) and arrhythmic (Neolamprologus crassus) cichlid species were crossed to produce hybrid generations (F1-F4) which will be used to perform quantitative trait loci mapping. Additionally, these results will be bolstered by a transcriptomic analysis to quantify differential gene expression between N. brichardi and N. crassus across different time points. Integrating the results from these three approaches (the genome wide association, quantitative trait loci mapping and differential expression analysis), will allow us to identify the genetic signature of crepuscular preference in cichlid fish.

P25

Selective dopamine transporter knock out in the adult ventral tegmental area leads to circadian period lengthening and emergence of infradian locomotor components

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We have previously shown that dopamine transporter knockout (DAT-/-) mice tend to exhibit a second rhythmic locomotor component in addition to the primary circadian component when submitted to constant darkness. These additional rhythms typically exhibit periods longer than 24 hours and are therefore referred to as infradian rhythms. This second locomotor component is observable even in the absence of the circadian timing system, suggesting that a second rhythm generator is operative in DAT-/- mice which can act independently from the chief circadian pacemaker in the suprachiasmatic nucleus (SCN). A similar secondary, infradian rhythm component can be induced by chronic methamphetamine treatment, which we previously showed to be abrogated upon elimination of DA neurons of the VTA or their capacity to produce DA. To further characterize the role of the VTADA neurons in infradian rhythm generation, we disrupted the DAT gene selectively in the VTA using a CRISPR-Cas9 based viral approach. We found that VTADAT-KO leads to expansion of the daily activity window, lengthening of the circadian locomotor period, and, ultimately, development of infradian rhythmic components. These new results together with our previous findings indicate that VTADA neurons are necessary and sufficient for infradian sleep-wake rhythm production in support of the notion that they harbor or are an integral component of the oscillator that drives these rhythms. The study is supported by grants from Canadian Institutes of Health Research (CIHR) and Natural Sciences and Engineering Research Council of Canada (NSERC).

P26

Going wild: circadian rhythms of lab rats living in social groups outdoors

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Our understanding of circadian rhythm and sleep regulation in mammals is based almost entirely on laboratory studies in which animals live under controlled but highly artificial conditions. Field studies are few, but among these, reports of temporal niche 'misbehaviour' are not uncommon. We built a large (25m2) seminatural enclosure to study circadian rhythms and sleep in lab-bred and wild-caught rats living in social groups outdoors. The enclosure is protected from rain and sun by a transparent roof and tree cover and contains enrichment and bedding materials, feeding and drinking stations, an insulated burrow annex with three ~ 0.5m2 interconnected light-proof nest chambers and infrared video recording cameras. Results of the inaugural study will be presented. Five young adult male rats (Long-Evans, Charles River Labs) were implanted with miniature accelerometers (Nanotags, Kissei Comtec) and radiofrequency ID tags (UID, USA) to record locomotor activity for 1 week in the lab and 6 weeks outdoors (Oct 8 - Dec 3, 2024). Three rats were housed in the seminatural and 2 rats in an adjacent modified lab cage for comparison. In the seminatural, the rats retained a strongly nocturnal chronotype. Total daily activity was markedly elevated. The timing of nocturnal activity onset (CT12) was delayed for a few days, but gradually advanced across the 6 weeks outdoors, consistent with tracking dusk. An unexpected, acute advance shift appeared to be induced when the rats were handled to retrieve data wirelessly, at dusk on days 30 and 34, an effect that we did not see in the laboratory. There were small but consistent individual differences in circadian phase and in specific behaviours (e.g., nest-building and food-hoarding behaviors). Analyses of feeding, drinking, and sleep, and associations of circadian parameters with daily variations in weather, are pending.

P27

Impact of osteocyte-specific Bmal1 deletion on bone mass, microstructure, and strength

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Background: Osteocytes modulate bone structure through osteoblast-mediated bone formation and osteoclast-mediated bone resorption. Studies have shown that the conditional deletion of circadian transcription factor Bmal1 in osteoclasts and osteoblasts results in high and low bone mass phenotypes, respectively. Thus, this project aims to investigate how the conditional deletion of Bmal1 in osteocytes (OcKO) affects cortical bone mass, microstructure and strength. Methods: OcKO mice were obtained using the Cre-loxP system and a Dmp1 promoter-driven Cre recombinase. Tibiae from 10-week-old female and male OcKO mice and their littermate controls (Bmal1fl/fl and Dmp1Cre) (n=7/genotype/sex) were scanned using in-vivo microCT (8μm voxel size) at baseline and 21 days later, after which the mice were euthanized. We analyzed bone strength in femora using three-point bending and bone formation in tibiae using time-lapse imaging and histomorphometry. One-way ANOVA followed by student`s T-tests determined the effect of genotype within each sex ($p<0.05$). Results: PCR results confirmed Bmal1 deletion in osteocytes. Significant differences were noted in female mice, with OcKO mice exhibiting greater cortical thickness and area compared to Bmal1fl/fl and Dmp1Cre mice. Total area was also significantly greater in OcKO female mice compared to Bmal1fl/fl mice. Male OcKO mice showed no microstructural differences between genotypes. There were no significant differences in bone strength or mineral apposition rate between genotypes within each sex. Discussion: The results demonstrate that while knockout of Bmal1 in osteocytes leads to an increase in cortical bone mass at the tibial mid-diaphysis in female mice, no distinct phenotypic changes were observed in male mice. Studies are ongoing to confirm that decreased bone resorption contributed to the greater bone mass in OcKO mice. Further investigations into the molecular mechanism underlying the sex-dependent differences we observed may lead to identification of novel molecular targets to improve bone health.

P28

Investigating transcriptional dynamics of circadian and cell cycle interactions via dual synchronization and RNA velocity

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The circadian clock and cell cycle are fundamental biological oscillators whose coordination ensures temporal regulation of cellular processes. Disruption of either of these biological processes is linked to pathologies, including cancer. While bidirectional interactions between the two biological processes are hypothesized, the exact molecular mechanisms remain elusive. This study aims to elucidate, at the transcriptional level, how the circadian clock gates cell cycle progression and how cell cycle phases feed back onto circadian rhythms in mouse NIH3T3 fibroblasts. We employed a dual synchronization strategy: serum deprivation (0.6% FBS, 48 hours) to arrest the cell cycle, followed by dexamethasone (100 nM) pulses administered 12 hours apart to synchronize circadian clocks at two distinct time points. Samples were collected every 2 hours over 48 hours post-synchronization for RNA sequencing to study transcriptional dynamics using RNA velocity analysis. In parallel, the dual synchronization was validated using both DBP-luciferase bioluminescence (30-minute intervals, 72 hours) and flow cytometry using propidium iodide staining (2-hour intervals, 72 hours). Preliminary luciferase data confirmed robust 24-hour circadian oscillations phase-shifted by 12 hours between the two time points, while flow cytometry confirmed the G0/G1 arrest during serum deprivation and release in the cell cycle upon serum addition. Future RNA velocity analysis will enable the study of the transcriptional dynamics of the expression of circadian (e.g., Bmal1, Per2) and cell cycle (e.g., Wee1, Cyclin D1, p21) genes and their respective interaction overtime. This integrated approach will clarify whether circadian phases restrict cell cycle transitions (e.g., S/G2) and if mitotic events reset circadian rhythms.

P29

Decoding the evolution and genetics of sleep architecture across cichlid fish

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Sleep is a complex, paradoxical behaviour observed and necessary to every animal studied. Sleep has been linked to many essential biological processes, including energy conservation, immune function, development, brain plasticity and cognition. While all animals sleep, the structure and composition of sleep varies widely across and within species. Sleep consolidation is a critical aspect of the sleep/wake cycle, referring to how long and concentrated sleep bouts are, which may be consolidated all at once (monophasic) or split into multiple bouts throughout the day (polyphasic). Due to vast taxonomic differences across species, it is difficult to interpret behavioural diversity, including diversity in sleep between species, due to confounding variation between taxa. For this reason, I use the model clade of cichlid fish to understand the evolution of differences in sleep architecture, their relation to cognition, and identify the genetic signatures associated with them. I take a comparative approach, integrating behavioural variability, evolutionary histories, and genomic analyses. Our work on cichlids identified that they display high inter-species variation in sleep behaviours, including total duration, circadian timing, and sleep consolidation. Sleep is also known to cycle between different states, which has been commonly observed and studied in mammals, but also likely present across the animal kingdom. Up until the discovery of sleep states in lizards, it was believed that sleep states evolved in endotherms. It is not clear whether distinct sleep states exist in fish, due to the electrophysiological correlates of mammalian sleep being divergent in fish and other ectothermic species. Using statistical modelling and behavioural experiments, I will determine whether these sleep states exist in cichlids to better understand the evolution of sleep. My research aims to comprehensively answer these important questions about the form, function, timing and evolution of sleep.

P30

Complex interactions between food and light-entrainable activity rhythms revealed by LD cycle shifts

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Circadian rhythms in mammals are regulated by light-entrainable circadian oscillators (LEO's) in the suprachiasmatic nucleus, and food-entrainable circadian oscillators (FEO's) elsewhere in brain and body. Some FEOs are thought to control daily rhythms of food anticipatory activity (FAA) that emerge when food is limited to a fixed time of day or night. SCN ablation eliminates light-entrainable but not food anticipatory rhythms, therefore FEOs and LEOs have been conceptualized as anatomically separate and zeitgeber specific. Early studies reporting effects of LD and mealtime shifts on food- and light-entrained rhythms were interpreted as evidence for weak coupling between LEOs and FEOs. Ehichioya et al (2023) reported that FAA in mice shifts in parallel with light-entrainable rhythms following a 6h LD shift. These effects were evident in per KO mice that lacked SCN cycling, suggesting that FAA was controlled by extra-SCN LEOs. We examined this issue in rats using operant levers and motion sensors to assay FAA and light-entrainable rhythms. In rats fed at ZT4, response to a 6h LD advance was variable. FAA was stable in some case, but advanced by a small amount in other cases, either for the first few days, or after a week or more, before returning to its initial phase. In rats fed at ZT4 and ZT16, a 6h LD advance affected FAA differentially. FAA to the ZT4 meal immediately advanced ~1h, and then delayed to its initial phase, whereas FAA to the ZT16 meal initially delayed and then advanced. When food was available ad libitum, the response to a 6h LD advance resembled re-entrainment 'by partition', with late-night activity delaying and early-night activity advancing. Changes in timing of FAA to ZT4 and 16 mealtimes may reflect beat phenomena created as advancing and delaying LEOs change phase relative to FEOs. Other interpretations are possible. Supported by NSERC.

P31

Circadian regulation of core body temperature in an androgen receptor mutant mouse model of metabolic syndrome

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Background: Metabolic syndrome is a rapidly escalating global health threat, affecting 25% of the population. Androgen receptor signalling is involved in metabolic homeostasis in men and, when disrupted, can cause metabolic abnormalities. Male mice with a humanized androgen receptor (AR-19Q), progressively develop symptoms resembling MetS by the time they are six months of age. Additionally, our preliminary data suggests a potential disruption in circadian function, supported by evidence of accelerated re-entrainment of running wheel activity following a 6-hour phase advance shift in the light-dark (LD) cycle in male mutant mice. Here, we aim to investigate whether the circadian disruption in AR-19Q mice is driven by the androgen mutation or the progression of the metabolic disease and to assess whether this accelerated re-entrainment is reflected in core body temperature, a reliable indicator of suprachiasmatic nucleus (SCN) output.

Methods: Using a humanized androgen receptor mouse model (AR-19Q), we investigated core body temperature as a measure of circadian rhythmicity. Body temperature was recorded in control and mutant male mice. Temperature rhythms, including mesor and amplitude, were compared at three and six months of age. Additionally, torpor was induced through food restriction to assess torpor recovery dynamics between both time points. Moreover, we implemented a 6-hour phase advance to assess core body temperature adaptations.

Results: Our data suggests that AR19-Q male mice show differences in patterns of torpor recovery. They also exhibit significantly faster re-entrainment of body temperature following an advanced LD cycle shift. This result provides further evidence of an alternative circadian phenotype in the AR19-Q. This accelerated re-entrainment could be attributed to disrupted oscillations of clock genes in the SCN of the AR19-Q.

Conclusions: These results expand the circadian profiling of the AR-19Q mouse model for metabolic dysfunction research and provide further evidence for the disruption of SCN function in MetS.

P32

The role of the TOR pathway in circadian rhythmicity in *Neurospora crassa*

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Circadian rhythms regulate diverse biological processes across species. While transcription-translation feedback loops (TTFLs) are fundamental in many systems, some organisms exhibit rhythmicity independent of TTFLs. In Neurospora crassa, FRQ-less oscillators (FLOs) generate rhythms without the core FRQ/WCC oscillator, suggesting alternative molecular mechanisms. Our lab identified the vacuolar TOR-associated protein (VTA) and its binding partner, GTR2, as components of the TOR pathway that influence circadian rhythmicity in both FRQ-sufficient and FRQ-less conditions. Given the conserved role of TOR in nutrient and energy sensing, we hypothesize that the TOR pathway could function as a FLO. My research investigates whether TOR activity maintains rhythmicity in frq knockout strains by assessing S6 phosphorylation patterns as a marker of TOR signaling. Preliminary results indicate that rhythmicity persists in frq mutants, supporting the idea that the TOR pathway operates as an independent oscillator. To further explore this, we are conducting experiments using heat pulse entrainment and analyzing the effects of additional genetic modifications, including mutant strains lacking frq, vta, and gtr2. Understanding the role of the TOR pathway in circadian regulation is crucial, as the TOR pathway is a central regulator of metabolism, growth, and stress responses in eukaryotic cells. If confirmed as an alternative circadian oscillator, this research could reshape our understanding of metabolic timekeeping mechanisms beyond the traditional TTFL model. Furthermore, given the conservation of TOR signaling across species, these findings may have broader implications for circadian biology in other organisms, including humans. Disruptions in circadian rhythms are linked to various metabolic disorders, and insights into TOR-based oscillatory mechanisms could provide new avenues for therapeutic interventions.

P33

Chemogenetic activation of orexin cells induces non-photic-like phase shifts in mice

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The intergeniculate leaflet (IGL) and its primary neurotransmitter, neuropeptide Y (NPY), participate in non-photic phase shifting, but precisely how non-photic stimuli activate the IGL remains unknown. One signal that could stimulate the IGL is the arousal-inducing peptide orexin (OX; i.e. hypocretin). In addition to non-photic manipulations activating OXergic cells and OX fibers densely innervating the IGL, ex vivo application of OX activates IGL cells, including NPYergic cells. Consistent with these findings, our lab recently discovered that in mice, a significant proportion of NPYergic IGL cells activated by sleep deprivation have close OX appositions. To further investigate this relationship, this study tested whether the activation of OXergic cells induces non-photic-like phase shifts. Using Hcrt-CRE mice subjected to viral infusions of an excitatory DREADD aimed at the OX-containing region of the lateral hypothalamus, preliminary results suggest that activation of OXergic cells with the selective DREADD agonist deschloroclozapine in male and female Hcrt-CRE mice produces non-photic-like phase shifts compared to control C57Bl/6J mice. Although these results are preliminary, this study provides supplementary support for OX as an arousal signal that could activate the IGL during non-photic phase shifts.

P34

Temporal patterns in social interaction as a motivated behaviour

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The mammalian timekeeping system operates as a hierarchy and biological rhythms manifest in a wide range of behaviours. Circadian rhythms in spontaneous locomotion are governed by the light-entrainable SCN, while more complex goal-directed behaviours, such as food anticipatory activity and time memory, utilize SCN-independent mechanisms entraining to significant events. Social interaction, however, is a uniquely complex behaviour that requires reciprocal entrainment between individuals. Both its rhythmic patterns and its place within the clock hierarchy remain unclear. Our study focuses on the circadian and ultradian rhythmicity in rodent social interaction, especially how these rhythms compare to the spontaneous wheel-running behaviour. We continuously tracked social interaction and wheel-running activity in paired mice. In a three-chamber apparatus, mice occupied the side chambers kept in constant darkness, where their wheel-running activity was recorded. Social interaction was recorded in the middle chamber, which was made mildly aversive by bright illumination and divided by a grid that permitted tactile contact but prevented mice from crossing to the other side. Active social interaction was quantified as the time both mice were simultaneously present by the grid, while social motivation was additionally measured by individual entries into and time spent in the middle chamber. Social interaction patterns were compared between paired mice and single-housed controls to distinguish social motivation from general exploratory activity. Half of the mice underwent SCN ablation to test whether circadian social rhythms persist independently of the SCN and whether social behaviours aligns with SCN-driven locomotion. The data will be analyzed to see whether social interaction follows its own oscillatory patterns or integrates into the broader circadian hierarchy. (This work was supported by the Natural Sciences and Engineering Research Council of Canada (NSERC) http://nserc-crsng.gc.ca: RGPIN-2018-06411 to M.R.R.)

P35

Site- and cell-type-specific miRNA and mRNA genes and networks across the CNS

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Biological rhythms control gene expression, but effects on central nervous system (CNS) cells and structures remain undefined. Gene expression rhythms can be both site- and cell-specific. Identifying patterns of gene rhythmicity across the CNS is necessary for both the study of chronobiology and to make sense of data obtained in the laboratory. We now identify cycling mRNAs, miRNAs, gene networks and novel mRNA-miRNA co-expression pairs in the cortex, hypothalamus, and corpus striatum using high-dimensional datasets. A searchable catalogue (https://www.ghasemloulab.ca/chronoCNS) was created to help refine the analysis of cellular/molecular rhythmicity across the CNS. Our study sheds light on the contribution of diurnal rhythms and mRNA-miRNA interactions to CNS function. This work was supported by grants from the Natural Sciences and Engineering Research Council of Canada (NSERC; #RGPIN-05604, to N.G.) and Brain Canada (to N.G.).

P36

Decoding the genomics of circadian and circannual rhythms in teleost fishes

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Circadian and circannual rhythms are primarily influenced by photoperiod, yet the genetic mechanisms governing these rhythms in vertebrates remain poorly understood. In this study, we adopt an evolutionary approach to investigate the genetic basis of these temporal rhythms by examining the genomes of teleost fishes, which represent approximately 50% of all extant vertebrate species and over 95% of aquatic vertebrates, and which exhibit remarkable diversity in their morphology, physiology, behaviour, ecology, and genetics. Circadian and circannual activity patterns also vary greatly across fish species, with different species being active at different times of day, and different species exhibiting different seasonal phenotypic changes such as reproductive behaviour and feeding. These variations provide a unique opportunity to explore how genetic factors may influence the regulation of daily and seasonal rhythms. The SV (saccus vasculosus), a fish-specific brain organ influenced by photoperiod, plays a role in seasonal regulation of activity patterns and varies in complexity across species, including complete absence in some. In collaboration with M. Policarpo (Max Planck Institute), we are developing a pipeline to identify gene duplications and pseudogenizations in teleost fish gene families through iterative BLAST searches, sequence alignment, and phylogenetic analysis. This pipeline will be used to explore gene repertoires of genes associated with circadian and circannual behavioural rhythms, as well as genes expressed in the SV, including opsins, hormones involved in food intake and reproduction, as well as clock genes and sleep/wake-related neuropeptides. We will look for correlations between the repertoire of these gene families and both the presence and degree of development of the SV across species, as well seasonal variations in the habitats of these species and associated seasonal phenotypic changes, temporal activity patterns, morphological traits, and ecological characteristics.

P37

Exercise modifies systemic core clock expression and promotes de-novo transcriptional programmes

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Introduction: Across organ systems, we have reported an age-related decline in the number of genes oscillating in a circadian pattern. In skeletal muscle, rhythmic coordination of key biological processes such as proteostasis are lost which likely contributes to a decrease in muscle size and muscle quality with age. We hypothesized that exercise training may modulate systemic core clock expression and restore 'youthful' transcriptional programmes in skeletal muscle with ageing.

Methods: In this study, we obtained male C57BL/6J mice from the National Institute of Aging colony with terminal endpoints at 6, 20 and 29 months of age, (n=106). Mice were assigned to sedentary control conditions, or a 32-day voluntary wheel running exercise intervention. After 32 days, wheels where manually locked for 48-hours and mice were exposed to constant darkness (DD), placing the mice into a 'free-running' circadian state. Mice were euthanized via live cervical dislocation under red light with gastrocnemius muscles, liver and peripheral tissues collected every 4-hours for 24-hours to generate a circadian time course. Combining transcriptomic profiling (RNA-seq) with the assay for transposase accessible chromatin with sequencing (ATAC-seq), we mapped the first aging, circadian transcriptome and chromatin landscape in skeletal muscle and studied its relationship with rhythmic gene expression across age and in response to exercise training.

Results: A large proportion of genes losing rhythmicity at the gene expression level with age in skeletal muscle, also had reduced transcription start site/promoter (TSS) accessibility suggesting epigenetic silencing contributes to the loss of their circadian expression pattern. Furthermore, we identified age dependent and age-independent exercise responsive chromatin loci/dynamics and de-novo circadian gene expression patterns with exercise training across the lifespan. Our results promote the potential efficacy of short-term exercise interventions in restoring healthier circadian transcriptional networks with ageing and potentially healthspan.

P38

The role of the cell adhesion protein NLGN1 in modulating the responses of the circadian clock to light

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Circadian rhythms are internally driven 24-h cycles in many physiological processes maintained by a self-sustained biological clock. In mammals, the main circadian clock is located in the suprachiasmatic nucleus (SCN) of the hypothalamus. The SCN network exhibits periodic changes in its communication properties allowing it to synchronize firing rhythms and adjust physiological functions to the light/dark (LD) cycle notably via glutamatergic neurotransmission. Neuroligin-1 (NLGN1) shapes the function of glutamatergic synapses. Hence, we aim to assess the impact of NLGN1 in modulating the circadian clock and its response to light. Running-wheel activity of Nlgn1 knockout (KO) and wild-type (WT) mice of both sexes was monitored under different lighting conditions. Under a 12h:12h LD cycle, Nlgn1 KO mice exhibited similar activity profiles in comparison to WT mice. However, Nlgn1 KO mice showed a longer endogenous period in constant darkness, and fewer activity counts under constant light compared to WT littermates. To understand the role of NLGN1 in light response, activity phase shifting and SCN cFOS staining were measured following a one-hour light pulse at circadian time 15 (CT15). Nlgn1 KO mice showed a reduced phase shift of activity in comparison to WT littermates. Moreover, KO showed less cFOS positive cells in the SCN than WT mice. To localize the actions of NLGN1 in the light response pathway and rule out alterations in retinal visual inputs, AAV-driven neuronal NLGN1 expression was introduced into the retinas of Nlgn1 KO or WT mice. Neither Nlgn1 rescue nor overexpression modified the electroretinogram (scotopic and photopic) or the light-induced phase shift of locomotor activity compared to control manipulations, suggesting a localized role for NLGN1 specifically in the SCN. Altogether, the results suggest that the synaptic adhesion molecule NLGN1 play a role in SCN functioning and photic entrainment, and further the understanding of entrainment pathways in the SCN.

P39

PKA instructs Drosophila Clock protein in regulating circadian transcription, mediating transcriptional synchrony in the circadian neuronal network

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Circadian rhythms are behavioural and physiological responses to rhythmic environmental changes, such as photoperiod and temperature. Such behavioural rhythms are regulated by a transcription/translation negative feedback loop called the circadian clock, which regulates the daily expression of several hundred genes. In Drosophila, the circadian clocks are found in ~240 neurons that are arranged into distinct clusters across the brain, suggesting a need for communication across the clusters to maintain coherent behavioural rhythms. Neurotransmitters connect of these clusters, often acting through G-protein coupled receptors (GPCRs), forming a neuronal network. Among the functions of GPCRs is regulation of cytosolic cAMP levels that serve as a secondary signal to relay extracellular instructions to internal cellular machinery. PKA is a kinase that responds to cAMP and activates a wide variety of proteins through phosphorylation. We have found that PKA phosphorylates CLK protein to repress function of the transcriptional activator complex of the circadian clock. This site is conserved across various species of insects, fish and mammals. When PKA is knocked down in distinct circadian neuronal clusters, both the local circadian clocks and overall behavioural rhythms change differently. Thus, PKA is a signaling molecule that responds to various instructions in distinct circadian neurons to regulate the circadian clock, maintaining both circadian clock synchrony and ensuring coherent behavioural rhythms.

NOTES