Parental
Brain 2025

Parental Brain 2025

Program and abstracts

Parental
Brain 2025

Table of Contents

Parental
Brain 2025

1. Program

May 7

1:30pm - Registration

2:30pm - Welcome and Keynote Speaker

NEUROANATOMICAL CHANGES ASSOCIATED WITH HUMAN PREGNANCY
Dr. Susana Carmona, Instituto de Investigación Sanitaria Gregorio Marañón, Madrid, Spain

3:15pm - Coffee Break

3:30pm - Symposium 1

THE FATHERING BRAIN: HOW GREAT DADS ARE MADE, NOT BORN
Dr. Darby Saxbe, University of Southern California, USA.

NEUROBIOLOGICAL CHANGES ACROSS THE TRANSITION TO HUMAN FATHERHOOD
Dr. James Rilling, Emory University, USA.

CARING DADS: THE SOCIAL NEUROSCIENCE OF ATTACHMENT AND CAREGIVING IN FATHERS
Dr. Pascal Vrticka, University of Essex, England.

SENSORY PLASTICITY IN CALIFORNIA MOUSE FATHERS
Dr. Wendy Saltzman, University of California Riverside, USA.

A NEURAL BASIS FOR REINFORCEMENT OF PARENT-INFANT INTERACTIONS
Dr. Lauren O'Connell, Stanford University, USA.

5:15pm - Poster Presentations

Young Investigator Aperitif

BeMother Exhibition (All Day)

May 8

9:00am - Keynote Speaker

NEUROENDOCRINE BASIS OF RODENT MATERNAL BEHAVIOUR: MY JOURNEY FROM OXYTOCIN VIA VASOPRESSIN TO CRF – AND BACK
Prof Dr Oliver Bosch, Fakultät für Biologie und Vorklinische Medizin, Universität Regensburg, Germany

9:45am - JNE Young Investigator Symposium

THE TRANSITION TO MOTHERHOOD: A MULTILEVEL STUDY ON THE BRAIN'S TRAJECTORY ACROSS PREGNANCY AND POSTPARTUM.
Camila Servin-Barthet, Universitat Autònoma de Barcelona, Barcelona, Spain

THE HYPOTHALAMUS UNDERGOES DYNAMIC ADAPTATIONS IN THE TRANSITION TO MOTHERHOOD
Maria Paternina-Die, Instituto de Investigación Sanitaria Gregorio Marañon, Madrid, Spain

SINGLE-CELL RNA SEQUENCING OF THE MATERNAL HYPOTHALAMUS REVEALS A DISTINCT NEUROENDOCRINE TRANSCRIPTOME IN PREGNANCY
Risha Amarsi, King's College London, London, United Kingdom

THE ROLE OF MIDBRAIN DORSAL RAPHE CRFR2 IN POSTPARTUM CAREGIVING AND AFFECTIVE BEHAVIORS
Taryn Meinhardt, Michigan State University, United States

EXAMINING THE ROLE OF IL-1R ANTAGONISM IN TREATING POSTPARTUM DEPRESSION USING A RODENT MODEL
Romina Garcia de Leon, University of Toronto, Canada

NEURAL SUBSTRATES IN THE POSTPARTUM BRAIN FOR FLEXIBLE MATERNAL CARE
Mingyu Yang, University Hostpital Cologne, Germany

11:15am - Coffee Break

11:30am - Symposium 2

SOCIAL PHYSIOLOGY: THE METABOLIC ROOTS OF CAREGIVING
Dr Shir Atzil, The Hebrew University of Jerusalem, Israel.

MOTHERS WITH OPIOID USE DISORDER: CLINICAL TRIAL OF MOM POWER PARENTING PSYCHOTHERAPY WITH MULTIMODAL NEUROIMAGING
Dr James Swain, Stony Brook University, USA.

DEVELOPMENT OF RAPID-ACTING NEUROACTIVE STEROID ANTIDEPRESSANTS FOR POSTPARTUM DEPRESSION
Dr. Kristina Deligiannidis, Feinstein Institutes for Medical Research, USA.

REDUCED EXTRACELLULAR FREE WATER IN THE BRAIN IN POSTPARTUM DEPRESSION
Dr. Daniel Bergé, Hospital del Mar Research Institute, Barcelona, Spain.

CAN TARGETING THE GUT-MICROBIOTA HELP US UNDERSTAND PLASTICITY OF THE MATERNAL BRAIN?
Dr. Jodi Pawluski, University of Rennes, France.

1:15pm Lunch Break (lunch not provided)

2:45pm - Symposium 3

DEVELOPING A RODENT MODEL OF POSTPARTUM ANXIETY THAT TRANSLATES TO HUMAN SAMPLES
Dr. Bronwyn Graham, University of New South Wales, Australia.

A PROLACTIN-SENSITIVE NEURAL CIRCUIT THAT REGULATES REWARD PATHWAYS AND PARENTAL BEHAVIOUR IN MALES AND FEMALES
Dr. Rosie Brown, University of Otago, New Zealand.

NEUROIMMUNE REGULATION OF PLASTICITY IN THE MATERNAL BRAIN FOLLOWING GESTATIONAL STRESS
Dr. Benedetta Leuner, Ohio State University, USA.

STATE-DEPENDENT FLEXIBILITY OF PARENTAL CIRCUITS
Dr. Jonny Kohl, The Francis Crick Institute, England.

LOVE, DEATH, AND OXYTOCIN: THE CHALLENGES OF MOUSE MATERNAL CARE
Dr. Robert Froemke, New York University, USA.

4:30pm - Coffee Break

4:45pm - Poster Presentations

6:30pm - Conference Dinner

BeMother Exhibition (All Day)

May 9

9:30am - Symposium 4

CELLULAR MECHANISMS MEDIATING THE LONG-TERM EFFECTS OF PREGNANCY, POSTPARTUM AND STRESS EXPERIENCES IN THE MATERNAL BRAIN
Dr. Jennifer Chan, Mount Sinai School of Medicine, New York, USA.

DIVERSE FORMS OF PLASTICITY SUPPORTING MATERNAL AGGRESSION IN FEMALE MICE
Dr. Takashi Yamaguchi, New York University School of Medicine, New York, USA.

UNCOVERING CONTRIBUTIONS OF THE MEDIAL PREOPTIC AREA TO MATERNAL SENSITIVITY
Dr. Mariana Pereira, Psychological & Brain Sciences University of Massachusetts, Amherst, USA.

PROMOTING LARGE-SCALE DATASETS AND COLLABORATION IN HUMAN MATERNAL BRAIN RESEARCH
Dr. Magdalena Martínez-García, University of California Santa Barbara, USA.

PUP PHEROMONES INDUCE MATERNAL BEHAVIOURS
Dr. Ferran Martínez-García, UP Medicine, Universitat Jaume I, Castelló de la Plana, Spain.

SEROTONIN RELEASE IN THE NAC AFFECTS MATERNAL BEHAVIOR
Dr. Clémence Simonnet, University of Geneva, Switzerland.

11:30am - Coffee Break

11:45am - Keynote Speaker

Maite Egoscozabal and Laura Baena
Malasmadres Club, Spain

12:30pm - Closing Comments

BeMother Exhibition (All Day)

2. Abstracts of the keynote speakers and symposia speakers

MAY 7

KEYNOTE SPEAKER

NEUROANATOMICAL CHANGES ASSOCIATED WITH HUMAN PREGNANCY

Dr. Carmona S

In this talk, I will present recent findings from longitudinal MRI studies that track women from preconception through the postpartum period. Current evidence reveals that pregnancy induces significant and enduring changes in the human brain. These changes appear to be linked to fluctuations in sex steroids and may play a crucial role in facilitating the maternal transition.

SYMPOSIUM 1

THE FATHERING BRAIN: HOW GREAT DADS ARE MADE, NOT BORN

Saxbe D

University of Southern California, USA

This talk will review several studies on brain changes across the transition to parenthood in first-time human fathers. We find that men show cortical volume decreases that are similar to those seen in mothers, but are less significant and more variable. We also show that when men express more motivation to parent, and more engagement in parenting, they show larger gray matter volume decreases. At the same time, gray matter volume decreases are associated with more postpartum mental health problems and poor sleep quality. The talk will also describe research on perinatal resting state connectivity and white matter changes in men, and functional studies on men reacting to infant stimuli and emotional faces.

NEUROBIOLOGICAL CHANGES ACROSS THE TRANSITION TO HUMAN FATHERHOOD

Rilling JK

Department of Psychology, Emory University, USA

Among biparental non-human species, males often experience neurobiological changes that prepare them for fatherhood. Recent studies in human fathers have demonstrated changes in cortical thickness across the transition to fatherhood, but changes in brain function have been only minimally explored. We recruited first-time expecting fathers and non-father controls for a longitudinal study that followed men across their transition to fatherhood to document changes in brain anatomy and brain function. Structural and functional MRI scans were acquired from expecting fathers between 4 and 5 months gestation and again at 4 postnatal months, after several months experience with their infant. Nonfather controls were scanned

over a similar time interval. Participants viewed infant photographs during the fMRI scan. New fathers experienced increases in cortical thickness in the right insula, pars opercularis, supramarginal gyrus and orbitofrontal cortex that were not found in nonfathers. In response to cues predicting infant pictures, new fathers showed a pre- to postnatal increase in activation of brain regions that are part of the mesolimbic dopamine system, a system involved with parental motivation, and this change was not found in non-father male controls. Compared with nonfathers, fathers also showed larger increases in activation to infant cues within the above cortical regions that showed volumetric increases. Finally, fathers, but not nonfathers, showed increased activation to infant pictures in brain regions implicated in empathy, such as the anterior insula. Our findings suggest that human fathers experience neuroanatomical and neurofunctional changes that may adapt them to their new parental role.

CARING DADS: THE SOCIAL NEUROSCIENCE OF ATTACHMENT AND CAREGIVING IN FATHERS

Vrticka P

University of Essex, England

Today's dads are more strongly involved in childcare activities than ever before, and attachment theory increasingly recognises fathers' importance as caregivers and attachment figures for their children. In our research, we aim at investigating the neurobiological processes underlying paternal caregiving and attachment. To do so, we are looking at fathers' brain activity and structure as well as father-child interpersonal neural synchrony (INS) and compare these measures to the same measures obtained from mothers, mother-child dyads and non-fathering men. In my talk, I will first show data from a functional magnetic resonance imaging (fMRI) study during which fathers and mothers play a virtual ball-tossing game "Cyberball" with their 5-6-year-old child and an unknown child. While our results reveal many similarities in fathers' and mothers' brain activity, we find stronger paternal versus maternal brain activity in areas related to mentalising during children's exclusive play interaction with another child. I will then summarise structural MRI findings revealing no differences in hypothalamus volume between fathers and non-fathering men but a significant positive correlation between self-reported caregiving beliefs and hypothalamus volume in fathers. Finally, I will show that fathers' caregiving beliefs are also positively correlated with father-child INS during a problem-solving task, and that father-child INS is higher than mother-child INS while the opposite pattern is present for behavioural synchrony. Altogether, our findings importantly advance our understanding of paternal brain activity and structure as well as father-child INS and particularly their similarities with and differences to data obtained from mothers, mother-child dyads and non-fathering men.

SENSORY PLASTICITY IN CALIFORNIA MOUSE FATHERS

Saltzman W

University of California Riverside, USA

In biparental species, fathers, like mothers, show increased attraction to sensory stimuli from infants, compared to reproductively naïve adults. In mothers, this increase is associated with plasticity in sensory systems that detect and process infant-related stimuli; however, little is known about sensory plasticity in fathers. We have been investigating effects of fatherhood on behavioral and neural responses to pup vocalizations and pup odors in the biparental California mouse (*Peromyscus californicus*), in which fathers, but not adult virgin males, are consistently attracted to and nurturant toward infants. When presented with pup odors and/or vocalizations, fathers, but not virgins, spent more time interacting with the pup cues than with control stimuli. Fathers had consistently lower Fos expression in the main olfactory bulbs, compared to virgins, but Fos responses to pup stimuli did not differ between the groups. Unexpectedly, auditory brainstem responses indicated that parents were less sensitive than virgins to tones around the frequency of pup vocalizations. Finally, the primary auditory cortex of fathers showed greater increases in spectral power in response to pup vocalizations and greater temporal fidelity across trials for pup calls, compared to virgin males. In spite of these differences in sensory processing, fathers and virgin males showed no differences in gene expression of the oxytocin receptor or vasopressin (V1a) receptor in the auditory and olfactory cortices. Collectively, these findings indicate that male California mice undergo changes in neural processing of pup vocalizations and odors during the transition to fatherhood, which might facilitate the onset of paternal care.

A NEURAL BASIS FOR REINFORCEMENT OF PARENT-INFANT INTERACTIONS

O'Connell, L

Stanford University, USA

Parenting quality has far-reaching impacts on many aspects of offspring survival. Signals of need by offspring require accurate and precise interpretation by their caregivers to provide care. However, little is known about the neural basis of communication between parents and offspring, and even less is known in biparental species about how synchrony between parents can influence offspring care. Filling this knowledge gap in parental behavior circuit architecture is essential for understanding the basic brain mechanisms underlying high quality parenting, and how this variation influences offspring development. Poison frog tadpoles are altricial and rely entirely on parental investment for healthy development. In the biparental Mimic poison frog (*Ranitomeya imitator*), mothers provide more food to tadpoles that beg (vibrate) more intensely, suggesting somatosensation (touch) is an important component of offspring signaling need. We found that parents, depending on sex, may use different offspring signals to make care decisions. In parallel, we explored how parental brains respond to the begging behavior of their offspring. We found that offspring touch coincides with activation of opioid pathways and suppression of nociceptive pathways. When opioid signaling is perturbed, we found that only high care fathers modify their contact with offspring. Currently, we are delineating what neural pathways are recruited during parental care, and what individual

variations drive increased or decreased attentiveness to offspring. Overall, we aim to better understand how endogenous opioids regulate bonding and motivation to care for offspring.

MAY 8

KEYNOTE SPEAKER

NEUROENDOCRINE BASIS OF RODENT MATERNAL BEHAVIOUR: MY JOURNEY FROM OXYTOCIN VIA VASOPRESSIN TO CRF – AND BACK

Bosch O

Group, Department of Behavioural and Molecular Neurobiology, University of Regensburg, Regensburg, Germany

Maternal behaviour in rodents has been the focus of my scientific interest ever since I moved to the field of neuroscience. Studying the various aspects of maternal behaviour in general, and the adaptations in the maternal brain in particular, never gets old. The neuroendocrine mechanisms underlying maternal behaviour are many-faceted and often brain region and context dependent, highlighting the complexity of the maternal brain. And studying maternal behavior in preclinical models bears indispensable translational value.
I will take you on my journey through the rat maternal brain and behaviour, from oxytocin controlling maternal aggression to vasopressin triggering maternal care and the rather “anti-maternal” corticotropin-releasing factor (CRF) system. At one point, the latter came into my focus - and with it the consequences of failed adaptations. In closing the circle, the CRF system can interact with the oxytocin system, which might culminate in a compensatory mechanism to reinstate the maternal allostasis in perturbed, and potentially detrimental, conditions.

While many advances have been made over the last decades to reach a better understanding of maternal brain adaptations, many more questions are waiting to be answered in the future.

JNE YOUNG INVESTIGATOR SYMPOSIUM

THE TRANSITION TO MOTHERHOOD: A MULTILEVEL STUDY ON THE BRAIN’S TRAJECTORY ACROSS PREGNANCY AND POSTPARTUM.

Servin-Barthet C

Pregnancy represents a transformative journey marked by critical psychological adaptations to motherhood. In humans, neuroimaging studies scanning women before and after pregnancy and around the peripartum suggest that first-time mothers experience a remodeling of brain architecture that predicts postpartum maternal attachment towards the newborn. However, no previous study has charted the complete trajectory of human brain change from pre-conception throughout pregnancy and postpartum, integrating multimodal neuroimaging data, endocrine assessments, and neuropsychological information.

In this communication I will present the results from my latest research. I will focus on describing the U-shaped trajectory that gray matter volume exhibits during the transition to motherhood, dipping in late pregnancy and partially recovering during postpartum. I will also talk about whether the observed neuroanatomical trajectory differs based on the functional location of the changes and how it is predominantly linked to gestational factors, as it is only present in gestational mothers and correlates with fluctuations in estrogens over time. Finally, I will discuss how the mother's mental health status mediates the relationship between postpartum gray matter volume recovery and maternal attachment. Together the presentation will shed light on the complex interplay between hormones, brain, and behavior during the transition to motherhood, therefore filling a critical void in the human maternal brain literature.

THE HYPOTHALAMUS UNDERGOES DYNAMIC ADAPTATIONS IN THE TRANSITION TO MOTHERHOOD

Paternina-Die M

Motherhood is a transformative experience that induces profound physiological and psychological adaptations. Neuroimaging studies have shown that human pregnancy causes pronounced changes in the cortical mantle associated with estrogen levels and maternal behaviors. Solid evidence from rodent data indicates that maternal behaviour is triggered by hormonal mechanisms within the hypothalamus. However, the effects of pregnancy on the human hypothalamus remain largely unexplored. Our aim is to delineate the hypothalamic changes throughout the transition to motherhood. We used a prospective longitudinal design that followed primiparous mothers at six time points: 1) before conception; 2) at 18 weeks of gestation; 3) at 34 weeks of gestation; 4) at one month postpartum; 5) at 6 months postpartum; 6) and at 18 months postpartum. We extracted the volumes of the hypothalamus and its subregions from T1-MRI acquisitions using Freesurfer. Data from the pregnant mothers were compared with a subset of their same-sex partners who did not undergo pregnancy (non-pregnant mothers) using Linear Mixed-Effects Models and Generalized Additive Mixed Models. Results suggest a dynamic trajectory in the hypothalamus of pregnant mothers, with volume increases during pregnancy followed by decreases after childbirth that fully recover at eighteen months. No hypothalamic changes were observed in non-gestational mothers throughout their partner's pregnancy or after parturition, highlighting the unique neurobiological adaptations associated with pregnancy. This trajectory suggests a negative association between the changes in the cortical mantle and those occurring in the hypothalamus.

SINGLE-CELL RNA SEQUENCING OF THE MATERNAL HYPOTHALAMUS REVEALS A DISTINCT NEUROENDOCRINE TRANSCRIPTOME IN PREGNANCY

Amarsi R

Background: Pregnancy is characterised by a profoundly changed endocrine environment. Although the maternal hypothalamus represents a critical hormonal target, the exact neuroendocrine pathways, which regulate widespread adaptations across various maternal organs, are scarcely known. To address this, we conducted a single-cell RNA sequencing (scRNA-seq) investigation of the pregnant mouse hypothalamus.

Methods: We generated four independent scRNA-seq datasets of the whole hypothalamus from fasted pregnant (embryonic day 16.5) and virgin mice (n=2 per group). Datasets were combined and then mapped to a recently published transcriptional reference atlas of the murine hypothalamus, the “HypoMap”, which provided a validated set of functional annotations of hypothalamic cell types. A stringent “pseudobulk” differential expression analysis was applied to identify pregnancy-induced genes within biologically relevant populations of the hypothalamus.

Results: A distinctive transcriptome in pregnant mice was observed across all hypothalamic cell-types. Within neuronal cell-types, two functional regions were observed as transcriptional hotspots of pregnancy: the arcuate nucleus and medial preoptic area. Detailed sub-region analysis of the arcuate nucleus revealed extensive transcriptional shifts within distinct neuronal sub-populations, particularly the dopaminergic neurons. Moreover, these sub-region analyses identified candidate genes involved in hormone receptor pathways, including the estrogen receptor co-regulator, Cited1.

Conclusion: This high-throughput, cell-specific comparison of the virgin and pregnant hypothalamus has unveiled a unique transcriptional landscape of pregnancy. Our work introduces neuroendocrine pathways in the arcuate nucleus as novel targets for the dynamic hormonal concentrations in late-gestation, and highlights the strength of scRNA-seq as an unbiased tool for deciphering the complex adaptations of the maternal hypothalamus.

THE ROLE OF MIDBRAIN DORSAL RAPHE CRFR2 IN POSTPARTUM CAREGIVING AND AFFECTIVE BEHAVIORS

Meinhardt T

The transition to motherhood is typically marked by high levels of infant caregiving that are accompanied by a positive affective state. Unfortunately, the neural mechanisms promoting positive postpartum affective behaviors are very poorly understood. While numerous forebrain sites have been examined for this role, midbrain sites such as the dorsal raphe (DR; the largest source of forebrain-projecting serotonin cells) have mostly been neglected. DR neurons express many neurochemical receptors that alter DR functioning, including stress-related CRF receptors. Interestingly, the DR is one of few brain regions that densely express the stress-related CRF type 2 receptor (CRFR2), which influences social and affective behaviors in males, but their role in postpartum caregiving and affective behaviors in females is unknown. We recently found that new mother rats have twice as many rostral DR cells expressing CRFR2 mRNA as compared to virgins. Therefore, we hypothesized that upregulated DR CRFR2s are necessary for positive affective states in the early postpartum period and thus facilitate the display of maternal caregiving, particularly after stress. To test this, we pharmacologically antagonized CRFR2s in the rostral DR of early postpartum mothers to investigate the effects on caregiving and anxiety-like behaviors after exposure to a mild stressor; we also mapped the neuroanatomical projections from DR CRFR2-expressing neurons to four forebrain sites critical for postpartum behavior (NAc, mPOA, CeA, AH).This research is providing novel insight to the mechanisms driving postpartum adaptations in behavioral susceptibility to stress, with implications for stress-related derailments in maternal affective state and infant caregiving in women.

EXAMINING THE ROLE OF IL-1R ANTAGONISM IN TREATING POSTPARTUM DEPRESSION USING A RODENT MODEL

Garcia de Leon R

Background: Depression risk is highest during the postpartum [postpartum depression (PPD)]. Selective serotonin reuptake inhibitors (SSRIs) are often prescribed for PPD, however, only 3.2% of females with PPD achieve remission with SSRIs. In our preclinical model of PPD, we administer high corticosterone (CORT) during the postpartum. We found increased levels of the proinflammatory cytokine IL-1β in the hippocampus was commensurate with reduced SSRI efficacy, indicating this may be an important target to boost SSRI efficacy. Our central hypothesis is that antidepressant efficacy in the postpartum is mediated by inflammatory signalling.

Methods: High CORT was administered during the postpartum period to dams starting on postpartum day 2 along with fluoxetine (FLX) and/or anakinra (KIN), an IL-1R antagonist. FLX efficacy was measured using the forced swim test (FST), and maternal care observations. All dams were euthanized 23 days later to examine inflammation and neuroplasticity in the hippocampus.

Results: Dams treated with KIN (with or without FLX) failed to rescue passive coping behaviours in the FST. However, FLX and KIN together were able to rescue reductions in neuroplasticity as noted in hippocampal perineuronal net (PNN) expression and doublecortin (DCX+ cells) expression. Current analyses are in progress to quantify PNNs in the frontal cortex, alongside postsynaptic density-95 (PSD-95) in both hippocampal and frontal cortex tissue. Lastly, we will quantify the percentage of phagocytic microglia (Iba1+/CD68+) in the hippocampus and frontal cortex.

Conclusions: These findings indicate that IL-1β may serve as a potential target for increasing antidepressant efficacy in people with PPD.

NEURAL SUBSTRATES IN THE POSTPARTUM BRAIN FOR FLEXIBLE MATERNAL CARE

Yang M

Flexible infant-oriented maternal behavior is driven by multisensory cues from the offspring. An example of such behavioral flexibility in maternal mice (dams) is the rapid transition from nursing in the nest to exiting the nest in search of misplaced pups. This involves a sensory competition between distress calls, emitted by pups outside the nest, and somatosensory contact with pups inside the nest. Inflexible maternal behavior can be a symptom of postpartum depression. While selective serotonin reuptake inhibitors are a common treatment, it remains unclear how serotonin regulates responses to infant cues in maternal brain networks. Therefore, understanding the neural mechanisms responsible for processing competing infant cues and modulating flexible maternal behavior is essential for improving maternal care. Here, we investigated the neural substrates involved in the processing of competing infant cues, and their modulation by serotonin. We identified a neural hub for infant cue processing: calbindin-expressing neurons in the posterior intralaminar thalamus (PILcb). Using channelrhodopsin-assisted circuit mapping, we found that PILcb neurons receive input

from primary sensory nuclei and send output to the paraventricular nucleus to control oxytocin release and maternal behavior. PILcb neurons were more excitable in dams than in virgins and showed a particular preference for input frequencies consistent with the frequency range of pup calls. We observed a dense distribution of serotonergic fibers in PIL, and bath application of serotonin significantly increased the resting membrane potential of PILcb neurons. Calcium imaging revealed that auditory stimuli activated PILcb neurons. Finally, using the GRAB5-HT sensor, we found that serotonin levels in PIL are modulated by pup calls. Our findings establish PIL as a bottleneck station, uniquely positioned for processing of multisensory infant cues, potentially modulated by serotonin.

SYMPOSIUM 2

SOCIAL PHYSIOLOGY: THE METABOLIC ROOTS OF CAREGIVING

Atzil S

Hebrew University of Jerusalem, Israel

Human physiology is inherently social. From birth, infants depend on caregivers for the regulation of their bodily states. Parental care is thus directed toward supporting the infant's allostasis—from basic metabolic needs to emotional arousal. Through affective communication and caregiving behaviors, parents serve as external regulators, ensuring the infant's survival and promoting healthy development.

In this talk, I will present a proof of concept for the framework of *Social Physiology* in humans. I propose that the neural infrastructure underlying parental and social care draws heavily on visceromotor circuits—brain systems responsible for regulating internal bodily states. These circuits enable parents to incorporate their infants into their own allostatic systems, modulating the infant's physiology as part of an ongoing regulatory loop that begins in pregnancy. I will discuss how the visceromotor system, with its roles in autonomic control, reward, and social cognition, provides a biological foundation for caregiving and shapes developmental trajectories. This framework also offers new insights into perinatal psychopathologies, such as postpartum depression, which may reflect a breakdown in these regulatory systems due to allostatic overload.

MOTHERS WITH OPIOID USE DISORDER: CLINICAL TRIAL OF MOM POWER PARENTING PSYCHOTHERAPY WITH MULTIMODAL NEUROIMAGING

Swain JE

Stony Brook University, USA

Background: Opioid Use Disorder (OUD) and related issues of stress, depression and anxiety disrupt maternal brain neurocircuits (MBN) that govern sensitive parenting despite medication assisted therapies. We studied the effects of evidence-based Mom Power (MP) psychotherapy on brain-behavior mechanisms.

Methods: Mothers with OUD (n=11) received MP—a 13-session evidence-based parenting group psychotherapy. We collected and analyzed (paired-sample t tests) pre vs. post MP survey and multimodal neuroimaging data. Surveys included Opiate Craving Scale (OCS), Edinburgh Postpartum Depression Scale, Post-Traumatic Stress Disorder (PTSD) Checklist & Parenting Stress Index (PSI). Neuroimaging included event-related potential responses (ERPs) to standardized photos of Crying, Laughing and Neutral unknown children, and functional magnetic resonance imaging (fMRI) of the MBN comparing "joining" vs. "observing" emotional photos of own vs. unknown child.

Results: Post- vs. Pre-MP, participants showed significant reductions in depression, PTSD and PSI. ERP N170 responses were reduced for Crying vs. Neutral faces and fMRI empathic attunement in the MBN were enhanced for Join vs. Observe own vs. other child's joyful vs. distressed face. Furthermore, post- vs. Pre-MP reduction in OCS correlated with concomitant reductions in depression and increased late positive potentials to Laughing vs. Neutral and Laughing vs. Crying faces (all p's <0.05).

Implications: For mothers with OUD, MP improved indices of mental health showcasing the benefits of interventions, such as MP, to optimize maternal mood and parenting quality. Furthermore, MP modulated the MBN, suggesting mechanisms that may lead to validated assessment methods that might be more broadly applicable to other perinatal states/disorders.

DEVELOPMENT OF RAPID-ACTING NEUROACTIVE STEROID ANTIDEPRESSANTS FOR POSTPARTUM DEPRESSION

Deligiannidis KM

Feinstein Institutes for Medical Research, USA

Perinatal depression is one of the most common complications of childbearing yet is underdiagnosed and undertreated. Untreated/undertreated perinatal depression is associated with adverse effects on the well-being of the mother, child and the family. For women requiring antidepressant treatment, conventional serotonergic antidepressants have been the mainstay of postpartum depression (PPD) treatment for many years. This presentation will highlight preclinical and clinical studies supporting a role for neuroactive steroids in the pathophysiology of perinatal depression and then discuss the clinical trial data that led to the U.S. Food and Drug Administration's (FDA) approval of two rapid-acting neuroactive steroid antidepressants for PPD. Brexanolone, an intravenous preparation of synthetic allopregnanolone, was FDA approved in 2019 for the treatment of PPD in females 15 years old and older. Brexanolone is administered as a 60-hour infusion in medically supervised settings. Zuranolone, an oral allopregnanolone analog, was FDA approved in 2023 for the treatment of PPD in adult females. Zuranolone is administered as a 14-day oral at-home treatment. Finally, the clinical use of conventional serotonergic and newly FDA-approved rapid-acting neuroactive steroid antidepressants will be discussed, including use in lactation.

REDUCED EXTRACELLULAR FREE WATER IN THE BRAIN IN POSTPARTUM DEPRESSION

Bergé D

Hospital del Mar Research Institute, Barcelona, Spain

Although abnormal periphery inflammatory markers have been reported in depression, little is known about the interplay between perinatal depression and the physiological inflammatory changes that occur during pregnancy and postpartum. Extracellular free-water in the brain (FW) has been suggested as an in-brain inflammatory marker which, surprisingly, has not yet been studied in perinatal depression.

Thirty-eight control mothers and 34 mothers with perinatal depression were evaluated at 8 weeks postpartum including an assessment for depression using EPDS and HDRS scales, and an MRI scan covering a structural and a diffusion sequence. FW was calculated for every voxel and then averaged across gray matter volume, and interpolated to gray matter (GM) cortical surface for every subject. Participants were grouped into controls, depression only during pregnancy, and depression involving the postpartum. Between-group comparisons and correlations with depression rating scales were implemented for average measures, and the corresponding regional differences were explored using surface-wise measures.

Between three-groups comparison ($F=4.131, p=0.020$) showed lower average FW in GM in postpartum depression as compared to controls ($p=0.019$), and regional differences in a large cluster involving right temporal, parietal and frontal cortical regions. FW in GM inversely correlated with HDRS score ($r=-0.289, p=0.014$), and showed a trend to significance with EPDS score ($r=-0.201, p=0.095$) across all participants.

Plot figures and statistical brain maps showing regional differences will be included in the oral communication, as well as a brief discussion of the hypothetical underpinnings of these findings in the context of physiological and pathological inflammatory changes during the perinatal period.

CAN TARGETING THE GUT-MICROBIOTA HELP US UNDERSTAND PLASTICITY OF THE MATERNAL BRAIN?

Pawluski JL

University of Rennes

The transition to motherhood is a time when nearly all aspects of a female's existence are modified – from her neurobiological processes to her social role. In recent years we have increased our interest in this developmental period on a woman's life with a focus on understanding the neurobiology of motherhood and maternal mental health. However, we have much to learn about plasticity in the maternal brain and the mechanisms behind these changes. Current research points to a key link between the gut microbiome and brain plasticity

showing that the gut-microbiome-brain axis is a fundamental biological system linked to a variety of health outcomes throughout life. How this system relates to neuroplasticity in motherhood, in health and illness, remains to be determined. Over the past few years, my research has aimed to 1) better understand the gut-microbiome-brain axis across pregnancy and motherhood, and 2) determine how targeting this axis may aid in our understanding of the maternal brain and perinatal mental illness. Focusing on these two general aims, I will briefly introduce how the gut-microbiome-brain axis changes with pregnancy in the adult female and the limited literature on how stress impacts the gut-microbiome of motherhood. I will then discuss our recent findings on how targeting the gut microbiome may be linked to neuroplasticity in the maternal brain. Further research is needed to understand the gut-microbiome-brain axis in motherhood, but there is no doubt that this is a promising target system for understanding the maternal brain and improving maternal mental health.

This work was funded in part by a grant from BINC Geneva and the INCR Rennes.

SYMPOSIUM 3

DEVELOPING A RODENT MODEL OF POSTPARTUM ANXIETY THAT TRANSLATES TO HUMAN SAMPLES

Graham B

University of New South Wales, Australia

Background: A major impediment to developing an understanding of the biological mechanisms of postpartum anxiety disorders in humans is the lack of an adequate animal model. Female rats and humans undergo similar hormonal changes across pregnancy, and the mechanisms of anxiety regulation are highly conserved across species. This suggests that studying the neurobiology of anxiety and its regulation in postnatal rats may provide novel insights into the biological factors that contribute to postnatal anxiety in humans.

Methods: We compared the hormonal, neural, molecular and behavioural mechanisms of anxiety regulation in virgin female rats and primiparous (one prior litter of pups) female rats, as well as samples of human participants with or without a prior history of pregnancies. We used validated models of fear conditioning and fear extinction, as well as tests of innate anxiety (e.g., the elevated plus maze, or ecological momentary assessment of anxiety in humans) that measure species-specific anxiety responses.

Results: We find that the hormonal, neural, molecular and behavioural mechanisms of anxiety regulation undergo a fundamental shift in both female rats and humans as a consequence of pregnancy. These changes are driven by pregnancy-induced long-lasting reductions in circulating levels of the sex hormone oestradiol, as well as a blunting in the neurosteroid allopregnanolone, a natural anxiolytic.

Implications: These findings validate the use of rodent models to develop knowledge on mental health conditions in humans in the postpartum period, and may point to novel hormonal treatments (e.g., allopregnanolone) for postpartum anxiety disorders.

A PROLACTIN-SENSITIVE NEURAL CIRCUIT THAT REGULATES REWARD PATHWAYS AND PARENTAL BEHAVIOUR IN MALES AND FEMALES

Brown R

Centre for Neuroendocrinology and Department of Physiology, University of Otago, Dunedin, New Zealand

Prolactin action in the medial preoptic area of the hypothalamus (MPOA) is critical for the display of maternal behaviour, and also required for normal paternal behaviour in males However, how prolactin-sensitive neurons in the MPOA integrate into the neural circuit that underlies parental behaviour has been unclear. Using *in vivo* fibre photometry, the specific components of parental behaviour during which MPOA prolactin-sensitive neurons show increased activity were characterised. We have identified a prolactin-sensitive MPOA projection to the ventral tegmental area, a key brain region in regulating reward behaviour. In both male and female mice, optogenetic activation of this circuit can drive dopamine release into the nucleus accumbens, and promote pup-directed aspects of parental behaviour.

NEUROIMMUNE REGULATION OF PLASTICITY IN THE MATERNAL BRAIN FOLLOWING GESTATIONAL STRESS

Leuner B

The Ohio State University

Pregnancy confers vulnerability to mental health disorders, with 20% of new mothers experiencing Postpartum Depression (PPD). The mechanisms contributing to mood dysregulation and impaired maternal care in PPD are not well understood, but stress during pregnancy is a strong risk factor. During pregnancy, the brain becomes highly plastic to allow for changes in maternal mood and caregiving behavior. Pregnancy is also accompanied by dynamic immune changes both peripherally and in the brain, and immune dysregulation has been implicated in postpartum mood disorders. Microglia, the main CNS immune cell, have a well-established role in regulating synaptic plasticity through phagocytic activity and the release of secreted factors in both non-stressed and stressed states; though little is known about microglia-regulated plasticity in the peripartum period. This talk will focus on our recent work using a rodent model showing that gestational stress exposure leads to a postpartum-depression-like behavioral phenotype accompanied by substantial alterations in the neuroimmune environment of the maternal brain. These neuroimmune changes include significant shifts in inflammatory mediators, microglia phagocytic properties, and downstream microglia-mediated remodeling of perineuronal nets within the prefrontal cortex, a region important for regulating both mood and maternal behavior. Understanding how gestational

stress-induced remodeling of perineuronal nets by microglia may contribute to the underlying pathophysiology of PPD is a novel avenue for future research and interventional strategies.

Funding Sources for the Research: National Science Foundation Award Number 211438; National Institute of Mental Health R21 MH117482-02.

STATE-DEPENDENT FLEXIBILITY OF PARENTAL CIRCUITS

Kohl J

The Francis Crick Institute, England

Parenting is an instinctive behavior supported by species-specific motor programs, yet it is flexible and shaped by experience and internal states. Using the mouse as a model, we are uncovering the mechanisms behind this flexibility. I will present recent findings showing how parental circuits are remodelled across long (days–weeks) timescales. During pregnancy, physiological changes prepare the body and brain for motherhood, yet the role of pregnancy hormones in remodelling parental circuits remains unclear. We found that action of estradiol and progesterone on galanin (Gal)–expressing neurons in the mouse medial preoptic area (MPOA) is critical for pregnancy-induced parental behavior. Whereas estradiol silences MPOA-Gal neurons and increases their excitability, progesterone rewires this circuit node by promoting dendritic spine formation and recruitment of excitatory synaptic inputs. This MPOA-Gal-specific neural remodeling sparsens population activity and results in persistently stronger, more selective responses to pups. Pregnancy hormones thus remodel parenting circuits in anticipation of future behavioral need. Additionally, I will present new data on how hunger and estrous state are integrated at the cellular level in the MPOA to flexibly tune pup interactions over shorter timescales (minutes–hours). These findings provide key mechanistic insights into the flexibility of parental behavior.

LOVE, DEATH, AND OXYTOCIN: THE CHALLENGES OF MOUSE MATERNAL CARE

Froemke R

New York University, USA

The neuropeptide oxytocin is important for maternal physiology and social behavior. In this talk, I will discuss new and unpublished data from our lab on when, where, and how oxytocin is released from hypothalamic neurons to enable maternal behavior in new mother mice. I will focus on maternal responses to infant distress calls, and how oxytocin enables rapid neurobehavioral changes for dams and alloparents to recognize the meaning of these calls. We have built a new system combining 24/7 continuous video monitoring with neural recordings from the auditory cortex and oxytocin neurons of the hypothalamus in vivo. With this documentary approach, we have identified behaviors of experienced and naïve adults learning to co-parent together which also activate oxytocin neurons. I will discuss circuits routing sensory information to oxytocin neurons leading to oxytocin release in target areas important for maternal motivation. Finally, I will discuss longer-term behavioral monitoring over months, examining how single mothers build nests to help ensure pup survival or how this sometimes goes awry.

MAY 9

SYMPOSIUM 4

CELLULAR MECHANISMS MEDIATING THE LONG-TERM EFFECTS OF PREGNANCY, POSTPARTUM AND STRESS EXPERIENCES IN THE MATERNAL BRAIN

Chan J

Pregnancy and postpartum periods represent incredible physiological stressors, yet while effects of psychosocial stresses are well-documented, how reproductive experiences persistently alter the maternal brain remain unknown. Moreover, parity (previously carrying one or more pregnancies to term) is a complex risk factor. In general, parity promotes parenting adaptations. However, in some individuals, parity increases susceptibility for perinatal or postpartum mood and anxiety disorders. Therefore, understanding the biological processes that orchestrate and disrupt parity effects in the brain is essential. Using mice, we performed brain-wide transcriptional profiling to identify regions sensitive to parity. The dorsal hippocampus (dHpc) exhibited greatest plasticity one month post-weaning, which associated with enhanced contextual fear conditioning and pup retrieval performance. Dissecting the contributions of pregnancy and postpartum experiences, we found that while pregnancy initiates dHpc programming, additional postpartum interactions are required for full transcriptional alterations. Thus, we next tested the impact of postpartum stress using a maternal separation with limited nesting model. We found that stress disrupted both parity-dependent transcriptional and behavioral adaptations. Using single nuclei RNA-sequencing to determine cellular origins of dHpc changes, we identified changes to dopamine receptor-expressing neurons, suggesting altered dopamine regulation contributes to dHpc plasticity. Chemogenetic inhibition of the VTA to dHpc projection further demonstrates the essential role of dopaminergic signaling in mediating the long-term adaptive effects of parity on both dHpc transcriptional and behavioral plasticity. These studies provide insight into the cellular mechanisms contributing to long-term effects of parity effects in brain, and the environmental triggers that interact to influence maternal brain health.

DIVERSE FORMS OF PLASTICITY SUPPORTING MATERNAL AGGRESSION IN FEMALE MICE

Yamaguchi T

To protect the helpless young, females dramatically increase aggression towards intruders during lactation, known as maternal aggression. However, attack is costly and risky. When pups no longer exist, maternal aggression loses its purpose and rapidly declines. Our study reveals the critical role of the pathway from estrogen receptor alpha-expressing (PAEsr1) cells in the posterior amygdala to neuropeptide Y receptor Y2 (VMHvlNpy2r) cells in the ventrolateral part of the ventromedial hypothalamus in the rise and fall of maternal aggression. Functional manipulations and photometry recordings demonstrate VMHvl-projecting PAEsr1 (PAEsr1□VMHvl) cells are naturally active and required for maternal aggression. In vitro slice recording showed that PA-VMHvlNpy2r connection strengthens and VMHvlNpy2r excitability increases to enhance VMHvlNpy2r responses to intruders and drive attack in lactating dams. Furthermore, we found oxytocin as a critical mediator to link pups' needs to the aggression

circuit output. Interestingly, PA, not VMHvl, is the key site for oxytocin to boost the aggression circuit output. The abundant expression of oxytocin receptor (OXTR) in PAEsr1 cells enables oxytocin to increase the input-output relationship of PAEsr1 cells by increasing the input resistance of the cell. The decreased maternal aggression by the oxytocin level drops after pup separation can be restored by optogenetic stimulation of oxytocin neurons in the paraventricular hypothalamic nucleus. This recovered maternal aggression can be canceled by blocking PA OXTR signaling. Thus, diverse forms of plasticity occur at the PAEsr1-VMHvlNpy2r circuit to support maternal aggression, while oxytocin signals the need of the young, enabling the female to rapidly adjust its aggression.

UNCOVERING CONTRIBUTIONS OF THE MEDIAL PREOPTIC AREA TO MATERNAL SENSITIVITY

Pereira M

Maternal behavior that is sensitive to the offspring's needs is essential for the healthy development and emotional wellbeing in mammals. Offspring have different physiological and behavioral needs as they grow and develop, and mothers must promptly and flexibly adjust caregiving and affective interactions to meet those needs. However, the brain mechanisms that dynamically coordinate caregiving decisions with the needs of the offspring are not well understood. Our previous work in rats demonstrated that the medial preoptic area (mPOA), a critical node in the maternal behavior circuitry, is essential for maternal sensitivity, allowing mothers to flexibly adjust caregiving decisions to resolve the everchanging needs of their offspring. The present study investigates the contribution of mPOA neurons to sensitive caregiving decisions. Our findings demonstrate that chemogenetic inactivation of mPOA-to-infralimbic medial prefrontal cortex (IL) neurons disrupts cognitive aspects of maternal sensitivity in multiparous healthy mothers, leading to uniform maternal behavior regardless of their offspring's needs. Conversely, chemogenetic activation of the mPOA ameliorated the significant disturbances in maternal sensitivity in the well-validated Wistar-Kyoto (WKY) rat model of depression, with WKY mothers now spending more time providing sensitive caregiving behaviors. Retrobeads retrograde tracing analysis revealed upregulated cFos expression in mPOA projections to the IL and ventral tegmental area (VTA) during maternal adjustments of care. Additionally, catFISH analysis of c-fos indicated that a distinct population of mPOA neurons play a crucial role in coordinating sensitive caregiving behaviors. This work expands on our understanding of the mPOA's contribution to sensitive parenting.

PROMOTING LARGE-SCALE DATASETS AND COLLABORATION IN HUMAN MATERNAL BRAIN RESEARCH

Martínez-García M

Each year, nearly 140 million women around the world experience one of the most transformative events of their lifetime - pregnancy. Yet, scientific knowledge of how pregnancy shapes the maternal brain—impacting mental health, cognition, and neurobiology- is still in its infancy. Over the past decade, pioneering longitudinal studies have revealed profound, dynamic, and lasting neurobiological changes in the maternal brain, laying the foundation for a burgeoning field of research. Despite these advances, current progress is constrained by the lack of large-scale datasets and global collaboration to account for variability in hormonal

and immune signals, links to perinatal mental health, and the influence of socioeconomic factors and parental leave policies. The Global Maternal Brain Project (MBP Global), a key initiative of the Ann S. Bowers Women's Brain Health Initiative, seeks to address this gap by creating the world's largest longitudinal maternal neuroimaging database. We aim to recruit >1,000 first-time pregnant women across global strategic sites, tracking participants from pre-conception through years postpartum. Data collection includes standardised MRI scans at multiple time points, blood and stool samples for multi-omics profiling, assessments of sleep, cognition, and lifestyle factors, and evaluations of reproductive health and pregnancy outcomes. This initiative will generate an unprecedented open-access resource, empowering researchers to explore neurobiological questions previously out of reach and providing clinicians with critical insights for risk assessment.

PUP PHEROMONES INDUCE MATERNAL BEHAVIOURS

Martínez-García F

In rodents, pup directed behaviours change with hormonal condition and experience. While female mice are maternal, motivation increases during motherhood due to pregnancy hormones. Virgin males are infanticide whereas fathers are paternal. This involves poorly understood changes in the response of adults to pup chemosignals. Here, we report the results of experiments checking the working hypothesis that pup pheromones detected by the vomeronasal organ (VNO) become rewarding for females during motherhood, leading to pup(goal)-directed maternal behaviours.

We show that pup volatiles induce place-preference in mothers, but only elicit transient investigation (novelty effect) in virgin females. Late-pregnant females already show persistent attraction to pup chemosignals, and egr-1 expression indicates that they activate the VNO. Indeed, pup-induced neural activity (cFos expression) increases in late-pregnant, as compared to virgin females, in key centres of the olfactory (piriform cortex), vomeronasal (posteromedial cortical amygdala), sociosexual (ventrolateral PAG) and motivational (AcbC) brain circuits. We have identified 11 specific volatiles from neonatal (3-4 day-old) pups using GC-MS based untargeted metabolomics. Most of them activate isolated VNO cells in vitro, as shown by means of calcium-imaging techniques.

In addition, when applied onto pup dummies, pup wash or mixtures of the identified pup volatiles, induce licking in females and paternal males (but attacks in virgin males), while reducing occasional attacks (virgin females). As a conclusion, pups emit rewarding pheromones that are induce pup(goal)-directed maternal behaviours in dams, but exacerbate attacks in infanticide adults (virgin males). In other words, pup pheromones help identifying pup-like objects (dummies) as true pups.

SEROTONIN RELEASE IN THE NAC AFFECTS MATERNAL BEHAVIOR

Simonnet C

Maternal care is a core component of mammalian behavior, involving the detection of offspring signals, execution of caregiving actions such as nest building, nursing, and thermoregulation, and the motivation to provide care despite stress or perceived threats. In our study, we

observed that both primiparous and nulliparous mice perform pup retrieval in a familiar environment. However, only dams exhibit this behavior under anxiogenic conditions. These observations led us to investigate the neural circuits differentially engaged in dams versus nulliparous females during maternal behavior. We hypothesize that the nucleus accumbens (NAc) acts as a central hub integrating multimodal inputs related to maternal behavior. Specifically, we focused on afferent signals from serotonergic (5-HT) and dopaminergic (DA) neurons, which are implicated in regulating motivation, parental behavior, and the establishment of mother-offspring bonds.

Using fiber photometry, we observed that medium spiny neurons in the NAc respond oppositely in dams and nulliparous females during pup retrieval, indicating that distinct inputs may drive this activation. To further explore this, we used sensors to examine DA and 5-HT release in the NAc during pup retrieval. Unexpectedly, we found a decrease in 5-HT release correlating with successful pup retrieval under anxiogenic conditions in dams. Using optogenetic inhibition of 5-HT neurons, we enhanced pup retrieval behavior in dams. These findings suggest that changes in NAc activity and connectivity during the postpartum period enable maternal care behaviors to occur independently of external stressors.

KEYNOTE SPEAKER

Maite Egoscozabal and Laura Baena

Presentation of Malasmadres Club, Spain

3. Abstracts of the posters

SINGLE-CELL RNA SEQUENCING OF THE MATERNAL HYPOTHALAMUS REVEALS A DISTINCT NEUROENDOCRINE TRANSCRIPTOME IN PREGNANCY.

Amarsi R

Background: Pregnancy is characterised by a profoundly changed endocrine environment. Although the maternal hypothalamus represents a critical hormonal target, the exact neuroendocrine pathways, which regulate widespread adaptations across various maternal organs, are scarcely known. To address this, we conducted a single-cell RNA sequencing (scRNA-seq) investigation of the pregnant mouse hypothalamus.

Methods: We generated four independent scRNA-seq datasets of the whole hypothalamus from fasted pregnant (embryonic day 16.5) and virgin mice (n=2 per group). Datasets were combined and then mapped to a recently published transcriptional reference atlas of the murine hypothalamus, the “HypoMap”, which provided a validated set of functional annotations of hypothalamic cell types. A stringent “pseudobulk” differential expression analysis was applied to identify pregnancy-induced genes within biologically relevant populations of the hypothalamus.

Results: A distinctive transcriptome in pregnant mice was observed across all hypothalamic cell-types. Within neuronal cell-types, two functional regions were observed as transcriptional hotspots of pregnancy: the arcuate nucleus and medial preoptic area. Detailed sub-region analysis of the arcuate nucleus revealed extensive transcriptional shifts within distinct neuronal sub-populations, particularly the dopaminergic neurons. Moreover, these sub-region analyses identified candidate genes involved in hormone receptor pathways, including the estrogen receptor co-regulator, Cited1.

Conclusion: This high-throughput, cell-specific comparison of the virgin and pregnant hypothalamus has unveiled a unique transcriptional landscape of pregnancy. Our work introduces neuroendocrine pathways in the arcuate nucleus as novel targets for the dynamic hormonal concentrations in late-gestation, and highlights the strength of scRNA-seq as an unbiased tool for deciphering the complex adaptations of the maternal hypothalamus.

EARLY POSTPARTUM DEVELOPMENT OF OLFACTORY-GUIDED MATERNAL PREFERENCE: THE ROLE OF MOM-PUP INTERACTIONS AND URINE CUES

Andreu V

Motherhood is characterized by pronounced changes in the brain and body. During pregnancy and after birth, the reproductive, endocrine, and nervous systems undergo significant modification to support the growth and care of offspring. While the olfactory system plays a critical role in pup retrieval and nesting behaviors in mice, how the olfactory system adapts during motherhood remains unclear. Using odor preference testing, we have demonstrated that first-time mothers develop a specific preference for pup urine following parturition and early postpartum care, which is not observed for other social or neutral odors. This preference is absent in late-pregnant females, first-time mothers separated from their pups after parturition, and virgin females exposed either to pups or to pup urine. This suggests that this

preference for pup urine requires both internal (hormonal) and external (pup chemosensory) cues to develop. Finally, liquid chromatography-mass spectrometry and gas chromatography-mass spectrometry analyses identified specific compounds in pup urine that may drive this behavior. These findings may provide valuable insights into how motherhood influences the sense of smell, with chemosensory cues playing a key role in shaping maternal responses and enhancing olfactory-guided behavior.

ATTACHMENT STYLES AND THEIR RELATIONSHIP WITH AFFECTIVE STATES, SLEEP QUALITY, AND CHRONOTYPE DURING PREGNANCY AND EARLY POSTPARTUM.

Arrieta-Laurent A

Neurobiological changes that occur throughout pregnancy and motherhood influence maternal attachment styles and affective states, which can impact maternal well-being and the quality of the mother–child bond. In recent years, attention has also turned to understanding how circadian rhythms relate to affective disturbances; however, the role of chronotype in these processes during the perinatal stage remains insufficiently explored.

The present study aimed to: 1) Characterize attachment styles (measured by ECR), trait anxiety (STAI), depressive symptoms (EPDS), and sleep quality (PSQI) in 25 pregnant women in Uruguay during the last trimester of pregnancy and early postpartum. 2) Explore the associations between sleep quality during pregnancy and maternal chronotype with postpartum affective states.

Our results indicate that anxious and avoidant attachment styles measured in the postpartum period were positively correlated with anxiety (r=0.469, p=0.02; r=0.593, p=0.01) and depressive symptomatology (r=0.451, p=0.03; r=0.445, p=0.03;) a. Sleep quality was positively correlated with anxiety (r=0.617, p=0.01), depression (r=0.622, p=0.01), and avoidant attachment (r=0.592, p=0.02) during the postpartum period. Moreover, participants with a more morning-oriented chronotype showed higher trait anxiety and a tendency to have a higher anxious attachment (Median(SIQR)=38(3.5); 19(2.5)) compared to those with a more evening-oriented chronotype (Median(SIQR)=30(2.5),p=0.04; 15(3), p=0.05; Mann-Whitney test).

Taken together, these findings suggest the importance of considering maternal attachment styles and chronotype as potential affective risk markers in the perinatal period, as well as highlighting the role of sleep quality in supporting maternal emotional health

NEUROANATOMICAL SIGNATURES OF POSTPARTUM DEPRESSION: INSIGHTS FROM A CROSS-SECTIONAL STUDY

Attolini S

Previous structural MRI studies have reported long-lasting grey matter volume (GMV) decreases in the maternal brain. However, evidence on neuroanatomical changes in mothers with postpartum depression (PPD) remains inconclusive. This cross-sectional study aimed to investigate GMV differences between healthy nulliparous women, healthy mothers and mothers with PPD, and how these correlate with maternal psychological and bonding

variables. Our sample included n = 20 healthy nulliparous women, n = 32 healthy mothers and n = 18 mothers with PPD (0-18 months postpartum for both groups), who underwent structural MRI scans. Mother-infant bonding, depressive symptomatology and maternal self-confidence were assessed through validated self-report measures. The GMV of twelve Regions of Interest was compared across groups and correlated with maternal variables. Statistically significant GMV differences were found in the bilateral amygdala, thalamus, globus pallidus, inferior and superior frontal gyrus across groups. Post-hoc tests showed that while healthy mothers presented lower GMV in the amygdala compared to healthy nulliparous women, mothers with PPD exhibited higher GMV in the amygdala, thalamus and globus pallidus compared to healthy mothers, and in the inferior and superior frontal gyrus compared to both healthy mothers and healthy nulliparous women. Furthermore, mothers with PPD showed significantly higher bonding impairment than healthy mothers and a significant positive correlation between right insular GMV and maternal self-confidence scores. All reported findings survived False Discovery Rate correction. In conclusion, our results suggest that mothers with PPD may display GMV increases, contrasting with the GMV reductions seen in healthy motherhood, particularly in reward-related brain regions.

BONDING BEFORE BIRTH: MATERNAL-FETAL ATTACHMENT AND MATERNAL CORTICAL CONNECTIVITY IN LATE PREGNANCY

Ayala K

Emerging research suggests that pregnancy and motherhood are associated with neural adaptations that support caregiving. Maternal-fetal attachment (MFA), the emotional bond between a pregnant individual and their fetus, is thought to be an early precursor to maternal-infant bonding and sensitive caregiving, yet its neural underpinnings remain largely unexplored. Resting-state electroencephalogram coherence is a well-established measure of regional cortical connectivity and has been implicated in cognitive, attentional, and emotional processes related to parenting. Recent findings indicate that intrahemispheric alpha coherence between frontal and parietal regions in the left hemisphere is higher during pregnancy than postpartum, suggesting a preparatory role in maternal cognition and regulation. Extending this line of work, we investigated alpha coherence as a potential neural correlate of MFA. Thirty-five pregnant people in their third trimester (mean 36.8 gestational weeks) participated. MFA was assessed using the Prenatal Attachment Inventory-Revised (PAI-R). Our central finding was that higher scores on two PAI-R subscales, reflecting increased anticipation about the baby and more frequent interactions with the fetus, were associated with increased left intrahemispheric frontoparietal alpha coherence. These associations remained after controlling for parity and gestational age. Our findings suggest that neural mechanisms underscoring attachment may emerge during pregnancy, aligning with findings of changing left-lateralized connectivity during the transition to parenthood more generally. Identifying neural markers of MFA provides evidence that the foundation of maternal attachment may begin before birth and offers insight into the neurobiological basis of early bonding.

STATE-DEPENDENT PROCESSING OF OLFACTORY INFORMATION IN THE MEDIAL AMYGDALA

Bailey-Smith S

Flexibility in instinctive social behaviours is crucial to survival, and relies on the ability of the brain to interpret broad social sensory stimuli for ethologically appropriate actions. In mice, pup-directed behaviours provide a promising model to study the flexible processing of sensory information. Following sexual experience, males undergo a striking transition from infanticide to parenting, dependent on either the main or accessory olfactory pathways relaying volatile and non-volatile signals respectively. The medial amygdala (MeA), which receives axonal inputs from both olfactory pathways, has been implicated in the scalable control of pup-directed behaviours. However, the circuit logic underlying the behavioural transition remains unknown. Here, we sought to explore how sensory representations of conspecifics are altered by reproductive state in the MeA. We first established robust parental behaviour in CD1 mice, finding that cohousing with female mating partners, and 5 days of pup exposure was sufficient for reliable expression of pup-retrieval. Then, using Neuropixels 2.0 probes we recorded acutely from the MeA in head-fixed virgins and fathers whilst presenting a range of volatile and non-volatile stimuli. Non-volatile stimuli elevated MeA population activity across both reproductive groups, but marked responses to pup-derived volatiles were only observed in a small neuronal subpopulation in fathers. Finally, we recorded chronically from MeA during resident-intruder assays to determine how volatile and non-volatile signals differentially contribute to naturalistic interactions. We observed distinct neural responses to infants between reproductive states. Altogether we propose the brain can leverage parallel sensory pathways to flexibly process conspecific information for ethologically-relevant behaviour.

LINKING BIRTH EXPERIENCE AND PERINATAL DEPRESSION SYMPTOMS TO NEUROANATOMICAL CHANGES IN HIPPOCAMPUS AND AMYGDALA

Ballesteros C

Childbirth is a life-changing event in a mother’s life. While the transition to motherhood has recently been recognized as one of the most neuroplastic periods in adulthood, no study has yet explored whether the hippocampus and amygdala change during the peripartum in relation to childbirth experience and perinatal depression symptoms. In this longitudinal neuroimaging study, we assessed 88 first-time gestational mothers in late pregnancy and early postpartum and 30 nulliparous control women. We used optimized high-resolution MRI scans to quantify volumetric changes in the hippocampus and amygdala, along with their substructures. We found that increases in depression symptoms during the peripartum were positively correlated with changes in the right amygdala. A more challenging birth experience was associated with bilateral increases in hippocampal volume. These findings show that studying the neuroanatomical changes during the transition to motherhood can inform not only about adaptive processes but also about potential vulnerabilities, highlighting the importance of tracking perinatal experiences to enhance women’s health.

PERINATAL DEPRESSION AND ITS LONG-LASTING IMPACT ON INFANT NEURODEVELOPMENT

Benet G

Background:
Motherhood involves significant changes that increase the risk of mental health disorders, such as perinatal depression (PD) and postpartum anxiety (PPA), potentially influencing the mother-infant bond and infant neurodevelopment. Although PD is well documented, the impact on child neurodevelopment remains poorly understood.

Methods:
This cross-sectional study assessed n= 44 mother-infant dyads with PD and n= 43 control dyads at 8 weeks postpartum. Maternal mental health was assessed using EPDS, PSAS, and PBQ, and infant neurodevelopment with NBAS. Participants were categorized by the timing of depression (each trimester and postpartum). Statistical analyses included correlations and group comparisons.

Results:
Infants whose mothers experienced perinatal depression exhibited a significant decrease in NBAS scores compared to infants of healthy control mothers ($p = 0.01$), after adjusting for personal psychiatric history, socio-economic status, and birth experience. In secondary results, both PD and PPA impaired mother-infant bonding ($p < 0.0001$). Mothers with PPA exhibited worse mother-infant bond ($p < 0.001$) compared to healthy control mothers. Strong correlations between PD and PPA ($r = 0.79$, $p < 0.0001$) were found, consistent with prior research, highlighting frequent comorbidity and cumulative adverse effects on maternal and infant outcomes.

Conclusions:
Perinatal mental health significantly impacts infant neurodevelopment. Findings highlight the critical role of biological factors during maternal depression, with pregnancy being a sensitive period where hormonal and neurological changes profoundly influence infant neurodevelopment. The robust link between PD, PPA and mother-infant bond highlights the need for early screening and multidisciplinary interventions to improve outcomes for both mothers and infants.

NEUROIMAGING OF PERINATAL DEPRESSION

Benet G

Background:
During pregnancy and postpartum, the brain undergoes structural changes, particularly in gray matter volume (GMV), mainly in the frontoparietal and default networks. These transformations follow a U-shaped trajectory, with GMV decline during pregnancy and partial recovery during early postpartum period in healthy mothers. Although these neuroanatomical changes are being documented, their manifestation during perinatal depression remains unclear.

Methods:

A total of N=83 participants were assessed, including n= 40 healthy control mothers and n=43 mothers diagnosed with perinatal depression, at least once. Clinical diagnoses were confirmed using DSM-V criteria. All participants underwent an MRI scan at 8 weeks postpartum using a 3T MRI. Data preprocessing and analysis were conducted using voxel-based morphometry (VBM) in SPM, applying parametric methods to identify group differences.

Results:
Findings revealed that mothers who experienced perinatal depression exhibited significantly lower GMV in the left posterior cerebellum, specifically in Crus I and II, compared to healthy control mother's (p-FWE corr = 0.018, Ke = 1341; p-FWE corr = 0.049, Ke = 27).

Conclusions:
Pregnancy and postpartum involve neuroplastic changes that emphasize the maternal brain's adaptability. These findings suggest a role of the cerebellum in perinatal depression, suggesting the involvement of the cerebello-cortical networks. The regions of GMV decrease in the cerebellum are linked to social cognition and emotional processing, redefining it not solely as a motor-related structure. Incorporating the cerebellum into neurobiological models could help identify biomarkers for early detection and intervention. Future research should explore the duration of these changes and their impact on perinatal depression.

LATE MOTHERHOOD LINKED TO ACCELERATED MEMORY DECLINE IN AMYLOID-POSITIVE COGNITIVELY UNIMPAIRED WOMEN

Brugulat-Serrat A

Even female sex is a risk factor for Alzheimer's disease (AD), how women-unique experiences, such as pregnancy, may influence AD women's risk across their lifespan is unclear. We explored the association between age at first live birth and cognitive change in cognitively unimpaired (CU) parous women at risk of AD. We included 174 CU postmenopausal parous women and 123 men with children from the ALFA+ cohort. Age at birth of first child was defined using continuous and categorical (tercile split) approaches. Positive Amyloid (Aβ) status was defined using the CSF Aβ42/40 ratio<0.071 cut-off (A+). Aβ42/40 was measured using the NeuroToolKit (Roche Diagnostics International Ltd). Cognitive change (3-year follow-up) was measured with the PACC and domain-specific composites. Multivariable regression models predicting cognitive change were adjusted for age, education, APOE-e4, reproductive span, and number of childbirths. Interaction terms between age at birth of first child and Aβ status was modeled. Results showed that younger age at first live birth was significantly associated with greater number of childbirths, lower years of education, and better longitudinal memory performance. Multivariable models showed that A+ women with older age at first live birth showed greater memory decline over time, supported by the stratified analysis. We did not find significant results among other cognitive domains. No significant associations among men were found. This finding contributes to our understanding of how female reproductive events may influence later-life cognitive decline in females predisposed to AD and helps to target interventions to females at higher risk for cognitive decline.

CRYING BABY ELICITS DIFFERENT ELECTROENCEPHALOGRAPHIC RESPONSES IN TEENAGE AND ADULTS' MOTHERS

Canela D L

The capacity to reproduce begins in early adolescence; however, at this stage brain, cognitive, and psychological maturity have not yet been fully developed. These factors are necessary for the optimal deployment of maternal behavior, which enables the infant´s integral development. Considering this, teenage and adult mothers may exhibit different brain responses to infant stimuli. This study examines electroencephalographic (EEG) activity in mothers in response to a recording of a baby crying. The sample included a group of eight teenage mothers (TM) aged 15-19 years and a group of eight adult mothers (AM) aged 25-35 years, who were 6 to 19 months postpartum. Absolute Power (AP) and EEG Correlation were measured under three conditions: baseline, baby crying, and white noise. The results show that TM exhibited higher AP in delta and beta1 waves in the prefrontal-dorsolateral areas across all three conditions compared to AM. This may reflect developmental differences in TM´s brain, regardless of the stimulus. Furthermore, the TM group showed lower interhemispheric correlation (F3-F4) in the theta wave when listening to a baby crying. The opposite EEG pattern has been observed in tasks requiring cognitive flexibility. When comparing conditions, only the AM group showed lower correlation in the frontopolar-dorsolateral areas in theta and alpha waves when listening to a baby crying, a pattern associated with greater cognitive control. Flexibility and cognitive control are essential for detecting, interpreting, and responding to an infant's signals, functions that may not yet be fully matured in TM, as reflected in their distinct brain activity.

SOCIAL TRANSMISSION OF INFLAMMATION DURING THE POSTNATAL PERIOD AND ADULTHOOD

Castany S

The ability to detect and respond to sickness promotes survival, especially during the postnatal period when immune challenges represent significant threats to both mother and infants. This phase is critical for mother-infant bonding and attachment processes, yet few studies have examined the physiological and behavioral responses of mothers to sick offspring.

In this study, we investigated how exposure to sick conspecifics affects behavior and inflammation in pup-mouse mothers (dams) dyads and adult female mice. Our study shows that dams respond to immune-challenged pups by mirroring their inflammatory response. Dams with sick pups showed a marked increase in inflammatory mediators in both the brain and periphery, along with increased maternal behaviors and elevated corticosterone levels. Notably, this social transmission of inflammation occurred even without physical contact and contributed to the stress hormone response in the dams. In adult female dyads, the interaction with an immune-challenged cagemate did not induce a strong inflammatory response but increased sensitivity to subsequent immune challenge. This suggests that social transmission of inflammation may prime immune function, influencing hormonal status and behavior. In dams, this adaptation may facilitate close contact with sick pups and/or transfer immune mediators through milk.

Our findings reveal a novel mechanism of social transmission of inflammation, expanding our

understanding of maternal care and social behavior during the postnatal period. These insights could potentially have some implications for evolutionary biology and maternal-infant health.

ROLE OF HYPOTHALAMIC ESTROGEN SIGNALING IN THERMOREGULATORY CHANGES DURING PREGNANCY

Cortés LR

Many mammals, including humans and mice, exhibit decreased core body temperature as pregnancy progresses. This decrease in core body temperature may protect fetuses from excess heat. My work aims to understand the neural mechanism(s) that contribute to thermoregulatory changes during pregnancy. Circulating estrogen levels rise as pregnancy progresses, and in non-pregnant female rodents, estrogen administration lowers body temperature. We hypothesize that hypothalamic estrogen-sensitive neurons coordinate the decrease in core body temperature during pregnancy. The medial preoptic area (MPO) is considered the center of thermoregulation and contains many estrogen-sensitive neurons. Our lab previously tied estrogen receptor (ER) alpha expressing neurons in the MPO to thermoregulation in non-pregnant mice. We use a novel estrogen response element reporter (NeuroSeeER) to show that estrogen signaling in MPO ER alpha+ neurons is elevated in pregnant mice relative to non-pregnant mice. Next, we tested whether estrogen signaling in MPO neurons is critical for maternal thermoregulatory changes. We ablated ER alpha in the MPO and monitored core temperature in control and KO mice throughout pregnancy. We report that eliminating ER alpha expression in the MPO increased core body temperature (i.e. blunted the reduction in core temperature associated with pregnancy). This work expands our knowledge on how steroid hormones impact thermoregulation during the transition into parenthood. Understanding the hormonal modulation of homeostasis is especially important as an increasing number of pregnant people are exposed to environmental thermal challenges.

THE GENETICS OF REPRODUCTIVE SUBTYPES OF DEPRESSION IN FEMALES: WHAT DO WE KNOW?

Crestol A

Reproductive subtypes of depression, including premenstrual dysphoric disorder, postpartum depression, and perimenopausal depression are tightly linked to hormonal fluctuations. However, it remains unclear whether these subtypes share underlying genetic architecture. In this commentary, we address the known genetic etiology of these reproductive subtypes of depression, as well as existing knowledge gaps, challenges, and ways forward. We found that postpartum depression has been extensively studied, while genetic studies on premenstrual dysphoric disorder and perimenopausal depression are currently lacking. No genome-wide association studies (GWAS) exist for premenstrual dysphoric disorder or perimenopausal depression. Several GWAS have been conducted for postpartum depression, however the largest GWAS to date found no significant loci, indicating insufficient power. Similarly, numerous candidate gene studies have been conducted for postpartum depression while considerably fewer exist for premenstrual dysphoric disorder, and results are inconsistent across studies. A small number of candidate gene studies have investigated depression in females at midlife, and of those, only one included an interaction with menopausal status.

Overall, there are insufficient studies to make any conclusions regarding overlapping genetic architecture across reproductive subtypes of depression. Across existing studies, a major limitation is an inconsistency in terminology and clinical guidelines. Further, studies primarily include only white Europeans. Moving forward, large, well-powered studies with consistent diagnostic criteria across diverse ethnicities are needed. The identification of potential differences in the genetic architecture of premenstrual dysphoric disorder, postpartum depression, and perimenopausal depression would advance our understanding of their pathogenesis and could foster the development of new therapeutic targets.

THE ROLE OF PROVIDERS AND MEDICAL RACISM IN DISPARITIES IN BLACK MOTHERS

D'Anna-Hernandez K

Black women have historically faced worse perinatal outcomes compared to other racial groups, with stress, system barriers, and discrimination contributing to these disparities. However, the specific impact of healthcare experiences, discrimination, and healthcare providers within the medical system on Black women's perinatal outcomes remains less understood. Qualitative research has suggested that medical racism is a factor in the maternal healthcare experience for Black women, but this has not yet been quantitatively addressed. In general, existing research has shown that women who feel more respected during the perinatal process tend to have better outcomes. Doulas have also been associated with more reports of maternal satisfaction, suggesting that their involvement in perinatal care could play a significant role in improving outcomes for Black women. This study seeks to explore the role of provider type on healthcare experiences and birth outcomes in Black women. Black women reported the least satisfaction with and less respect (due to their ethnicity) from medical doctors, relative to other providers (midwives, nurse practitioners, physicians assistant, etc.). The quality and trust of the patient-provider relationship was associated with more postpartum anxiety and depression. Women also reported high rates of preterm birth. Analysis is ongoing to determine if healthcare experience moderate the effect of provider type on birth outcomes and if the role of doulas may be protective. Overall this work adds to the growing literature on the role of obstetric racism in perinatal health disparities.

MEASURING INTERGENERATIONAL TRANSFER EFFECTS REFLECTED THROUGH PARENT-CHILD SIMILARITY OF THE CORTICOLIMBIC TRACT

Federici E

Introduction: Intergenerational-transfer-effects refer to the transmission of traits from parents to children, with parents playing a key role in shaping their children's brain development, socioemotional skills, and mental health. Socioemotional skills, essential for daily life and well-being, are supported by corticolimbic circuits (CLC). Aberrant CLC structure or function is associated with mental disorders, highlighting the critical influence of parents on children's brain development. Methods: We aim to investigate intergenerational transfer effects on corticolimbic brain structures in parent-child dyads. Neuroimaging and behavioural data from 71 families were collected. Analyses, focusing on structural brain similarity, included data from 173 individuals (66 children, 6-14y, 30 girls; 107 adults, 30-61y, 62 mothers; 32 mother-son, 25 mother-daughter, 26 father-son and 19 father-daughter dyads). T1-weighted images were

acquired on a GE 3T scanner and pre-processed in FreeSurfer. Gray matter volume was extracted from regions in the CLC (neocortical: anterior cingulate, medial orbitofrontal areas; subcortical: bilateral amygdala, hippocampus, nucleus accumbens) using the Desikan/Killiany atlas. Dyadic similarity was calculated with Pearson's correlation coefficients. Results: Results indicated significant structural brain similarity in all circuits (CLC, neocortical and subcortical) for mother-son (r=.47–.52,p<.016) and mother-daughter dyads (r=.44–.51,p<.031). For father-son dyads, significant correlations were found in CLC (r=.56,p=.003) and neocortical circuits (r=.63,p<.001), but not subcortical (r=.29,p=.157). No significant correlations emerged for father-daughter dyads (r=.10–.19,p>.462). Future analyses will incorporate behavioral data exploring neural-behavioral interactions. Conclusion: Understanding underlying parent-child similarity mechanisms enhances our insight into how socioemotional skills are transmitted across generations, revealing developmental trajectories and factors shaping risk and resilience.

YOU'RE NOT ALONE: THE EFFECT OF ROMANTIC PARTNER PHYSICAL PRESENCE ON CORTICAL RESPONSE TO INFANT STIMULI IN NULLIPAROUS WOMEN

Filippi B

Infant cry is a salient stimulus that elicits caretaking behaviors from adults, but can also be a source of stress, highlighting the need for effective emotion regulation abilities. Yet, most research has focused on how individual factors (e.g., attachment style, individual emotion regulation) influence neural responses to infant stimuli, with less attention on interpersonal dynamics. Emotion regulation is inherently relational, and evidence from behavioral studies suggests that the mere physical social presence of another individual, especially a romantic partner, can modulate emotional and behavioral response to infant distress. This is particularly relevant as romantic relationships, in most cases, evolve into co-parenting dynamics, a crucial protective factor for both child development and partner well-being. Using functional Near-Infrared Spectroscopy, the present study investigated the effect of a romantic partner's physical presence on individuals' hemodynamic cortical responses to infant auditory stimuli in the prefrontal and parietal cortex areas. Forty nulliparous women and their partners underwent a passive listening task, where women were presented with novel infant cries, infant laughter, and control sounds in a randomized order, under two conditions: (1) alone; (2) in the same room as their partner, without physical contact. To monitor the attention level, participants were informed that they might be asked to evaluate the emotional valence of the sound stimulus just presented in an unpredictable way. The results will be discussed in terms of their implications for parental support interventions and future research directions on interpersonal neural regulation in caregiving contexts.

LATE-LIFE TRACES OF PARENTHOOD IN STRUCTURAL BRAIN MRI DATA

Fischer JL

Structural brain MRI studies have reported effects of motherhood in the human brain, even decades after childbirth. Whether these reflect persisting traces of pregnancy or effects of parenthood is unclear. Here, we compared effects of past live birth in women to effects of fatherhood in men, targeting the identification of shared patterns of parenthood. Aiming to isolate pregnancy from parenting, we also tested for effects of past pregnancy loss.

From the UK Biobank we selected N=3240 mothers (1-8 children) and N=3240 age-matched nulliparous women, all without past pregnancy losses. For fathers and non-fathers, we selected age-matched samples of the same size. Univariate analyses across 212 regional brain volumes revealed significant group differences in 13 regions for mothers and in 12 for fathers, with 4 regions overlapping between sexes. Association statistics for past live birth and fatherhood correlated across regions (r=0.51). In a subset of N=945 per group we compared nulliparous women to women without live births but pregnancy losses, and mothers without losses to mothers with losses. No significant effects of pregnancy loss were identified.

Overall, our findings suggest that effects associated with parenthood - but not pregnancy loss - may reflect traces of parenthood itself, rather than solely persisting traces of past pregnancies. Caution is warranted given the limited power and characterization of the pregnancy loss data. Our own ongoing recruitment efforts for pregnancy loss data but also projects on same-sex couples entering parenthood suggest promising data to further study the extent and nature of maternal neuroanatomical adaptations.

LONGITUDINAL CHANGES OF BRAIN STRUCTURES ACROSS THE FEMALE REPRODUCTIVE LIFESPAN

Freund M

Hormonal fluctuations across the female reproductive lifespan have been associated with increased neuroplasticity as well as increased vulnerability to mental health disorders. Identifying similarities and differences between different hormonal transition phases and their impact on the brain might help to translate findings from well-studied fields, such as the neuroscience of puberty, to emerging research areas, such as the neuroscience of pregnancy and pregnancy loss. Here, we aimed to characterize the brain anatomical architecture of two hormonal transition phases, (1) menarche as an event leading to raising levels of steroid hormones, and (2) menopause, as a time of declining levels.

Using linear mixed-effect models on two longitudinal MRI datasets, we explored the effects of menarche onset (ABCD study, N=611) and menopause onset (UK Biobank, N=122) on the volumes of 201 brain regions, controlling for age-related variance. We found 56 volumes significantly associated with menarche beyond age (P<.05 FDR-corrected). Whereas no menopause effect survived FDR correction, three of the regions significantly associated with menarche were nominally significant also for menopause (P<.05 uncorrected); specifically, the rostral middle frontal gyrus in both hemispheres and the right medial orbitofrontal cortex.

We will next integrate these preliminary findings with further studies of the hormonal fluctuations in pregnancy and pregnancy loss, examining the degree and spatial profiles of volume changes also for reproductive events. As such, by combining longitudinal windows into different phases of the reproductive lifespan we seek to build up a system-level understanding of the neural foundations of women’s reproductive neuroplasticity and mental health.

EXPLORING THE IMPACT OF SOCIAL FACTORS AND NUMBER OF CHILDBIRTHS ON WHITE MATTER HYPERINTENSITY IN POST-MENOPAUSAL WOMEN AT RISK OF AD

Gallay C

Hormonal changes caused by pregnancy impact the cerebrovascular and central nervous systems. Additionally, social factors play a role in health and pregnancy outcomes. Our previous results show that higher number of childbirths relates to less white matter hyperintensities (WMH) in frontal regions and basal ganglia. Here, we examine the influence of socioeconomical factors on WMH and its moderating or mediating role in the relationship between childbirth and WMH in healthy cognitively unimpaired (CU) postmenopausal women at increased risk of AD.

Our sample includes 201 CU postmenopausal women from the ALFA+ study. Regional WMH volumes were obtained averaging lesions within five regions: frontal, temporal, parietal, occipital lobes, and basal ganglia. Social factors were years of education and household income. Linear regression models assessed the relationship of each social factor to WMH volume and their moderating or mediating role in the childbirth and WMH relationship. All models covaried for APOE-ε4 status, age and amyloid positivity (CSF Aβ42/40 ratio<0.071).

Subjects' age ranged between 49.61 and 73.43 (m=60.78, sd=4.73). Number of childbirths ranged between 0 and 4 and had no significant relationship with age or social factors. We did not find a significant main effect of social factors on WMH volume. No moderation or mediation effect was found.

Results imply that previous associations found between childbirths and lower WMH load in frontal regions and basal ganglia are driven by biological mechanisms related to pregnancy and cardiovascular health rather than socioeconomic factors. Findings may differ in diverse populations with varying socioeconomic backgrounds and risk profiles.

EXAMINING THE TOLE OF IL-1R ANTAGONISM IN TREATING POSTPARTUM DEPRESSION USING A RODENT MODEL

Garcia de Leon R

Background: Depression risk is highest during the postpartum [postpartum depression (PPD)]. Selective serotonin reuptake inhibitors (SSRIs) are often prescribed for PPD, however, only 3.2% of females with PPD achieve remission with SSRIs. In our preclinical model of PPD, we administer high corticosterone (CORT) during the postpartum. We found increased levels of the proinflammatory cytokine IL-1β in the hippocampus was commensurate with reduced SSRI efficacy, indicating this may be an important target to boost SSRI efficacy. Our central hypothesis is that antidepressant efficacy in the postpartum is mediated by inflammatory signalling.

Methods: High CORT was administered during the postpartum period to dams starting on postpartum day 2 along with fluoxetine (FLX) and/or anakinra (KIN), an IL-1R antagonist. FLX efficacy was measured using the forced swim test (FST), and maternal care observations. All dams were euthanized 23 days later to examine inflammation and neuroplasticity in the hippocampus.

Results: Dams treated with KIN (with or without FLX) failed to rescue passive coping behaviours in the FST. However, FLX and KIN together were able to rescue reductions in neuroplasticity as noted in hippocampal perineuronal net (PNN) expression and doublecortin (DCX+ cells) expression. Current analyses are in progress to quantify PNNs in the frontal cortex, alongside postsynaptic density-95 (PSD-95) in both hippocampal and frontal cortex tissue. Lastly, we will quantify the percentage of phagocytic microglia (Iba1+/CD68+) in the hippocampus and frontal cortex.

Conclusions: These findings indicate that IL-1β may serve as a potential target for increasing antidepressant efficacy in people with PPD.

MATERNAL ELECTROPHYSIOLOGICAL RESPONSE TO INTERACTIONS WITH THEIR OWN CHILD: A PRELIMINARY STUDY IN A SAMPLE OF SAME-SEX MOTHERS

Gemignani M

Previous research explored the links between maternal electrophysiological responses and caregiving quality. However, these patterns remain underexplored in same-sex mothers, and prior studies often employed designs with limited ecological validity. Moreover, no research has investigated how maternal involvement in childcare associates with event-related potential (ERP) responses to child stimuli.

Thirty-two same-sex mothers participated in a study involving a 15-minute structured play session with their child (ages 3–11 years), videotaped and coded using the Emotional Availability Scales. Stimuli for the EEG task were extracted from these recordings. During EEG, mothers viewed videos of their own and other parent-child interactions, displaying successful and unsuccessful exchanges. Maternal involvement in childcare was assessed using the Child Caregiving Involvement Scale.

Results revealed that same-sex mothers exhibited an enhanced Late Positive Potential (LPP) response to interactions with their own child compared to interactions involving other parent-child dyads. Mothers with higher involvement displayed an increased LPP activation in response to unsuccessful interactions with their own child. However, this result did not remain significant after post-hoc corrections. Mothers who exhibited greater sensitivity, non-intrusiveness, and non-hostility showed an amplified LPP response to unsuccessful interactions with their own child.

These findings advance the understanding of the neural correlates of parenting considering the diversity of contemporary family structures. Employing a novel experimental paradigm, we highlight the neural mechanisms underlying sensitive caregiving in same-sex families of two mothers. These families, particularly in the Italian context, face significant societal challenges, underscoring the importance of continued research and policy efforts to support them.

EARLY EXPERIENCES WITH CAREGIVERS AND NEURAL RESPONSES TO INFANT FACES: BEHAVIORAL AND ELECTROPHYSIOLOGICAL EVIDENCE FROM NULLIPAROUS ADULTS

Gemignani M

Early experiences with caregivers play a critical role in shaping individual adjustment and modulating responses to socially relevant stimuli, such as infant faces. Within the framework of Interpersonal Acceptance-Rejection Theory (IPARTheory), this study explored how perceptions of childhood acceptance or rejection from caregivers are associated with behavioral and electrophysiological (EEG) responses to adult and infant faces.

Sixty nulliparous adults (30 males, 30 females) completed an Emotion Recognition task with emotional and neutral infant and adult faces while undergoing an EEG recording. Participants completed the Parental Acceptance-Rejection Scale to assess perceived care experiences during childhood.

Results revealed that higher levels of perceived maternal rejection were associated with slower reaction times (RTs) in recognizing adult and infant faces, particularly among males. At the neurophysiological level, higher perceived paternal rejection was linked to an increased N170 amplitude in response to infant faces, suggesting a greater discrimination effort. Females who reported higher paternal rejection exhibited a larger N170 amplitude increase and a more pronounced decrease in LPP amplitude in response to emotional faces compared to males.

These findings highlight how perceptions of parental rejection influence social cue processing in adulthood at both behavioral and neural levels. Maternal rejection was associated with slower behavioral recognition of faces, whereas paternal rejection was linked to heightened cognitive discrimination demands during early processing of infant faces. These associations were further modulated by sex, highlighting the complex ways in which early care experiences shape adult social cognition.

INFLUENCE OF MATERNAL METABOLISM ON NEONATE EATING BEHAVIOR

Goll N

Introduction: Maternal metabolism before and during pregnancy is assumed to influence eating behavior in the offspring, but respective results in neonates are lacking. We investigated whether eating behavior assessed objectively and subjectively in the very early days of life is modulated by maternal BMI and maternal weight gain during pregnancy.

Methods: Two weeks after birth, food intake of 21 neonates was assessed by weighing breast-fed babies before and after feeding, or directly in bottle-fed babies. In addition, mothers filled in the Baby Eating Behavior Questionnaire (BEBQ). Results were analyzed by multivariate regression analyses and group comparisons according to preconceptual BMI and to the range of pregnancy-related body weight gain according to Institute-of-Medicine guidelines.

Results: Pregnancy-related maternal weight gain predicted BEBQ ‘food responsiveness’ ($\beta=0.11$, $P<0.01$), reflected by increased values in neonates born to females with increased

vs. reduced weight gain (P<0.03). Neonates born to females with recommended weight gain displayed increased 'satiety responsiveness' compared to neonates of females with increased (P<0.02) or reduced weight gain (P<0.09). Satiety responsiveness also tended to be inversely related to preconceptual maternal BMI (β=-0.07, P<0.10). While subjective and objective measures of food intake largely corresponded, the effects were less pronounced in the latter. Birth weights of neonates born to the different maternal groups were generally comparable (mean across all neonates: 3447 ± 131 g).

Conclusion: Dysregulations of maternal metabolism before and during pregnancy may predispose neonates to dysfunctional hunger and satiety regulation at a very early age, with potential ramifications for subsequent body weight trajectories.

COLD ADAPTATION OF MECHANOSENSATION IN A MAMMALIAN HIBERNATOR

Greenberg R

The thirteen-lined ground squirrel is an obligate hibernator that seasonally drops its body temperature from 37° in the active state to 2-4°C during torpor. While such temperatures typically inhibit peripheral nervous function in homeotherms, torpid squirrels remain sensitive to mechanosensory cues through unknown cellular mechanisms. We performed patch clamp electrophysiology of squirrel dorsal root ganglia (DRG) neuronal cultures across seasonal states and temperatures to assess the hypothesis that the species possesses functional adaptations at the DRG supporting mechanosensation in the cold. Candidate adaptations include modification of ion channels pertaining to (i) action potential induction or (ii) mechanotransduction. Torpid neurons maintained at 10° demonstrated largely unchanged resting membrane potential, input resistance, and action potential kinetics relative to active neurons. Meanwhile, inactivation time constants of mechanically activated (MA) currents shifted from mostly rapidly-inactivating (0-10 ms) in active neurons, to almost exclusively slowly-inactivating (>30 ms) in torpid neurons. Across vertebrates, the slowing of MA current inactivation in response to cold potentiates mechanotransduction via increased ion conduction per stimulus, suggesting this modification in torpid neurons may be an adaptation to enhance signaling at low temperatures. Furthermore, torpid neurons incubated at 37° displayed a dominant proportion of rapidly-inactivating current as in active neurons, suggesting the torpid squirrel DRG mechanotransduction phenotype depends on prolonged cold exposure. These findings bring forward a subcellular candidate mechanism for mammalian adaptation to peripheral signaling in the cold. Broadly, this line of work will elucidate molecular underpinnings of nervous system resilience in response to an extreme physiological challenge.

MAPPING NEUROVASCULAR ADAPTATIONS ACROSS PREGNANCY: INSIGHTS FROM THE MATERNAL BRAIN PROJECT

Grotzinger H

80% of women experience pregnancy at least once in their lifetime, yet the neuroscience of human pregnancy is still in its infancy. Only recently has longitudinal research begun to illuminate the pronounced structural brain changes that occur over the perinatal period: gray matter volume (GMV) and cortical thickness (CT) consistently decrease across pregnancy

with a partial recovery in the postpartum. Estradiol, a potent vasodilator, drives a ~30-50% increase in blood flow and cardiac output during pregnancy. However, there is virtually no knowledge of how these pregnancy-induced cardiovascular adaptations impact cerebral blood flow (CBF). Here, we used a precision imaging design to map the structural and cerebrovascular adaptations of first-time mothers throughout pregnancy and postpartum. Three females planning a first-time pregnancy completed ~20 Magnetic Resonance Imaging (MRI) visits from pre-conception up to one year postpartum, including a whole-brain anatomical sequence and a pseudo-continuous arterial spin labeling sequence to assess CBF. As expected, all pregnant participants showed significant GMV and CT decreases ($p < 0.001$) across gestation. Additionally, two pregnant participants displayed increases in CBF from baseline to a peak around week 22 in the second trimester, followed by a subsequent decline (Subject 1: $p < 0.001$; Subject 2: $p = 0.010$), while a third participant with hypertension showed no such pattern ($p = 0.439$). Together, these findings reveal that the brain undergoes profound structural remodeling and cerebrovascular changes throughout gestation. Future investigations incorporating peripheral biofluids will be essential to uncover the biological mechanisms underlying these neural adaptations.

PREGNANCY RESHAPES DOPAMINERGIC CIRCUITRIES AND INDUCES FOOD CRAVING-LIKE BEHAVIOURS

Haddad-Tóvolli R

The transition to motherhood requires profound physiological and behavioral adaptations to ensure optimal conditions for embryonic development. Among these, food cravings for highly palatable foods are prevalent during pregnancy and are a contributing factor to gestational overweight and obesity. Here, we demonstrate that mice, similar to humans, experience gestational food craving-like episodes, which are associated with functional reorganization of brain connectivity within key components of the dopaminergic mesolimbic circuitry. Pregnancy engages a dynamic modulation of dopaminergic signalling through Nucleus Accumbens D2R neurons, which directly modulate food craving-like episodes. Persistent maternal food craving-like behaviour leads to intergenerational effects, thus impacting offspring neuropsychological and metabolic health. In particular, progeny born to dams experiencing persistent food craving-like episodes develop anxiety-related states and binge eating-like disorder during adolescence and adulthood. Remarkably, targeted manipulation of maternal brain circuits underlying food craving-like behaviors can effectively rescue offspring's anxiety and eating disorder traits. Our results reveal the cognitively motivated nature of pregnancy food cravings and highlights a direct neurobiological link between maternal food cravings and offspring mental health.

NEURAL SIGNAL VARIABILITY AND THE MATERNAL BRAIN

Halmans S

Pregnancy induces profound changes in brain structure and function, reflecting dynamic adaptations supporting the transition to motherhood. However, the mechanisms driving these changes and their behavioral implications remain unclear. This study focuses on neural signal variability, a measure of moment-to-moment fluctuations in brain activity associated with cognitive capacity and known to decline with age.

Using data from a prospective cohort study, we analyzed resting-state fMRI from 40 first-time mothers scanned before conception and at early and late postpartum stages. A control group of 40 nulliparous women underwent two scans over a comparable time period. Signal variability was quantified as the voxel-wise standard deviation of the BOLD signal after manual denoising.

When comparing changes in pre- and post-pregnancy signal variability between the pregnancy and the control group, significant clusters were observed in the bilateral superior/middle temporal gyrus. Within-group analyses revealed a pattern of pronounced and large-scale reductions in signal variability between sessions in the control group. In contrast, only a few localized clusters of signal variability decrease were observed in the pregnancy group.

These findings indicate that women who become mothers show reduced declines in the variability of neural fluctuations in comparison to nulliparous control women. These reductions are in accordance with previously observed age-related declines in signal variability, suggesting a potential protective effect of pregnancy against normal aging processes. These findings thus point to the possibility that pregnancy may modulate typical brain aging, offering a protective mechanism.

STRUCTURAL BRAIN CHANGES DURING HORMONAL TRANSITION PERIODS

Holm MC

Puberty and pregnancy are hormonal transition periods marked by steep increases in sex steroid levels and changes to immune functions, alongside shifts in the psychosocial environment. Research shows heightened neuroplasticity during these life phases which suggests may be linked to the higher incidence of psychiatric conditions normally onsetting at puberty and during post-partum. Despite advancement in research on neural changes during puberty and pregnancy, the full scope of alterations remains unclear. To advance understanding of these periods, we studied: 1) the relationship between pubertal markers and brain development, and 2) pregnancy-related structural brain changes in a study under analysis. Using a deep convolutional network on minimally processed T1 data from a longitudinal sample of 9807 youth (9-12 years) from the adolescence brain and cognitive development (ABCD) study, we analyzed associations between brain age and pubertal status assessed via the pubertal development scale. We found that one step increase in pubertal maturation correlated with a 2.22-month higher brain age across time points ($\beta = 0.10$, $p < .001$), and that annualized change in pubertal development was weakly related to the rate of change in brain age ($\beta = .047$, $p = 0.04$). In our ongoing study on pregnancy-related brain changes, we are assessing changes in brain structure from pre-conception to 5 months post-partum in a sample of 118 females aged 25-42. In this data we are currently testing the hypotheses that pregnancy leads to a) differential structural brain changes depending on parity status, and b) change in brain age.

PREOPTIC CIRCUIT REMODELLING UNDERLIES ALLOPARENTAL CARE IN JUVENILE MICE

Jamieson BB

In mice, parental behaviour is controlled by brain-wide circuits, the functional organisation of which is increasingly well understood. However, the relevance and function of these circuits in early life remains unknown. Here, we uncover the functional circuit architecture of parental circuits in juvenile mice and address whether they control alloparental social interactions at this age.

We have observed that juvenile mice start to display spontaneous alloparental behaviour between postnatal day (P) 14 and 15, at levels similar to adult virgin females. This is independent of prior exposure to pups. c-Fos mapping revealed that this behaviour recruits galanin-expressing neurons in the medial preoptic area (MPOAGal neurons). We confirm that these neurons start exhibiting pup-evoked activity at P15, using in vivo calcium imaging.

While anterograde viral tracing from MPOAGal neurons in juveniles shows adult-like projection patterns, retrograde trans-synaptic tracing uncovers much more extensive inputs in juveniles. We find that MPOAGal neurons undergo extensive morphological remodelling between P14 and P15, accompanied by an increased frequency of spontaneous postsynaptic currents. This suggests that maturation of parenting-relevant synaptic inputs drives the onset of alloparental behaviour during this period. Concurrent changes in microglial morphology suggest that glial activation may play a role in the mechanisms underlying this cellular remodelling.

Our results indicate that morphological and biophysical alterations in juvenile MPOAGal neurons contribute to the onset of alloparental behaviour. This work provides valuable insights into the neurodevelopmental processes that underlie the expression of caregiving behaviours during early life.

MAPPING ASB4: MATERNAL IMPRINTING IN THE PARENTAL HUB NEURONS OF THE MPOA

Jones RA

Genomic imprinting is a form of epigenetic regulation in which expression is limited to one parental allele only and, in animals, found only in mammals. Although only a small subset of the genome is subject to genomic imprinting (~260 genes and ncRNAs) these are crucial for development and prominent in a few key physiologies. For instance, imprinted gene expression is predominant in the brain and their roles in neural processes are becoming more appreciated. Recent in silico analyses of published RNA-seq data show an enrichment of imprinted gene expression in the “parental hub” of the hypothalamus. Specifically, imprinted genes were over-represented in the transcriptomic profile of Galanin positive (Gal+) neurons in the medial preoptic area (MPOA) of the hypothalamus. Here I replicate and expand this finding by examining the transcriptomic profile of MPOA samples enriched for Gal+ cells. Again, imprinted genes were significantly over-represented in the transcriptomes of Gal+ cells. One of those imprinted genes was the maternally expressed Asb4. We hypothesise that Asb4 has a role in the function of the MPOA and influences parental behaviour. Following on from the RNA-seq analysis, I explore the spatial expression of Asb4 within the MPOA using

RNAscope. In particular, I examine whether Asb4 co-localises Galanin and/or Calcitonin Receptor (Calcr) expressing neurons within the MPOA.

EXPERIENCE-DEPENDENT REGULATION OF SOCIAL AND PARENTAL BEHAVIORS BY THE OXYTOCIN RECEPTOR-EXPRESSING NEURONS IN THE LATERAL SEPTUM

Keller D

Social behaviors are crucial for the survival and reproduction. The role of lateral septum (LS) in the control of maternal responses and social novelty is well-established. Despite the important role of the LS in regulating both parental and social behaviors, the exact mechanism of balancing between these behavioral forms remains to be elucidated. The role of oxytocin and oxytocin receptor (OxtR)-expressing cells in these behaviors has been also established. We hypothesize that the OxtR-expressing cells of the LS play a significant role in mediating between social and parental behaviors in both male and female and the posterior intralaminar thalamic (PIL) input plays significant role in this mechanisms.

We used calcium imaging in behaving mice to record activity of a large number of OxtR-LS cells across different phases of parental and social behaviors in both male and female mice.

We identified distinct coding patterns of OxtR cells in response to parental and social interactions. In virgin animals, OxtR cells are found to be specifically inhibited by pup stimuli. However, this inhibition decreases following sexual experience, after which OxtR cells instead become inhibited by social stimuli. We also found that those OxtR cells in virgin animals, that are inhibited by pup stimuli, are excited by social stimulus.

Additionally, LS-OxtR cells exhibits inhibition during sexual behavior. Furthermore, optogenetic stimulation of PIL input to LS-OxtR cells significantly increased their activity. In summary, our findings suggest that OxtR-expressing cell populations in the LS function in a complementary manner to regulate both social and parental behaviors.

PROFILE OF STEROID METABOLITES IN HUMAN BREAST MILK IN DIFFERENT STAGES OF LACTATION.

Khymenets O

Background: Steroids play a primary role in establishing of mother-placenta-fetus relationship during curse of pregnancy. However, their role in postpartum period is not very well studies, especially in relation to breastfeeding, a functional link between mother and child where breast milk (BM) acts as a physiological mediator. BM, as an optimal food, provides the newborn with a variety of minor compounds relevant for health and wellbeing. Endogenous steroids, also minor constituents, are mainly secreted in BM as conjugated metabolites. Recent research has revealed the relevance of steroid conjugates in many physiological processes. Thus, their presence in BM appears to be very intriguing, especially in relation to breastfeeding.

Study´s objective: The objective of our study was to profile steroid metabolites present in BM in relation to the lactation stage, and to promote further evaluation of their importance in breastfeeding.

Methodology: We developed and used a direct UHPLC-MS/MS metabolomics approach capable to detect more than 60 conjugated metabolites (mono-sulfated, mono-glucuronylated, bis-sulfated and sulfate-glucuronylated) from all steroid families. We compared the occurrence of these metabolites in 62 samples collected from breastfeeding mothers and stratified by lactation stages: colostrum, transitional and mature milk.

Results: Our results showed that many biologically relevant steroids are secreted in BM. The concentrations were highest in colostrum, decreased remarkably in transitional and were much lower in mature milk, with some exceptions. The profile of metabolites also differed considerably between lactation stages. The approximate daily secretion in BM indicated that infants are exposed to significant oral doses of steroid metabolites during the first week of lactation. The supply of these metabolites in BM declined and became constant after the second week postpartum.

Conclusions: Overall, our data provide a foundation for further investigation on the physiological relevance of BM secreted steroid metabolites in relation to both mother and child.

DYNAMICS OF SALIVARY STEROIDOME THROUGHOUT THE COURSE OF PREGNANCY.

Khymenets O

Background: The endocrinology of pregnancy is very complex with steroid hormones acting as primary players in its establishing and evolution. During gestation drastic changes occur in the biosynthesis and metabolism of all steroid families: progestogens, androgens, estrogens and corticosteroids. Comprehensive steroid profiling and exploration of longitudinal changes in steroidome can provide an opportunity for better monitoring and understanding physiology of pregnancy. In this respect, saliva, as non-invasive and stress-free biological sample, could be of specific interest, since it provides an information on freely available and biologically active unbound steroids rather than on total circulating metabolites. Therefore, the assessing of salivary steroidome can provide an interesting asset for tracking hormonal changes occurring on the systemic levels during pregnancy.

Study´s objective: To explore salivary steroidome and its fluctuation through the course of normal pregnancy in order to evaluate its potential in monitoring hormonal changes in this biological fluid.

Methodology: Two direct UHPLC-MS/MS targeted metabolomics approaches capable to detect a wide variety of both unconjugated steroids and conjugated metabolites were developed. These methods were applied for analysis of saliva samples collected in 5 women every two weeks over the course of a normal gestation.

Results: The presence of numerous unconjugated steroids and conjugated metabolites belonging to different steroid families was detected in saliva samples, all together establishing dimensions of salivary steroidome. We also monitored the changes in steroid metabolites through the course of gestation and reported on the pregnancy related dynamics of salivary steroidome.

Conclusions: Our study shows that the salivary steroidome, represented by both unconjugated and conjugated steroids, can be a valuable tool for monitoring of pregnancy related hormonal rearrangements on the level of steroid synthesis and metabolism.

THE PROSPECTIVE ASSOCIATIONS BETWEEN PRENATAL SOCIOECONOMIC RISKS AND POSTPARTUM BRAIN RESPONSES TO INFANT CRIES AMONG NEW BIRTHING PARENTS

Kim P

Non-human animal studies suggest that prenatal stress disrupts normative plasticity in brain regions critical for parental motivation and behavior. However, little is known about the impact of prenatal stress—particularly exposure to environmental stressors—on postpartum brain and behavioral outcomes in human birthing parents. This prospective study examined the associations between socioeconomic risks (poverty and income instability) during pregnancy and postpartum brain responses to infant cues. A total of 120 participants were recruited during pregnancy and included in the subsequent fMRI analysis. At one month postpartum, participants underwent fMRI while listening to four sound types: their own infant's cry, a control infant's cry, white noise matched to their own infant's cry, and white noise matched to the control infant's cry. Lower income during pregnancy was associated with reduced parental sensitivity during interactions with their infants, $r(104) = 0.21$, $p = 0.027$. Neuroimaging revealed that lower income was linked to dampened brain responses to infant cries compared to white noise in the right superior temporal gyrus and right precentral gyrus—regions implicated in empathy and parental response preparation, $ps < 0.05$, corrected. Moreover, income instability during pregnancy was associated with reduced responses to infant cries in the left inferior frontal gyrus, a region involved in emotion and social information processing, $p < 0.05$, corrected. These findings highlight that socioeconomic risk during pregnancy prospectively contributes to attenuated brain responses to infant cries, potentially impairing parents' ability to respond sensitively to their infants during early interactions.

INVESTIGATING THE BRAIN CRF AND OXT SYSTEMS IN THE NUCLEUS ACCUMBENS: IMPLICATIONS FOR POOR MOTHERING IN LACTATING RATS

Köck A

Females undergo various adaptations to prepare for motherhood, resulting in a balanced interplay of various neurotransmitter systems, like corticotropin-releasing factor (CRF) and oxytocin (OXT). Their dysregulation can potentially lead to maternal neglect. The nucleus accumbens (NAc), a heterogenous brain region at the interface of the reward and maternal circuits, plays a key role in these processes. Here, we investigated the NAc CRF and OXT systems' involvement in maternal behaviour in early lactating rats. First, maternal aggression was monitored during the maternal defence test (MDT) against a virgin female intruder after bilateral, local injections of vehicle or CRF (1 µg/0.5µL/side) in the NAc shell. In addition, maternal care was monitored before and after the MDT. Acute CRF infusion reduced the number of attacks and total nursing. Microdialysis during the MDT revealed increased intra-NAc OXT release during maternal defence. Interestingly, retrodialysis of CRF, but not of Urocortin 3, also resulted in OXT release within the NAc. Unilateral microinfusion of a

retrograde transported virus in the NAc shell of virgin female rats revealed CRF+ projections descending from the basolateral amygdala, medial prefrontal cortex, and paraventricular thalamus. Using in-situ hybridisation, we further characterised the nature of CRF receptor-expressing neurons in the NAc, indicating differential expression of Crhr1 and Crhr2 throughout the NAc. This research highlights the critical role of NAc CRF and OXT in regulating maternal behaviour and provides novel insights into the NAc's neuronal underpinnings.

ASSOCIATION OF HIPPOCAMPAL VOLUME AND TREATMENT RESPONSE IN POSTPARTUM DEPRESSION

Koeppel CJ

Postpartum depression (PPD) is a highly prevalent postpartum complication, impairing maternal quality of life, mother-infant bonding and child development. The peripartum is a critical phase for the development of affective disorders and closely linked to alterations in hippocampal volume. Smaller hippocampal volume presents a reliable brain structure as predictor for treatment outcome in major depressive disorder (MDD). Still, studies focusing on associations between hippocampal volume and treatment outcome in PPD remain scarce. We analyzed T1-weighted MRI scans and behavioral data from 18 mothers suffering from PPD, admitted for in-patient treatment at the specialized psychiatric parent-child unit at Charité Berlin. Separate logistic and linear regression analyses were performed for each left and right hippocampal volume as predictor of treatment outcome. Smaller right hippocampal volume was significantly associated with treatment outcome in PPD, representing an inverse effect to prior findings in MDD. Our findings introduce first insights into structural markers for treatment outcome in postpartum depression. The inverse effect compared to MDD is likely due to the neuroadaptive processes observed during the peripartum with widespread cortical grey matter reductions being linked to better mother-infant attachment, potentially having a positive impact on treatment outcome.

LONG-TERM EFFECTS OF POSTNATAL CLOMIPRAMINE EXPOSURE ON CENTRAL AMINERGIC SYSTEMS IN A POSTPARTUM RAT MODEL OF OBSESSIVE-COMPULSIVE DISORDER

Kosaraju H

Obsessive-compulsive disorder (OCD) is characterized by difficulty controlling thoughts and impulses and disproportionately affects postpartum women. OCD is associated with low central serotonin (5-HT) and dopamine (DA) levels and decreased hippocampal volume, indicative of impaired mood stabilization, cognitive ability, and memory formation. Clomipramine, a tricyclic antidepressant that targets serotonin and norepinephrine reuptake, is one current treatment for OCD in pregnant and lactating individuals. The long-term effects of clomipramine on maternal aminergic systems are unknown. Although clomipramine is used to treat OCD in adults, male rat pups administered postnatal clomipramine contrarily exhibit OCD-like behavior and increased central 5-HT and DA receptor expression in adulthood. Although OCD-like behavior and neurotransmitter levels due to clomipramine exposure have been analyzed in male rats, this model has not been examined in the hippocampus or in female rats. Based on previous studies, we hypothesized that administering clomipramine to female rats during their early postnatal period causes decreased adult postpartum 5-HT and

DA levels in the hippocampus compared to controls. To test this hypothesis, during postnatal days 9-16, 30 Sprague-Dawley female rats received intraperitoneal injections of either 0.9% saline (control) or 15 mg/kg clomipramine (experimental) twice daily. High-performance liquid chromatography revealed that dams exposed to early-life clomipramine exhibited a 51.07% decrease in 5-HT and a 61.17% decrease in DA in their hippocampus versus controls. These decreased adult amine levels suggest that drug exposure during a sensitive developmental period affects later postpartum aminergic systems, further warranting increased research and consideration in addressing maternal health.

BIO-PSYCHO-SOCIAL BACKGROUND FACTORS OF NEAR-LETHAL CHILD MALTREATMENT CASES IN JAPAN: COMMON FEATURES WITH OFFSPRING DESERTION / ATTACK IN MAMMALS

Kuroda KO

Child maltreatment has been associated with multiple risk factors at the caregiver, child, household, and community levels. However, the relative importance of each factor and their interrelationships remain elusive because the available information, particularly on perpetrators, is often fragmentary. Here we examined the convicted cases of maltreatment and the control caregivers in Japan for 402 items inferring evolutionary adaptive and non-adaptive causes of offspring desertion and attack conserved in mammals. We found a significant accumulation of multiple developmental, neurobiological, and environmental factors in the Case participants with gender differences. Developmental pathway modeling with 391 caregivers identified the childhood abuse received, low educational attainment, and cohabitation with adults biologically unrelated to the victimized child as the top three contributors to the conviction for severe child maltreatment. This proof-of-concept study suggests two foci for intervention: parenting assistance for families with multiple vulnerabilities, and educational support for children in early adversity, as a societal responsibility to prevent severe child maltreatment.

DISRUPTION OF BIDIRECTIONAL DAM-PUP INTERACTIONS FOLLOWING GESTATIONAL BISPHENOL EXPOSURE

Lapp HE

Decades of research has illustrated the importance of “micro-behaviors” in human caregiver-infant interactions. These multi-modal second-by-second interactions have predictive power for infant development. Exposures to endocrine disrupting chemicals, such as bisphenols, during the perinatal period impact can impact maternal behaviors, but their impact on the bidirectional interplay between parent and offspring is not well understood. Bidirectional micro-coding approaches with animal models are limited by the lack of tools to acquire, code, and analyze the high-density data that characterizes dyadic social interactions. To address this methodological gap, we developed the Automated Maternal Behavior during Early Life in Rodents (AMBER) pipeline, which uses open-source machine learning software to automatically track rodent dams and pups in home cage recordings and extract behaviors with behavioral classifiers that have frame-level temporal resolution and high accuracy. We then used AMBER to investigate the effect of gestational exposure to exposures of BPA, BPS, and bisphenol mixtures on parent-infant contingency in Long-Evans rats. Similar to human micro-

coding studies, we assessed bidirectional dam-pup contingency using two second windows and dynamic structural equation modeling during focal 5-minute periods when the dam reenters the nest to attend to pups and identified dose and mixture-dependent disruptions in pup movement following nursing and dam nest attendance. We also examined dam-pup interactions more broadly by applying AMBER to continuous recordings from day of birth through postnatal day 10. Using these advanced tools for behavior analysis, we are able to uncover effects of bisphenols on reciprocal dam-pup behavior for the first time.

THE STILL-FACE EFFECT ON MOTHER–INFANT INTERPERSONAL DISTANCE: BEHAVIORAL AND PSYCHOLOGICAL CORRELATES

Lebert A

The Still-Face Paradigm provides a unique lens for examining how brief disruptions in maternal responsiveness (i.e., an unresponsive “still face”) affect infants’ emotional regulation and mothers’ interactive behaviors. This study first investigates changes in mother–infant interpersonal distance before and after the still face, and then explores their associations with maternal psychological and relational factors. Using a person-detection algorithm, we quantified mother–infant distance and maternal approach versus withdrawal behaviors, and subsequently correlated these measures with indices of attachment, postpartum depression, perceived stress, sleep quality, and cognitive empathy. Our findings underscore the importance of integrating spatial measures with traditional affective and behavioral indices within the Still-Face Paradigm, offering new insights into early socio-emotional dynamics and the mother–infant bond.

EXPOSURE TO PUPS INCREASES SEROTONIN RELEASE IN THE FEMALE MOUSE NUCLEUS ACCUMBENS

Lonstein J

It is well known that nucleus accumbens (NAc) dopamine (DA) signaling is required for high maternal motivation. However, we recently found a peripartum increase in NAc serotonin 5-HT1A receptor expression, with selective NAc knockdown of these receptors disrupting postpartum mothering and anxiety-like behaviors (Vitale, Ford, Ahearn & Lonstein, in press). Because NAc 5-HT facilitates local DA release, we used in vivo fiber photometry to examine NAc 5-HT release when females interact with pups. Nulliparous mice received the 5-HT sensor, AAV2/9-hsyn-5HT3.0 (BrainVTA, China), and a fiberoptic cannula into the NAc shell (n=6). Mice were pseudorandomly exposed to a palatable food pellet, a foster pup, and a plastic pup for 3-10 min each. Changes in 5-HT-dependent (490 nm) fluorescence were determined with reference to scaled 5-HT-independent fluorescence (405 nm) as a proxy for 5-HT release. The first 20 min of recording was the baseline. Mean z-scores were determined one min before and one min after first contact with the stimuli. Results revealed significant NAc 5-HT release only to the live pup (z-score=0.76±1.06 to 5.99±1.22, $p<0.01$) with 5-HT release unexpectedly sustained for the duration of pup contact. This contrasts with our work (Perkinson & Brown, unpublished) showing elevated DA release in the virgin mouse NAc to either pups, objects, or food and all followed by a rapid decline. This study provides critical information about how NAc 5-HT relates to maternal caregiving. Ongoing studies are

investigating temporal dynamics between 5-HT and DA release in the maternal NAc to further explicate the neurochemical control of motherhood.

OXYTOCIN-MEDIATED CORTICAL PLASTICITY UNDERLYING MATERNAL BODILY ADJUSTMENTS DURING NURSING

Maier E

Maternal care, especially through early tactile contact, is essential for survival and well-being of the infant. Tactile experiences are processed and stored in the somatosensory cortex (S1). Hence, this area might play an important role for maternal care. This is supported by previous studies that have shown plastic changes in S1 of lactating rats. Tactile experiences, as well as maternal behavior have both been linked to oxytocin (OT). However, we still have little understanding about the neurobiological mechanisms underlying the relationship between OT, social touch and maternal behavior. We conducted electrophysiological recordings in lactating rats and found that neural plasticity was impaired following oxytocin receptor knock-out (OTR-KO) in S1. To investigate the relevance of this plasticity we analysed maternal behavior during nursing of these OTR-KO animals and found a reduction of bodily adjustments towards the litter. To investigate the underlying mechanisms of lactation induced receptive field plasticity, we used a combination of genetic, viral and anatomical techniques and found that the OTR neuronal population in the ventral trunk / nipple representation largely consisted of GABAergic interneurons. Using multi-shank recordings, we are currently investigating whether receptive field plasticity in lactating rats arises through lateral inhibition of principal cells by OTR expressing inhibitory interneurons from neighbouring cortical columns. Summarized, our results suggest that OT is essential for receptive field plasticity in S1, which in turn may facilitate precise mother-pup coordination.

NEURAL PROCESSING OF ADULT VS INFANT FACES IN MOTHERS OF CHILDREN WITH AUTISM SPECTRUM DISORDER: AN ERP STUDY OF N170 AND P2 RESPONSES AND THEIR ASSOCIATION WITH MATERNAL SENSITIVITY.

Márquez C

Introduction: Face processing is a critical aspect of social cognition and essential for effective communication and bonding, especially between mothers and their children. Face processing in parents helps us understand how adaptive strategies, emotional responses, and maternal sensitivity (MS) might be achieved, particularly in women raising children with Autism Spectrum Disorder (ASD). It remains unclear whether mothers of children with ASD process infant facial expressions differently from adult facial expressions at the neural level. Therefore, this study examined the processing of infant versus adult faces using the event-related potential (ERP) technique in mothers of children with ASD or neurotypically developing children. Method: We analyzed and compared the N170 and P2 ERP components of electroencephalogram (EEG), in 20 mothers of children diagnosed with ASD (MA group) and 20 mothers of neurotypically developing children (Reference group) when presented with infant and adult faces. Results: For infant faces, the MA group displayed larger N170 amplitudes in the right vs. left hemispheres, compared with no inter-hemispheric differences in the Reference group. For adult faces, there were no significant differences between or within groups for any condition in N170 or P2. Discussion: Our findings suggest that the observed

differences are related to the processing of faces during specific developmental stages (infancy or adulthood). These neural patterns highlight the relevance of infant faces for mothers regardless of whether their children are diagnosed with ASD or not. Understanding how mothers process faces at the neural level is critical for elucidating their social and emotional dynamics.

ASSESSMENT OF NEUROPSYCHIATRIC BEHAVIORAL TRAITS IN CD-1 MICE INDUCED BY MATERNAL IMMUNE ACTIVATION

Márquez C

Introduction: Maternal immune activation (MIA) has emerged as a significant animal model for the study of neurodevelopmental disorders, particularly Schizophrenia (SZ) and Autism Spectrum Disorder (ASD). Prenatal administration of the RNA-viral mimicking molecule: poly-inosinic/cytidylic acid [poly(I:C)], acts as a toll-like receptor (TLR)-3 agonist and triggers the production and release of pro-inflammatory cytokines. Poly(I:C)-MIA results in numerous neurobehavioral abnormalities in the adult offspring. However, this model has been evaluated mainly in the inbred C57 mouse strain. Strengthening of translational research requires replication of the MIA model in a different strain. CD-1 mouse strain, known for its outbred genetic diversity, seems to represent a promising opportunity to assess the MIA-induced behavioral traits. Therefore, we explored MIA in CD-1 mice, focusing on the effects of sex differences on behavioral outcomes in the offspring of mothers whose immune response was activated during pregnancy.

Methods: We administered poly(I:C) at gestational day 12 in CD-1 mouse dams followed by the behavioral phenotyping of MIA-induced females and males.

Results. Poly (I:C) CD-1 mice exhibited anhedonia at 48 hours in the sucrose preference test, and deficits in social interaction, but not in marble burying. Also, there was a significant effect of sex in sociability.

Discussion: Although CD-1 seems an appropriate strain to assess MIA-induced behavioral traits, further research should focus on a genetic comparison between CD-1 and C57. These findings allow us to understand the etiology of neurodevelopmental disorders and the importance of selecting appropriate mice strains for experimental research.

BRAIN-AGE CHANGES DURING HUMAN PREGNANCY AND POSTPARTUM

Martin de Blas D

Brain-age prediction is emerging as a potential biomarker for mental health aging. Longitudinal data indicates reduced brain-age during the early postpartum, and large-scale cross-sectional studies in middle-aged women find associations between parity and younger-looking brain structural and functional characteristics. Here, we study brain-age changes across gestation and postpartum using two unique longitudinal datasets that include Magnetic Resonance Imaging (MRI) data from women across their first pregnancy. The first dataset, the largest maternal brain database to date, includes more than 200 women scanned at preconception, 18 and 34 gestational weeks, and at one, six and 18 months postpartum. The second dataset corresponds to a dense-sampling study of 3 women scanned up to 26 temporal points from

preconception through 2 years postpartum, offering a unique high-resolution of maternal brain changes. For one dense-sampled participant, we integrated imaging data with DNA methylation epigenetic clocks, providing a detailed individual map of how pregnancy-induced brain aging trajectories align with biological aging markers. We predicted brain-age from structural MRI images and computed the difference with the chronological age, known as brain-age gap. In both databases, Hierarchical Generalized Additive Models show that brain-age gap increases across pregnancy and subsequently declines throughout the postpartum period. By 1.5-2 years postpartum, brain-age gap appears lower than at pre-conception, although this result was not significant across all algorithms used. These brain trajectories mirror patterns observed in peripheral epigenetic clocks, offering compelling evidence that pregnancy functions as both a stressor and a catalyst for recovery, influencing both brain and biological aging.

LEVERAGING BRAIN SEX CLASSIFICATION MODELS IN THE LIMBIC SYSTEM TO INVESTIGATE FEMALE HEALTH ACROSS THE LIFESPAN

Matte-Bon G

Machine learning models that classify individuals according to their biological sex based on structural neuroimaging data have been used to study sex differences in brain structure and function. These models usually rely on the whole brain, potentially overlooking regional-specific effects. Limbic structures, key players in emotional processing, show high degree of sex differences and undergo structural and functional changes across different hormonal and mental health states. Here, we tested whether regionally constrained machine learning models for brain sex could better reveal the association with sex-specific processes across the lifespan. We trained brain sex classification models based only on limbic or non-limbic structures and validated them in independent samples, investigating the associations of the model-derived sex estimates with puberty, pregnancy and mental health. For puberty, we observed that brain sex was associated with pubertal development with strongest effects in females. Menarche was significantly associated with a more female-like brain (i.e. higher estimates) only for the limbic model. For pregnancy, using longitudinal data of a single subject over the course of her pregnancy, preliminary results show that the brain becomes more female-like across pregnancy, with a peak in the third trimester that partially reverts in the post-partum period. Finally, for mental health we observed significant sex-specific associations of limbic brain sex with mood-related mental health in youths, and in adults with major depressive disorder. Taken together, our findings highlight the potential of regionally constrained machine learning models for brain sex to investigate female-specific variance and set the basis for further research.

WIDESPREAD DECREASES IN GRAY MATTER VOLUME AND INCREASES IN BRAIN IRON CONCENTRATION IN HUMAN PREGNANCY: A CASE-CONTROL STUDY

McCormack CM

Background: Pregnancy is a transformational period in which cognitive and behavioral adaptations are accompanied by heightened neuroplasticity in the maternal brain, yet the nature of brain changes underway during pregnancy itself and their neurobiological correlates have rarely been examined. Brain iron is a candidate mechanism given its established role in

neuroplastic processes and cognitive changes at other life stages such as adolescence, yet has not been examined in pregnancy.

Methods: We conducted repeat MRI scanning at 12 time points (9 during pregnancy from 18 to 38 weeks, and at 3 postpartum time points from 2 to 12 months), in a case study of 1 healthy pregnant participant and one nulliparous control. We leveraged novel MR sequences to quantify biological parameters including iron and myelin.

Results: A linear decrease in total brain volume and gray matter volume across pregnancy was observed in the pregnant participant, followed by gains in the postpartum. We also observed increasing R2f, a marker of brain iron, over pregnancy in multiple regions of interest. Change was particularly pronounced in basal ganglia regions, including the putamen.

Discussion: We demonstrate change in regional brain iron concentrations over human pregnancy for the first time. Structural findings converge with other recently emerging data to show a linear decrease in gray matter volume across pregnancy followed by postpartum gains. Further study of perinatal changes to brain iron, and individual difference in trajectories, is a promising approach that builds on the established role iron plays in both healthy neurodevelopment and mood disorders.

A PROLACTIN-SENSITIVE NEURAL CIRCUIT THAT GATES INFANTICIDAL BEHAVIOURAL IN MALE MICE

McQuillan J

The medial preoptic area (MPOA) of the hypothalamus plays a well-established role in the expression of parental behaviour in mice. Our laboratories have shown that the hormone prolactin, acting via the prolactin receptor (Prlr) in the MPOA, plays a critical role in establishing parental care in both males and female mice. Importantly, virgin male mice do not typically exhibit paternal behaviour, either ignoring or attacking pups and transition to pup-directed caregiving only following successful mating. How prolactin-sensitive MPOA neurons facilitate this transition to parenting behaviour is a key question. Using in vivo fiber photometry we show that during first pup contact, the activity dynamics of a sub-population of medial preoptic area (MPOAPrlr), can predict future infanticide in male mice with 90% accuracy. Furthermore, using optogenetics, we show that activation of inhibitory MPOAPrlr neurons that project to the ventral tegmental area (VTA) induces dopamine release in the nucleus accumbens, and blocks infanticidal behaviour in virgin male mice. Our data highlight a prolactin-sensitive neural mechanism that regulates the transition from pup directed aggression towards paternal behavior.

BRAIN-WIDE NEURAL ACTIVITY ENHANCING AUDITORY-GUIDED MATERNAL BEHAVIOR

McRae B

From the moment of giving birth, a mother must quickly adapt to the new demands of motherhood, attending to signals from her offspring and using them to inform her behavior. For instance, crying is one of the only ways infants can communicate their needs. Research

in mice has begun to disentangle innate and learned features of the neural circuitry underlying maternal responses to cries emitted by isolated mouse pups, termed “pup calls.” Pup calls elicit maternal behavior and time-locked neural activity in the left primary auditory cortex in mothers and virgins with maternal care experience, but not pup-naïve virgin females. Given the complexity of the pup call-evoked behaviors we observe, we hypothesize that pup calls engage distinct neural circuitry in animals of different maternal experience backgrounds, beyond the known differences in auditory areas. We have begun to reveal differences in how mothers versus experienced virgins behaviorally respond to pup calls, despite both groups successfully performing maternal behaviors. Through whole-brain activity mapping via immediate early genes, we have begun to characterize the neural representation of pup calls in animals of different maternal experience backgrounds throughout the brain. Our findings suggest that while mothers and experienced virgins both care for pups, the motivation or underlying neural circuitry supporting this behavior may differ significantly.

THE ROLE OF MIDBRAIN DORSAL RAPHE CRFR2 IN POSTPARTUM CAREGIVING AND AFFECTIVE BEHAVIORS

Meinhardt T

The transition to motherhood is typically marked by high levels of infant caregiving that are accompanied by a positive affective state. Unfortunately, the neural mechanisms promoting positive postpartum affective behaviors are very poorly understood. While numerous forebrain sites have been examined for this role, midbrain sites such as the dorsal raphe (DR; the largest source of forebrain-projecting serotonin cells) have mostly been neglected. DR neurons express many neurochemical receptors that alter DR functioning, including stress-related CRF receptors. Interestingly, the DR is one of few brain regions that densely express the stress-related CRF type 2 receptor (CRFR2), which influences social and affective behaviors in males, but their role in postpartum caregiving and affective behaviors in females is unknown. We recently found that new mother rats have twice as many rostral DR cells expressing CRFR2 mRNA as compared to virgins. Therefore, we hypothesized that upregulated DR CRFR2s are necessary for positive affective states in the early postpartum period and thus facilitate the display of maternal caregiving, particularly after stress. To test this, we pharmacologically antagonized CRFR2s in the rostral DR of early postpartum mothers to investigate the effects on caregiving and anxiety-like behaviors after exposure to a mild stressor; we also mapped the neuroanatomical projections from DR CRFR2-expressing neurons to four forebrain sites critical for postpartum behavior (NAc, mPOA, CeA, AH).This research is providing novel insight to the mechanisms driving postpartum adaptations in behavioral susceptibility to stress, with implications for stress-related derailments in maternal affective state and infant caregiving in women.

COORDINATED NEURAL ACTIVITY OVER THE MATERNAL EXPERIENCE: EXPLORING MATERNAL ELECTRICAL DYNAMICS AND THE IMPACT OF EARLY LIFE STRESS

Mitchell SB

The onset of motherhood initiates a cascade of change in the maternal brain. This change not only impacts structure, but also brain function, including electrical dynamics. While typically viewed as adaptations aiding parental proficiency, these neural alterations may also contribute

to negative maternal outcomes. This is particularly pertinent in populations with heightened vulnerability, following such adversities as early life stress (ELS). This work investigates patterns of brain wide electrical dynamics in the maternal mouse brain. These neurophysiological measures are examined in relation to maternal time course and parental behavior in addition to their interaction with ELS, as neural pathways impacted by stress largely overlap with those underlying parental care. To induce vulnerability, an ELS paradigm combining maternal separation, limited nesting material, and early weaning was performed in CD1 mice. Once adults, female control and ELS offspring were surgically implanted with multi-site in vivo recording electrodes for the continued observation of brain-wide electrical dynamics. Electrodes targeted regions having known putative roles in depression as well as involvement in maternal behaviors: the prelimbic and infralimbic cortices, nucleus accumbens, basolateral, medial, and central amygdala, ventral hippocampus, and ventral tegmental area. Recordings were captured in the homecage prior to conception, across maternal stages, and in the context of naturalistic and task-specific behaviors. Application of previously identified stress-relevant electrical brain networks demonstrated the significance of these networks over maternal time course and in behavior. A supervised autoencoder approach enabled the identification of novel maternal-relevant networks, showcasing the coordination of neural activity changes with maternal experience.

LONGITUDINAL PATHWAYS FROM MATERNAL DEPRESSIVE SYMPTOMS TO CHILD OUTCOMES: THE ROLE OF MATERNAL SELF-EFFICACY AND SEX-SPECIFIC EFFECTS

Morin E

Maternal depressive symptoms (MDS) in the postpartum period are a significant risk factor for child internalizing and externalizing problems, yet the mechanisms underlying this association remain unclear. This study examines the longitudinal pathways linking MDS to child internalizing and externalizing problems from 3 months to kindergarten entry, focusing on the mediating role of maternal self-efficacy (MSE) and potential sex-specific effects. Data were drawn from a longitudinal cohort, with maternal depressive symptoms and self-efficacy assessed from 3 to 24 months postpartum, and child internalizing and externalizing problems measured at kindergarten entry. Findings revealed a bidirectional relationship between MDS and MSE, where higher depressive symptoms predicted lower self-efficacy, which in turn contributed to sustained maternal depressive symptoms. MSE emerged as a key mediator, partially explaining the link between early maternal depression and later child outcomes, particularly externalizing problems. Additionally, moderation analyses indicated that boys were more vulnerable to the effects of maternal depressive symptoms on hyperactivity. These results highlight the importance of early intervention, as strengthening MSE in the first two years postpartum may mitigate the adverse effects of maternal depression on child emotional and behavioral development. Screening for self-efficacy in pediatric settings and extending maternal mental health support beyond the perinatal period could improve long-term child outcomes.

EFFECT OF MEDITERRANEAN DIET INTERVENTION DURING PREGNANCY ON MATERNAL BRAIN: A SECONDARY ANALYSIS OF THE IMPACT BCN RANDOMIZED CLINICAL TRIAL.

Nakaki A

Aim: To evaluate a structured Mediterranean diet (MD) intervention during pregnancy on maternal brain cortical structure.

Methods: A secondary analysis of the IMPACT BCN, a randomized clinical trial with 1221 pregnant women randomly allocated into three groups at mid gestation: MD intervention, Stress Reduction program, usual care. MD group participants had monthly visits with trained nutritionists, a free provision of extra virgin olive oil and walnuts. Maternal brain magnetic resonance (MR) was performed at third trimester in randomly selected participants from the three study groups. For this study, data from MD and usual group were analyzed. Maternal dietary intake, adherence to the MD and biomarkers of metabolites were evaluated with Food Frequency Questionnaire, 17-item MD adherence and plasma/urine samples, respectively. Cluster-wise analysis was used to assess cortical brain morphometric differences between intervention groups.

Results: MD women (n=34) had significantly larger surface areas in the right precuneus (90%CI: <0.0001–0.0004, p<0.001) and left superior parietal areas (90%CI: 0.026–0.033, p=0.03), compared to usual care participants (n=37). Right precuneus area was larger in the participants with high adherence to MD (D 177.2mm2, 95%CI 12.0-342.4), high intake of walnuts (D 210.8mm2, 95% CI 13.2-408.4) and was positively associated with concentrations of urinary hydroxytyrosol (b 74.3mm2, 95% CI 21.3-127.4). Left superior parietal area was larger in mothers with high intake of walnuts (D 375.7mm2, 95% CI 78.9-627.4) and was positively associated with urinary hydroxytyrosol (b 119.3mm2, 95% CI 39.0-199.6).

Conclusion: Promotion of MD during pregnancy has a significant effect on maternal brain structure.

DECODING THE FATHERING BRAIN: DISCRETE NEURAL RESPONSES TO INFANT AND FAMILIAR STIMULI IN FIRST-TIME FATHERS

Newsome P

Extant work implicates mentalizing, reward, and salience networks in own-infant neural processing; however, it is not clear whether these responses are driven by self-relevance or unique infant features. Here, we examine these distinctions in 32 first-time fathers by contrasting video stimuli of their infant, pregnant partner, and unfamiliar infant using univariate and multivariate pattern analyses. In addition, we test associations between own-infant neural responding and parental bonding and stress. Greater activation was observed in the precuneus, posterior cingulate, orbitofrontal cortex, and inferior frontal gyrus for the own-infant>unfamiliar-infant contrast (z≥3.1, pFWE<.05). For the own-infant>partner contrast, heightened activation was observed in the precuneus. Fathers who reported stronger antenatal and postpartum bonding, and lower parenting stress, subsequently showed stronger activation in the precuneus and posterior cingulate to their own infant (all ps<.05, TFCE-corrected). Searchlight analyses revealed that in addition to these regions, parahippocampus

and visual cortex differentiated own-infant versus other stimuli significantly above chance (>66.4%). Neural patterns distinguished infant (vs. adult) and familiar (vs. unfamiliar) stimuli in mentalizing, visual, and affective areas (78.1% and 67.2%, respectively). These findings extend previous research on the parental brain and suggest that cortical midline mentalizing regions, as well as visual and reward areas, are particularly important in first-time fathers' processing of their own infants.

INVESTIGATING SHARED RISK FACTORS OF PREGNANCY-RELATED DISORDERS AND BRAIN DISORDERS USING GENETIC APPROACHES

Oppenheimer H

Pregnancy-related disorders, such as hypertensive disorders and postpartum depression, are common and have short- and long-term consequences for maternal brain health, increasing risk for disorders such as depression and Alzheimer's disease. Observational studies show intertwined pathophysiologies of pregnancy-related disorders and brain disorders with cardiovascular disease. However, the genetic associations and causal effects of shared cardiovascular risk factors have not yet been fully established. Here, we used female-specific summary statistics from genome-wide association studies (GWAS) to estimate genetic correlations using linkage disequilibrium score (LDSC) regression and causal associations using Mendelian randomization between cardiovascular risk factors (c-reactive protein (CRP), HDL-cholesterol, LDL-cholesterol, triglycerides, and BMI), pregnancy-related disorders (hypertensive disorders of pregnancy and postpartum depression), and brain disorders (Alzheimer's disease and major depressive disorder). We found widespread genetic correlations between blood lipids, BMI, and pregnancy-related disorders. Using Mendelian randomization, triglycerides and HDL-cholesterol were significantly linked to hypertensive disorders of pregnancy, and LDL-cholesterol was significantly linked to postpartum depression. Further, CRP, LDL-cholesterol, and triglycerides were significantly associated with Alzheimer's disease. However, when including BMI in multivariable analyses, only the positive effect of triglycerides on hypertensive disorders of pregnancy remained significant. Further, postpartum depression was positively correlated and causally associated with major depressive disorder. Largely in line with findings from observational studies, the results suggest some shared underlying causal cardiovascular risk factors between pregnancy-related disorders and brain disorders. Thereby, cardiovascular mechanisms may explain the intertwined pathophysiologies of these disorders, highlighting BMI as an important modifiable risk factor.

NEUROACTIVE STEROID BIOSYNTHESIS DURING PREGNANCY PREDICTS FUTURE POSTPARTUM DEPRESSION

Osborne LM

Background: Postpartum depression (PPD) affects approximately 10-15% of childbearing individuals, with deleterious consequences for two generations. Recent research has explored the biological mechanisms of PPD, particularly neuroactive steroids (NAS). We sought here to investigate associations between NAS levels and ratios during pregnancy and the subsequent development of depressive symptoms with postpartum onset.

Methods: NAS levels and psychological scales were measured in individuals with and without mood disorders at up to 8 visits across pregnancy and postpartum. Generalized linear mixed-effects regression models were used to assess relationships in euthymic pregnant individuals between each of the NAS biomarkers and ratios and subsequent PPD.

Results: Participants with a one-unit increase in the log isoallopregnanolone/pregnanolone ratio at T3 had higher odds (OR=1.64, 95% CI: 1.13 to 2.37 , FDR adjusted p = 0.038, C-index=0.82), and those with a one-unit increase in the log pregnanolone/progesterone ratio at T3 had lower odds (OR=0.64, 95% CI: 0.47 to 0.88, FDR adjusted p = 0.036, C-index=0.82) of developing PPD, and those with a one-unit increase in the log progesterone at T3 had higher odds of developing PPD (OR=4.00, 95% CI: 1.54 to 10.37, FDR adjusted p = 0.035, C-index=0.80).

Conclusions: We found key differences in the progesterone metabolic pathway at the third trimester, indicating likely decreased activity/expression of the 3α-HSD enzyme and increased activity/expression of 3b-HSD.

IMPACT OF PARITY AND HORMONE LEVELS ON WOMEN'S PARASYMPATHETIC RESPONSES TO INFANT CRY

Peltola M

Parasympathetic responses to infant cry reflect regulation of arousal and they have been associated with caregiving behaviors. When measuring heart rate variability, reduction of respiratory sinus arrhythmia (RSA) in response to infant cry has been associated with maternal sensitivity. Whether multiple reproductive experiences (i.e., parity, conceptualized as the number of births) may modulate women's parasympathetic responses to infant cry is still unknown. Our aim was to test whether and how women's RSA in response to infant cry was associated with parity. In addition, given that pregnancy also entails major hormonal alterations, we assessed whether salivary hormonal levels (testosterone, estradiol, and cortisol) associate with women's RSA responses and parity. Participants included 184 Finnish women (62 nulliparous; 86 primiparous; 36 multiparous). RSA was measured while women watched a neutral baseline video, followed by videos of crying infants. In both nulliparous and multiparous women, watching the cry videos was associated with a significant RSA withdrawal compared to the baseline condition. However, a statistically significant RSA withdrawal was absent among primiparous women, possibly reflecting more sustained physiological arousal to infant cry in first-time mothers. Regarding the hormonal data, testosterone levels were highest in multiparous women, and in this group higher testosterone levels were related to lower RSA levels in both the baseline and cry conditions. In summary, new motherhood may be associated with more sustained arousal to infant cry, which may both support an increased focus on infant signals but also predispose new mothers to greater stress.

THE EFFECTS OF SOCIAL SUPPORT ON MOTHER-INFANT BRAIN AND BEHAVIORAL INTERACTIONS

Peoples SG

The Late Positive Potential (LPP) is a prolonged attentional and motivationally-relevant neural response critical for caregiving. Specifically, relative increases in LPP response to emotional stimuli (e.g., faces, cries) during the perinatal period reflect a caregiver adaptation that supports healthy parent-infant interaction. However, a previous study in our lab showed that lower perceived social support was associated with reduced LPP processing of emotional relative to neutral stimuli in expectant mothers (Nyman et al., 2020), which may interfere or negatively impact their ability to engage in adaptive infant interactions postpartum.

The current study tested whether mothers' (N=139) perceived social support (Interpersonal Support Evaluation List) moderated relations between mother-infant emotion processing, indexed by correlated LPP activity, and maternal-reported interaction quality (Parenting Stress Index [Parent–Child Dysfunctional Interaction Subscale]) one year postpartum. Correlations between LPP amplitudes were used as a proxy for neural synchrony as mothers (M=31.96, SD=4.76) and infants (M=13.00 months, SD=1.84) simultaneously viewed pictures of emotional faces (Tottenham et al., 2009).

When mothers perceived lower social support, less correlated mother-infant LPP predicted more dysfunctional interactions with infants (β=0.57, SE(β)=0.25, p=0.02). Results were not specific to one aspect of perceived social support (appraisals, tangibles, beliefs), but rather, reflect their cumulative impact.

Results suggest altered maternal emotion processing interferes with mother-infant interactions in the context of low levels of social support, and multigenerational effects of low social support may be observable on both the neural and behavioral level in the first year postpartum.

FROM AVOIDANCE TO MATERNAL CARE: INVESTIGATING THE NEUROBIOLOGY OF MATERNAL MOTIVATION IN RATS

Pérez-Gozalbo C

Motherhood entails neural changes associated with increased motivation for pups. Pregnancy-related hormones alter sensory processing and the activity of social and motivational brain circuitry, triggering highly motivated pup-directed behaviours, as observed in mice. Pup-derived stimuli also play a relevant role in inducing motivation, although differently in mice, with spontaneous maternal care, and rats, in which virgin females avoid pups, and only after 7-8 days of continuous exposure to pups (in the absence of their mother) they become maternal (maternal sensitisation). Hence, we have explored this process under more naturalistic conditions, modelling the "godmother" effect in rats (virgin females cohabiting with the dam and pups). Virgin female rats were continuously exposed to pups with their dam during most of pregnancy and postpartum, and we analysed anxiety-related, social and maternal behaviours in these females. Despite this prolonged exposure, virgin rats did not display maternal sensitization and showed no interaction with pups. These findings reveal clear-cut differences in maternal motivation between virgin and lactating rats, positioning this species as an optimal model to analyse the neuroendocrine basis of maternal motivation. In

this context, we have used cFos expression to test the hypothesis that the dopaminergic tegmento-striatal pathway signals reward prediction error when pups serve as a reward for mothers, including the rostromedial tegmental nucleus as a potential key element in the acquisition of maternal motivation during pregnancy and postpartum.

STRAIN DIFFERENCES IN MEDIAL AMYGDALA AND MEDIAL PREOPTIC AREA TRANSCRIPTOMIC PROFILES IN VIRGIN MALE MICE ASSOCIATED WITH PATERNAL CARE AND INFANTICIDE

Rada KR

Biparental care occurs in approximately 5% of mammalian species, including humans and rodents, with paternal care playing a crucial role in offspring development and well-being. While maternal neurobiology has been extensively studied, the neural mechanisms and molecular pathways underlying paternal behavior remain less understood. This study investigates the transcriptomic signatures in the medial amygdala (MeA) and medial preoptic area (MPOA) associated with paternal care and infanticide in virgin CD-1 and CD-1 x C57BL/6J F1 hybrid male mice. Virgin CD-1, and F1 hybrid male mice were socially housed for 3 weeks to assess social status. Following 24-hour isolation, males were behaviorally tested for 5 days to characterize phenotypes as paternal, infanticidal, or ignoring towards pups. F1 hybrids exhibited predominantly paternal or ignoring behaviors, while CD-1 males displayed approximately equal proportions of paternal and infanticidal behavior. Individual phenotypes were significantly stable across days. Social status was not predictive of phenotype. Using 3′-Tag RNA-seq and single-nucleus RNA sequencing, we identified transcriptomic signatures in the MeA and MPOA associated with each phenotype. Specifically, in both regions, we found high expression of genes encoding neuropeptides and their receptors associated with paternal behavior (e.g. Oxtr, Esr1, Prlr, Avp). We also found strain differences in the expression of genes related to the regulation of stress and alloparental behavior (e.g. Crh, Calcr, Crhbp) in the MPOA. These findings advance our understanding of the molecular underpinnings of paternal care and provide insights into evolutionarily conserved neuropeptides that may regulate paternal care.

EXPLORING THE IMPACT OF THE EXPOSOME ON POSTPARTUM DEPRESSION (PPD): UNDERSTANDING EXTERNAL AND INTERNAL FACTORS USING MACHINE LEARNING AND XAI

Romano D

Background: Postpartum depression (PPD) is a significant mental health concern that affects approximately 10-20% women after childbirth, with potential long-term consequences for both mothers and their children. This study investigates the use of exposomic data collected during and after pregnancy to identify women at higher risk of developing PPD. Using machine learning (ML) and explainable machine learning (XAI) approaches, we developed predictive models to estimate PPD risk and uncover the most influential factors contributing to these predictions.

Methods: We trained ML classification models using data from 1080 participants in the BiSC project, including 378 variables covering socio-demographic, lifestyle, clinical, biological, and

environmental chemical factors. Postpartum depression (PPD) symptoms were measured using the self-administered Edinburgh Postnatal Depression Scale (EPDS), with a cut-off threshold of 10 to classify participants as having significant PPD symptoms. The ML model was trained using 10-fold cross-validation repeated 20 times, combined with an undersampling technique to address class imbalance. Shapley Additive Explanations (SHAP) values provided interpretable insights into the decision-making processes of the models.

Results: The most effective model achieved an Area Under the Receiver Operating Characteristic (ROC) Curve (AUC) of 65%, indicating moderate predictive performance. SHAP analysis identified the top 20 predictors of postpartum depression (PPD) risk, highlighting the critical role of prior maternal mental health and exposure to environmentally associated chemical substances, such as perfluorinated compounds (PFAS).

Conclusion: The study underscores the importance of further exploration into how environmental exposures influence maternal mental health. Expanding datasets and incorporating additional factors may enhance model performance and provide deeper insights into PPD etiology.

FROM ATTRACTION TO AGGRESSION: EFFECTS OF MOTHERHOOD ON THE RESPONSE TO MALE PHEROMONES.

Sanahuja S

Motherhood constitutes a period of dramatic changes in the life of females. In mice, these changes include the appearance of maternal behaviours that ensure the survival and wellbeing of the pups and the reduction of social interactions with adult conspecifics. As a result, females furiously attack unknown adults (particularly males) that approach the nest during the postpartum period (what is known as maternal aggression).

There is evidence indicating that maternal aggression is triggered by the detection of the male-derived sexual pheromone MUP20 (darcin). Therefore, darcin has different effects throughout females' lifespan, eliciting attraction during adulthood and aggression only during peripartum. This suggests adaptations in the central processing of MUP20 and/or in its detection by vomeronasal organ (VNO) cells associated with motherhood. This study aims to understand the neural mechanisms underlying these changes and how are they related to the shift in female responses to male stimuli, from attraction to aggression.

For this, we exposed virgin females and dams to clean or male-soiled bedding and, 90 minutes later, we processed their brains and VNOs for cFos and pS6 immunohistochemistry, respectively. In this way, we combined the analysis of females' chemoinvestigation and social behaviour (made with the software Deeplabcut) with the assessment of the patterns of activity of the sociosexual, motivational and chemosensory (olfactory and vomeronasal) brain networks (cFos expression) and VNO function (pS6 expression).

The results suggest that motherhood reduces VNO sensitivity and the analysis of neural activity across the brain, indicates sharp changes in the pattern of male chemosignals-induced activation.

IMMUNE ACTIVATION DURING PREGNANCY DYSREGULATES MATERNAL REWARD SYSTEM, INDUCING A POSTPARTUM DEPRESSIVE-LIKE PHENOTYPE IN SPRAGUE DAWLEY RATS

Santoni M, Mastio A, Concas L, Frau R, Pistis M

Environmental factors, such as prenatal stress and infections, can trigger maternal immune activation (MIA), potentially impacting both the offspring and the maternal brain. While research on MIA has predominantly focused on neurodevelopmental outcomes in the offspring, less attention has been given to its effects on the maternal brain. Pregnancy and the postpartum period are marked by neuroplastic adaptations, particularly within the reward system, which plays a crucial role in maternal caregiving and in the emergence of depressive symptoms.

Here, we used a well-established MIA model in pregnant Sprague Dawley rats, administering a single intravenous injection of a viral mimetic [poly (I:C)] or vehicle on gestational day 15. This study aimed to assess whether inflammation during pregnancy increases the risk of postpartum depressive-like symptoms in the dams.

To investigate the impact of MIA on the maternal reward system, we performed in vivo extracellular recordings of ventral tegmental area(VTA) dopamine neurons at two time-points: (i)3 hours post-injection and (ii)at postpartum day (PPD) 28. Additionally, we performed the sucrose preference test to assess anhedonia.

In controls, VTA-dopamine neuron firing frequency physiologically decreases during pregnancy and returns to baseline postpartum. However, MIA dams displayed an increased frequency during pregnancy and a reduction in the postpartum. This neurobiological alteration correlated with decreased sucrose preference in MIA dams, suggesting a depressive-like phenotype.

These findings highlight the critical role of MIA models in investigating maternal brain adaptations and underscore the need for further research on how MIA alters maternal brain function and contributes to long-term mood disturbances.

DIFFERENCES IN INTEROCEPTION ACROSS PREGNANCY AND ADVERSITY EXPOSURE

Savoca PW

Pregnancy is a period of tremendous neurobiological plasticity and change in metabolic demand. In our recently published theoretical model, we propose interoception – the process by which the brain senses, perceives, and models the internal state of the body – changes over the course of pregnancy in order more precisely track metabolic needs to support the well-being of mother and developing child. Our model also suggests that pregnancy-related alterations in interoception may differ based on maternal exposure to early-life adversity (ELA). In an online study (n = 192), we found that between subject differences in self-reported interoception between never-pregnant women and first-time pregnant women in their second trimester depended on ELA exposure (Interoceptive Attention Regulation (Int = -0.15, p = 0.038), Interoceptive Self-Regulation (Int = -0.19, p = 0.023), and Interoceptive Noticing (Int = -0.17, p = 0.014). Generally, pregnant women with low ELA exposure reported greater

interoception, while pregnant women with high ELA exposure reported lower interoception. In an ongoing in-person study (n=16), we have found that performance on an objective measure of interoception (heartbeat detection task) is greater in women at later gestational weeks ($r = 0.54$, $p = 0.032$). Importantly, lower levels of interoception during pregnancy may also be associated with peripartum depression. However, interoception has also been shown to be modifiable by non-invasive interventions, such as mindfulness trainings, highlighting a potentially key mechanism to be targeted in the treatment and prevention of peripartum depression.

EMOTIONAL CONSEQUENCES OF PUP LOSS IN RAT MOTHERS: EVIDENCE FOR CRFR2 INVOLVEMENT

Sheibani-Tezerji S

The "pro-maternal" oxytocin system and the "anti-maternal" corticotropin-releasing factor (CRF) system are crucial components for the development and maintenance of the mother-infant bond, which is essential for their psychological and physical well-being. Disrupting this bond, e.g., through pup loss, is a stressful experience that affects maternal brain functions and behavior. Here, we studied rat mothers who had one day of maternal experience, followed by total pup loss for 19 days (LD1+19), or were left undisturbed with their pups (non-maternally separated, NMS). We analyzed the mRNA expression of CRF and its receptors, CRFR1 and CRFR2, in different brain areas relevant to maternal behavior. Notably, mRNA expression of CRFR2, but not of CRFR1, was elevated in the PVN and the VMH of LD1+19 versus NMS mothers. In addition, LD1+19 mothers showed increased passive stress coping in the forced swim test. To further examine the functional role of CRFR2 in maternal stress coping, we administered the CRFR2 antagonist Astressin-2B acutely in the VMH, which decreased passive stress-coping behavior in LD1+19 but not in NMS mothers. Currently, we investigate the potential role of the OXT system in the VMH after pup loss, with findings to be presented at the meeting. So far, our data suggest that region-specific alterations in CRFR2 signaling underlie the emotional consequences of pup loss.

EMPATHETIC RESPONSES TO INFANT EMOTIONS IN MOTHERS AND NON-MOTHERS

Sinisalo H

Becoming a parent is a major life event having significant impact on one’s brain anatomy and function. Sensitive caregiving requires the ability to recognize emotions as quickly and accurately as possible. The automatic and unconscious reactions on certain facial muscles to other people’s emotions have been associated with the ability to recognize other people’s emotions and can be measured using electromyography (EMG). Currently, there is no research investigating how these empathy related processes might change during the transition to parenthood. In this study, we compared first time mothers of small infants and non-mothers in their empathy related physiological responses in two facial muscle areas (corrucator supercilia and zygomaticus major) to dynamic emotional infant and adult faces. In addition, we examined whether the EMG responses have hormonal associations with testosterone.

Methods. Participants performed an emotion recognition task with dynamic infant and adult

emotional expressions while we measured the muscle activity. The aim was to answer the following questions: 1) Do mothers (n = 54) and non-mothers (n = 63) differ in their EMG responses to emotional facial stimuli especially when viewing infant faces? (ANOVA) 2) Is there correlation with EMG responses and salivary testosterone levels?

Results. Both groups had a significant zygomaticus response to smiles in general, but the response to smiling infants was heightened in mothers compared to non-mothers. In addition, testosterone was negatively associated with smiling responses to infant smiles in non-mothers. These results indicate that new mothers might have heightened reactivity to smiling infants.

AUDITORY RESPONSES TO OFFSPRING BEGGING CALLS IN PARENTAL AND NON-PARENTAL ZEBRA FINCHES

Smiley KO

Parental care is critical for offspring survival. For many species, including humans, auditory cues unique to dependent offspring, such as baby cries, elicit the necessary behavior from parents to care for young. Despite this, we know little about how the brain encodes auditory cues specific to offspring. Zebra finches are an excellent model to study this. Like humans, male and female zebra finch pairs raise the young together and rely on auditory cues (begging calls) to elicit chick feeding responses (parental behavior). It is well established that the caudomedial nidopallium (NCM), a higher-order region of secondary pallial cortex (analogous to the mammalian secondary auditory cortex), is involved in the perception of complex auditory signals. It is unknown, however, if/how NCM responds to offspring begging calls. To begin testing this, we recorded NCM activity using in vivo extracellular single-unit electrophysiology in adult zebra finches during an auditory playback experiment. Subjects were either parenting or non-parenting adult birds. Subjects were exposed to playbacks of their own and novel begging calls, male songs, and pure tone controls. Preliminary analyses indicate parenting females respond stronger (i.e., higher evoked firing rates) to both their own and novel begging calls relative to non-parenting females. Furthermore, females show more selectivity to their own chick begging calls, whereas males do not show similar levels of selectivity. These studies will lay the essential groundwork for future studies which will aim to test how auditory responses can elicit parental behavior and how these responses may change over the chick-rearing period.

PREGNANCY RENDERS ANATOMICAL CHANGES IN HYPOTHALAMIC SUBSTRUCTURES OF THE HUMAN BRAIN THAT RELATE TO ASPECTS OF MATERNAL BEHAVIOR

Spalek K

Animal studies have shown that pregnancy is associated with neural adaptations that promote maternal care. The hypothalamus represents a central structure of the mammalian maternal brain and hormonal priming of specific hypothalamic nuclei plays a key role in the induction and expression of maternal behavior. In humans, we have previously demonstrated that becoming a mother involves changes in grey matter anatomy, primarily in association areas of the cerebral cortex. In the current study, we investigated whether pregnancy renders

anatomical changes in the hypothalamus. Using an advanced delineation technique, five hypothalamic substructures were defined in longitudinal MRI scans of 107 women extracted from two prospective pre-conception cohort studies, including 50 women who were scanned before and after pregnancy and 57 nulliparous control women scanned at a similar time interval. We showed that becoming a mother is associated with volume reductions in the anterior-superior, superior tuberal and posterior hypothalamus. In addition, these structural changes related to hormonal levels during pregnancy and specific aspects of self-reported maternal behavior in late pregnancy, including maternal-fetal attachment and nesting behavior. These findings show that pregnancy leads to changes in hypothalamic anatomy and suggest that these contribute to the development of maternal behavior in humans, supporting the conservation of key aspects of maternal brain circuitry and their role in maternal behavior across species.

PREGNANCY ALTERS THE ORGANIZATION OF THE STRUCTURAL BRAIN NETWORK

Straathof M

Pregnancy induces widespread volumetric changes across the brain. These neural changes have been linked to gestational and postpartum maternal behavior, suggesting an adaptive process that facilitates the transition to motherhood. However, it is currently unknown whether the network organization of the brain is also changed due to pregnancy. Therefore, we set out to explore the structural and functional brain network organization across pregnancy in a prospective cohort study involving 80 nulliparous women. Half of these women became mothers for the first time during the study, and we acquired 3T diffusion-weighted MRI and resting-state fMRI scans before and after pregnancy. The other 40 women did not get pregnant during the study but underwent two MRI sessions with a similar time interval. We found an increase in global clustering coefficient and small-worldness and a decrease in density across pregnancy in the structural network. More locally, the increased clustering coefficient and reduced density were found only in the frontoparietal and visual network. The increased clustering coefficient and reduced density of the frontoparietal network were associated with less reductions in self-reported language difficulties and verbal memory. An additional follow-up MRI session in the late postpartum period showed that the changes in structural brain network organization partly reversed to the pre-pregnancy values. Hereby, we show that the organization of the structural brain network changes during the transition of becoming a mother, which may reflect a compensatory mechanism for language and verbal memory disruptions, characterized by the specialization and fine-tuning of specific brain networks.

PARENT-, PARENTING-, AND CHILD-RELATED CORRELATES OF PARENTAL PHUBBING

Unternaehrer E

Mobile Devices have become an essential part of our everyday life. The permanent accessibility of these devices offers many benefits, but also bears some risks, including distraction during face to face interactions (termed phubbing) with family and friends. The aim of this study was to examine a potential link between parental phubbing and child socio-emotional development and to identify parental factors linked to higher levels of parental phubbing.

In a cross-sectional online study, we collected data from German-speaking parents with children aged 2-16 years. We assessed parental phubbing (Parental Scale of Phubbing), child developmental outcomes (Strengths and Difficulties Questionnaire, Verhaltensskalen für das Kindergartenalter), and parenting-related factors. We examined associations of parental phubbing with child internalizing and externalizing symptoms and used machine learning to identify parental correlates of phubbing.

Preliminary analyzes (N = 196, 89% mothers, 53% girls, mean age parents = 40 ± 6.3 years; mean age children = 6.7 ± 3.4 years) suggested an association between greater parental phubbing and more child internalizing ($b=.222$, $p<.05$) but not externalizing ($b=.113$, $p>.05$) problems. Using LASSO regression, we found higher parental neuroticism, stress, and mindfulness to be the strongest correlates for parental phubbing.

Findings suggest that parental phubbing is associated with child internalizing symptoms. In addition, higher parental stress and lower resilience factors could be a risk factor for increased parental phubbing. Findings from this study will be relevant in the child psychiatric clinical setting and guide parents to limit their own digital media use.

EXTRACELLULAR MATRIX, HORMONES, AND MOTHERHOOD: A COMPLEX PUZZLE

Uriarte N

During motherhood, the female brain undergoes significant neuroplastic changes, particularly in regions involved in the expression of maternal behavior. While hormonal fluctuations drive adaptations in multiple brain areas, their impact on the extracellular matrix remains largely unexplored. We investigated whether perineuronal nets (PNNs)—extracellular matrix structures that regulate synaptic stability—are differentially affected by pregnancy in the medial preoptic area (mPOA) and the primary somatosensory cortex (S1). Our results reveal region-specific differences in PNNs plasticity. In the mPOA, PNNs organization is sensitive to hormonal fluctuations during pregnancy, suggesting dynamic remodeling of synaptic connectivity in this key maternal behavior area. In contrast, S1 showed no significant changes in PNNs density between diestrus and pregnancy. Additionally, PNN-coated (PNN+) neurons exhibited a distinct steroid receptor repertoire in these regions: while both mPOA and S1 PNN+ neurons expressed estrogen receptors (ERα), only mPOA PNN+ neurons expressed detectable levels of progesterone receptors (PR). These findings suggest that PNNs contribute to region-specific regulatory mechanisms influenced by steroid hormones, with the mPOA displaying greater extracellular matrix structural plasticity in response to pregnancy. Given that GABAergic neurons are the primary neuronal population associated with PNNs, express steroid receptors, and regulate GAD levels in response to circulating hormone levels, we are now focusing on this system. GABAergic neurons are key regulators of plasticity and the functional properties of neural circuits and are involved in the regulation of maternal behavior. Thus, understanding their interaction with PNNs will provide deeper insights into how extracellular matrix remodeling supports maternal adaptations.

INTRINSIC RESTING STATE CONNECTIVITY AND PERSONAL MEANING ACROSS THE TRANSITION TO FATHERHOOD

Vaccaro AG

New fatherhood is marked by profound psychological transformations, but there has been little investigation of neural changes in human fathers. Studies of resting state connectivity in mothers have found increases in the connectivity of default mode network and limbic regions, which are also important for emotion regulation and psychological adaptation. In this study, we investigated how resting-state intrinsic functional connectivity changed in 35 men between their partners' pregnancy and approximately 6-12 months after the birth of their first child. We observed increases in resting-state functional connectivity in the bilateral temporal lobes, right angular gyrus, thalamus, and right lateral occipital cortex, and decreases in regions such as the right frontal pole, left opercular cortex, and anterior cingulate. We additionally explored whether differences in connectivity change across fathers predicted their positive and negative feelings surrounding parenting, as well as their sense of life meaning and purpose. Notably, increases in insular cortex connectivity predicted greater postnatal personal meaning across multiple analyses, even after controlling for both positive and negative parenting-related feelings. These findings suggest that dynamic changes within the insula may support fathers' ability to form a higher-order sense of meaning and purpose during this transformative period.

PREGNANCY LEADS TO CHANGES IN SOCIAL BRAIN FUNCTION

Van't Hof SR

During pregnancy, structural brain changes occur in regions overlapping with the Theory of Mind (ToM) network.

In this prospective pre-conception cohort study, we examine changes in brain function in first-time mothers (n = 40), second-time mothers (n = 30), and a nulliparous control group (n = 40) during a social ToM task. We use a multi-method approach including structural and functional brain imaging, hormonal measures, ToM performance scores, self-reported ToM, and measures of observed and self-reported maternal behavior at multiple timepoints.

We show, for the first time, changes in social task-related brain function in first-time mothers. Our results reveal significant changes in ToM-related functional activity in the right precuneus/cuneus in first-time mothers compared to a nulliparous control group. These changes were selective for the women becoming mothers for the first time and were not observed in second-time mothers. Our longitudinal assessment reveals a return towards baseline levels of brain activity in the precuneus/cuneus cluster during a ToM task following the first pregnancy, with activity levels one-year postpartum between those observed pre-conception and early postpartum. First-time mothers also displayed higher effective brain connectivity but not structural connectivity after pregnancy compared to pre-conception. The changes in brain function in first-time mothers were significantly correlated with estriol and progesterone levels during pregnancy, as well as with ToM performance, self-reported ToM, and both observed and self-reported maternal behaviors.

Together, this study shows that becoming a mother is accompanied by changes in ToM-

related brain activity, suggesting that the social brain evolves across the transition to motherhood.

EMPATHIC RESPONSES TOWARDS EMOTIONAL CHILD STIMULI IN EXPECTING, FIRST-TIME, AND EXPERIENCED FATHERS

Veistola S

Parental empathy towards a child's emotional signals is crucial for effective caregiving. This is especially important with infants, who cannot express their needs verbally, requiring parents to interpret non-verbal cues during interactions. While recent research indicates physiological changes in men transitioning to parenthood, there is limited investigation into how these changes affect their empathy towards children. This study investigated whether first-time fatherhood represents a particularly sensitive phase, marked by heightened empathy towards a child's distress, as measured by electromyography (EMG; facial muscle activation).

Methods. In our laboratory study, we examined men's EMG responses to children's distress at different stages of fatherhood. Participating fathers viewed images of children in emotional situations while their EMG responses were recorded. Pre-registered analyses compared three father groups: expecting fathers (N = 35), first-time fathers (N = 44), and experienced fathers (N = 39). Our main hypothesis was that expecting and first-time fathers would exhibit stronger EMG reactions.

Results. First-time fathers demonstrated greater EMG responses to children's negative emotions compared to expecting fathers. This finding suggests that first-time fatherhood may be a particularly sensitive phase during the transition to parenthood, with empathy changes not yet as pronounced in expecting fathers.

PREGNANCY AND THE INTERPLAY BETWEEN MENTAL HEALTH AND COGNITIVE FUNCTIONING

Walther J

A commonly self-reported phenomenon by pregnant women is a decrease in cognitive abilities during pregnancy (Crawley et al., 2008). However, studies using standardized measures to investigate this area are rare. Here, we present a large-scale online study (n=205) using the app BrainExplorer for cognitive assessment (brainexplorer.net) with a cross-sequential design involving pregnant women. Participants completed multiple questionnaires and gamified cognitive tasks on their mobile phones to assess their mental well-being and performance in response inhibition, risk-taking and metacognition over eight weeks of their pregnancy. By combining data from participants during different pregnancy weeks, we examined women's mental and cognitive changes during pregnancy and the dependency on demographic, social and psychological background factors. While we found overall no significant change in the assessed cognitive abilities during pregnancy, there were interactions with environmental factors such as socioeconomic status and age. Additionally, we found that mental health factors such as anxiety can play an important role in mediating cognition during pregnancy. Together, our results indicate that women do not suffer from significant changes in domain-general cognitive abilities during pregnancy. Instead, previously reported cognitive change

might be due to an interplay between environmental factors and mental health, highlighting the need for greater support during pregnancy for vulnerable populations and additional research. In future studies, we will aim to use the present results to account for confounding factors when studying the mental health of women in particularly vulnerable conditions such as after pregnancy loss.

NEURAL EMOTION REGULATION DURING PREGNANCY - AN FMRI STUDY INVESTIGATING A TRANSDIAGNOSTIC MENTAL HEALTH FACTOR IN HEALTHY FIRST-TIME PREGNANT WOMEN

Weinmar F

Pregnancy is a psycho-neuro-endocrinological transition phase presenting a window of vulnerability for mental health. Emotion regulation, a transdiagnostic factor for psychopathology, is influenced by estradiol across the menstrual cycle on the behavioral and neural level. Whether this is also the case in the antepartum period remains unknown. For the first time, behavioral and neural emotion regulation were investigated in healthy pregnant females with extremely high estradiol levels during the second trimester (N=15) using a functional magnetic resonance imaging (fMRI) paradigm. Results were compared with naturally-cycling females with high (N=16) and low estradiol levels (N=16). Although pregnant females reported the lowest trait use of cognitive reappraisal, all participants successfully regulated their emotions by applying cognitive reappraisal in the scanner. During downregulation of negative emotions, all females had increased activity in the left middle frontal gyrus. Pregnant females showed no significant differences in functional connectivity (psychophysiological interaction, resting-state) related to emotion regulation compared to the nonpregnant groups. However, group differences emerged for amygdala activation. In pregnant females, increased amygdala activity predicted reduced regulation success and was positively associated with depression scores. This first fMRI study during pregnancy indicates that depression scores are reflected in heightened amygdala activity already observable in the antepartum period. Thus, through its association with reduced regulation success, increased amygdala activity suggests a neural risk marker for peripartum mental health. The findings highlight the importance of investigating neural and behavioral emotion regulation in the ante- and postpartum period, eventually allowing enhanced identification, prevention, and treatment of peripartum mental ill-health.

ANALYSIS OF OXYTOCIN RECEPTOR GENE EXPRESSION IN MEDIAL PREFRONTAL CORTEX AND ALLOPARENTING BEHAVIOR IN FEMALE RATS WITH JUVENILE PUP EXPERIENCE

Williams GE

Alloparenting, or animals caring for young that are not their biological children, occurs across the animal kingdom. Furthermore, alloparenting can be induced via maternal sensitization, in which nulliparous rats begin to show maternal behavior towards pups that are not their genetic offspring after prolonged exposure to them. Maternal sensitization achievement and latency can vary widely between subjects, and what makes some females more likely to successfully maternally sensitize remains elusive. Previous studies by our collaborators found that prolonged exposure to pups in juvenile female rats leads to faster latency and higher rates of

achievement of maternal sensitization. Furthermore, medial prefrontal cortex (mPFC) activity is necessary for the onset of maternal behaviors, such as pup retrieval and grooming. To follow up on these findings, we quantified oxytocin receptor (OTR) gene expression, a hormone essential for facilitating maternal behavior, in the mPFC in nulliparous female rats that did and did not demonstrate maternal behavior towards non-genetic offspring. We hypothesize that OTR expression is a positive indicator of maternal behavior towards both genetic and non-genetic offspring. Our results will demonstrate the potential effects of early pup exposure on OTR expression levels and oxytocin (OT) sensitivity, potential catalysts for maternal sensitization. Understanding a potential mechanism of maternal sensitization is essential to optimize infant care, as parental care is a critical aspect of proper physiological and psychological development.

HYPOTHALAMIC NEUROPEPTIDE SYSTEMS AND MATERNAL CARE DURING SICKNESS

Winokur SB

Sickness is a challenge for parents, requiring a balance between behaviors that support recovery and those essential for offspring survival. Through longitudinal monitoring of mouse maternal behavior during acute lipopolysaccharide (LPS)-induced sickness, we found that sick first-time mothers show reduced caregiving, resulting in elevated offspring mortality. Conversely, sick second-time mothers sustain caregiving. The paraventricular nucleus (PVN) of the hypothalamus contains oxytocin (OT) and corticotropin-releasing hormone (CRH) neurons, which are essential for enabling maternal and stress-related behaviors. We hypothesize that peripartum neuroplasticity and immune adaptations shape maternal behavior during sickness through changes to intra-PVN OT and CRH circuit activity. Using fiber photometry, we recorded maternal PVN OT and CRH neuron activity across acute LPS-induced sickness. We discovered that PVN CRH activity increased as fever peaked, coinciding with disrupted caregiving, and returned to baseline as mothers recovered. In contrast, PVN OT activity was temporarily suppressed during sickness, coinciding with reduced nursing. Although nursing resumed with recovery, milk letdown-related OT pulse characteristics were altered, suggesting sickness reshapes synchronized activity of OT populations critical for lactation. Given these findings, we hypothesize that maternal CRH and OT neuron populations in the PVN either directly or indirectly inhibit each other's activity, leading to a rebalancing of caregiving and sickness behaviors in response to LPS. Ongoing studies are examining whether activity of a subpopulation of co-expressing OT and CRH PVN neurons may promote robust maternal care under duress. Overall, this research aims to reveal the neural mechanisms that govern the balance between maternal self-preservation and offspring care.

DIVERSE FORMS OF PLASTICITY SUPPORTING MATERNAL AGGRESSION IN FEMALE MICE

Yamaguchi T

To protect the helpless young, females dramatically increase aggression towards intruders during lactation, known as maternal aggression. However, attack is costly and risky. When pups no longer exist, maternal aggression loses its purpose and rapidly declines. Our study reveals the critical role of the pathway from estrogen receptor alpha-expressing (PAEsr1) cells

in the posterior amygdala to neuropeptide Y receptor Y2 (VMHvlNpy2r) cells in the ventrolateral part of the ventromedial hypothalamus in the rise and fall of maternal aggression. Functional manipulations and photometry recordings demonstrate VMHvl-projecting PAEsr1 (PAEsr1àVMHvl) cells are naturally active and required for maternal aggression. In vitro slice recording showed that PA-VMHvlNpy2r connection strengthens and VMHvlNpy2r excitability increases to enhance VMHvlNpy2r responses to intruders and drive attack in lactating dams. Furthermore, we found oxytocin as a critical mediator to link pups' needs to the aggression circuit output. Interestingly, PA, not VMHvl, is the key site for oxytocin to boost the aggression circuit output. The abundant expression of oxytocin receptor (OXTR) in PAEsr1 cells enables oxytocin to increase the input-output relationship of PAEsr1 cells by increasing the input resistance of the cell. The decreased maternal aggression by the oxytocin level drops after pup separation can be restored by optogenetic stimulation of oxytocin neurons in the paraventricular hypothalamic nucleus. This recovered maternal aggression can be canceled by blocking PA OXTR signaling. Thus, diverse forms of plasticity occur at the PAEsr1-VMHvlNpy2r circuit to support maternal aggression, while oxytocin signals the need of the young, enabling the female to rapidly adjust its aggression.

NEURAL SUBSTRATES IN THE POSTPARTUM BRAIN FOR FLEXIBLE MATERNAL CARE

Yang M

Flexible infant-oriented maternal behavior is driven by multisensory cues from the offspring. An example of such behavioral flexibility in maternal mice (dams) is the rapid transition from nursing in the nest to exiting the nest in search of misplaced pups. This involves a sensory competition between distress calls, emitted by pups outside the nest, and somatosensory contact with pups inside the nest. Inflexible maternal behavior can be a symptom of postpartum depression. While selective serotonin reuptake inhibitors are a common treatment, it remains unclear how serotonin regulates responses to infant cues in maternal brain networks. Therefore, understanding the neural mechanisms responsible for processing competing infant cues and modulating flexible maternal behavior is essential for improving maternal care. Here, we investigated the neural substrates involved in the processing of competing infant cues, and their modulation by serotonin. We identified a neural hub for infant cue processing: calbindin-expressing neurons in the posterior intralaminar thalamus (PILcb). Using channelrhodopsin-assisted circuit mapping, we found that PILcb neurons receive input from primary sensory nuclei and send output to the paraventricular nucleus to control oxytocin release and maternal behavior. PILcb neurons were more excitable in dams than in virgins and showed a particular preference for input frequencies consistent with the frequency range of pup calls. We observed a dense distribution of serotonergic fibers in PIL, and bath application of serotonin significantly increased the resting membrane potential of PILcb neurons. Calcium imaging revealed that auditory stimuli activated PILcb neurons. Finally, using the GRAB5-HT sensor, we found that serotonin levels in PIL are modulated by pup calls. Our findings establish PIL as a bottleneck station, uniquely positioned for processing of multisensory infant cues, potentially modulated by serotonin.

SCREENING FOR FAMILIAL RESOURCES AND STRESSORS IN PEDIATRIC CARE: ASSOCIATIONS BETWEEN PARENTAL MENTAL HEALTH AND CHILD DEVELOPMENT

Zarifoglu L

Children's physical, cognitive, and emotional development is significantly influenced by parental mental health, yet, socio-medical data is rarely collected systematically in pediatric care. The Family-ReBel study (Screening for Family Resources and Strain in the Paediatric Setting) aims to identify familial stressors at an early stage and examine their relationship with the mental well-being of both, children and parents. Additionally, we seek to determine which psychosocial support services parents desire. Parents of children aged 2-8 years attending pediatric assessments in Switzerland are recruited via flyers with QR codes in pediatric practices, clinics, and care units. Participants complete an anonymous 10-15 minute online survey available in 14 languages, capturing parental stress factors using the Patient Health Questionnaire-4 (PHQ-4), parental resources using the CD-RISC, and children's strengths and difficulties using the Strengths and Difficulties Questionnaire (SDQ) and Behavior Scales for Kindergarten Age (VSK). We hypothesize that increased parental stress (symptom burden, functional impairment, and disability) will be associated with higher difficulty scores in children, while greater parental resilience will be associated with higher strength scores. Data is currently being collected and preliminary findings from our target sample of 150 families will be presented. The study will provide valuable insights into the relationships between parental mental health and resilience and child development, highlighting the importance of early screenings for familial resources and stressors. Identifying these factors during routine pediatric check-ups could facilitate timely interventions and appropriate psychosocial support, potentially enhancing both parental capabilities and children's developmental outcomes.

We look forward to welcoming you to the Parental Brain Meeting 2025 and appreciate your valuable contribution!

Should you have any questions or require clarification on any point, feel free to contact us at parentalbrain2025@teclat.com

Best regards,

The Organizers and the Technical Secretariat