# Fifth Parental Brain Conference

Regensburg 2013

Deutsche Forschungsgemeinschaft

Vielberth Stiftung

Journal of Neuroendocrinology

British Society for Neuroendocrinology

## Local Organizers

Oliver J. Bosch
David A. Slattery
Inga D. Neumann

## Speakers

Tallie Baram
Frances Champagne
Arpád Dobolyi
Alison Fleming
Liisa Galea
József Haller
Gordon Harold
Harm Krugers
Benedetta Leuner
Joe Lonstein
Stefania Maccari
Jamie Maguire
Gunther Meinlschmidt
Eydie Moses-Kolko
Wendy Saltzman
Carmen Sandi
Danielle Stolzenberg
James Swain
Moishe Szyf
Hiroki Tsukamura
Toni Ziegler


**July 11th – 14th, Regensburg, Germany**

## WELCOME TO REGENSBURG

We are delighted to extend a warm welcome to Regensburg to all the attendees of the 5th Parental Brain Conference. This conference hopes to build upon the success of the previous four conferences ("Maternal Brain" - Bristol 1999; "Mother and Infant" - Montreal, 2003; "Parental Brain" - Boston, 2007 and "The Parental Brain" - Edinburgh, 2010).

The broad scientific scope covered by the symposia, chosen by the international scientific programme committee, aims to provide something to excite everyone. In addition to the two plenary speakers and 19 invited speakers, nine investigators from the ~100 submitted abstracts were selected for two hot-topic symposia. The tradition to preferentially select presenters who did not speak at recent previous meetings has been preserved as far as possible.

The conference takes place in the "Altstadt", which has been designated as a UNESCO World Heritage Site since 2006, giving you the chance to explore this historic city with its unique medieval atmosphere. During this year's conference there will also be the chance to enjoy the Jazz Festival, which takes place throughout the city over the weekend.

We would like to express our gratitude to the sponsors of the meeting. Their financial contributions enabled us to put together a scientific programme with distinguished international speakers and to bestow travel awards for 6 young scientists, which are detailed in the programme.

We would like to particularly thank the many friends and colleagues "back stage" in Regensburg whose important contributions ensured the successful organization of the conference within the last 12 months.

We wish you both a pleasant and stimulating stay in Regensburg and at the 5th Parental Brain Conference.

Oliver Bosch
David Slattery
Inga Neumann

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2013 Parental Brain Conference
Local Organizing Committee

**TABLE OF CONTENTS**

## ACKNOWLEDGEMENTS

The 5th Parental Brain Conference organisers would like to thank the following sponsors for their financial support of the meeting, which was greatly appreciated:

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| **Dominik Moser** | (University of Geneva, Switzerland) |
| **Claudio Rocha** | (Federal University of Rio Grande do Sul, Brazil) |
| **Maria Zuluaga** | (Universidad de la Republica, Uruguay) |

## CONFERENCE INFORMATION

**Conference Venue**

Kolpinghaus, Adolph-Kolping-Strasse 1, 93047 Regensburg
Phone: 0049 941 595 000; Fax: 0049 941 595 0080

**Name badges**

Please wear your name badge at all times in the Conference building as well as at the Conference Dinner. The badges of the organizers and helpers are marked in red and speakers in yellow.

**Registration Desk**

Located on the 2nd floor of the Kolpinghaus, and will be open at the following times: Thursday 11th between 16:00 - 20:00, Friday 12th 08:00 – 15:30 and Saturday 13th 08:00 – 08:30. Services offered include delegate conference registration, details of the free Saturday afternoon programme, any fee payments, and local information.

**Speaker presentation**

Please present your memory stick / CD at the Registration Desk at least one Session ahead of the designated Symposium or the evening before (for speakers of the morning Sessions). There will be an opportunity to preview your presentation beforehand. It is not possible to use your own laptop for the presentation and the conference only supports ppt/pptx files.

**Poster presentation**

Posters can be mounted on Thursday, 11th, afternoon and should remain there until Saturday afternoon. Pins will be provided at the registration desk. There will be two poster sessions, the first on the 12th for odd-numbered posters and the second on the 13th for even-numbered posters. During the poster sessions, we will provide beer and brezel on the 12th and lunch on the 13th.

**Catering/Lunch**

During the coffee breaks coffee, tea, and complimentary snacks are offered. Lunch (Fri and Sat) is included in the registration fee and is provided at the catering area on the 2nd floor at the times indicated in the programme.

**Internet facilities** Two computers for e-mail and internet access are available at the Registration Desk (no printing facilities are available). It is also possible to pay for internet access at the Kolpinghaus by selecting the "telecom hotspot" (5 EURO for 24h).

**Health and safety** Delegates are responsible for their own health and safety. The Conference organisers take no responsibility for theft or damage of property or accidents (including on the free afternoon).

## USEFUL INFORMATION ABOUT REGENSBURG

The Bavarian city of Regensburg, located 120 km northeast of Munich, where the Danube is joined by the rivers Regen and Naab, is undoubtedly one of history's wonders. It is the only Gothic city in Germany to have retained its medieval face with hardly a blemish and remains from the first Roman settlers (circa 1st Century) can still be visited.
Regensburg's Old Town skyline, unique in the intact section towards the Danube, is considered to be one of the most impressive anywhere in the world. Visible from afar, the 105m high towers of St. Peter stand out, surrounded by towers, squares, houses, and lanes that tell the history of the Middle Ages in Germany like no others.
The oldest one in Germany, but still fully functional: the Stone Bridge has spanned the Danube for over 800 years. Even during the Middle Ages it was considered to be an example of Romanesque engineering to perfection. With its 16 square stone block arches rising towards the middle it was regarded as the eighth wonder of the world after its completion in 1145.

**Eating out** Both local and international cuisine is reflected in the many restaurants and pubs in Regensburg. In the heart of the city, situated between the train station and the river Danube, you will find good restaurants, pubs and bars.

**Shopping** The heart of the city, particularly the narrow medieval streets of the pedestrian zone, are famous for their shops. There are two Shopping Centres within walking distance.

## SOCIAL PROGRAMME

**Welcome reception** The welcome reception will take place in the foyer of the Kolpinghaus directly after the first plenary lecture. There will be drinks and a buffet with music provided by the *Spitzweg Quartet* (former singers of the famous boys choir *Domspatzen*) for all registrants and accompanying persons.

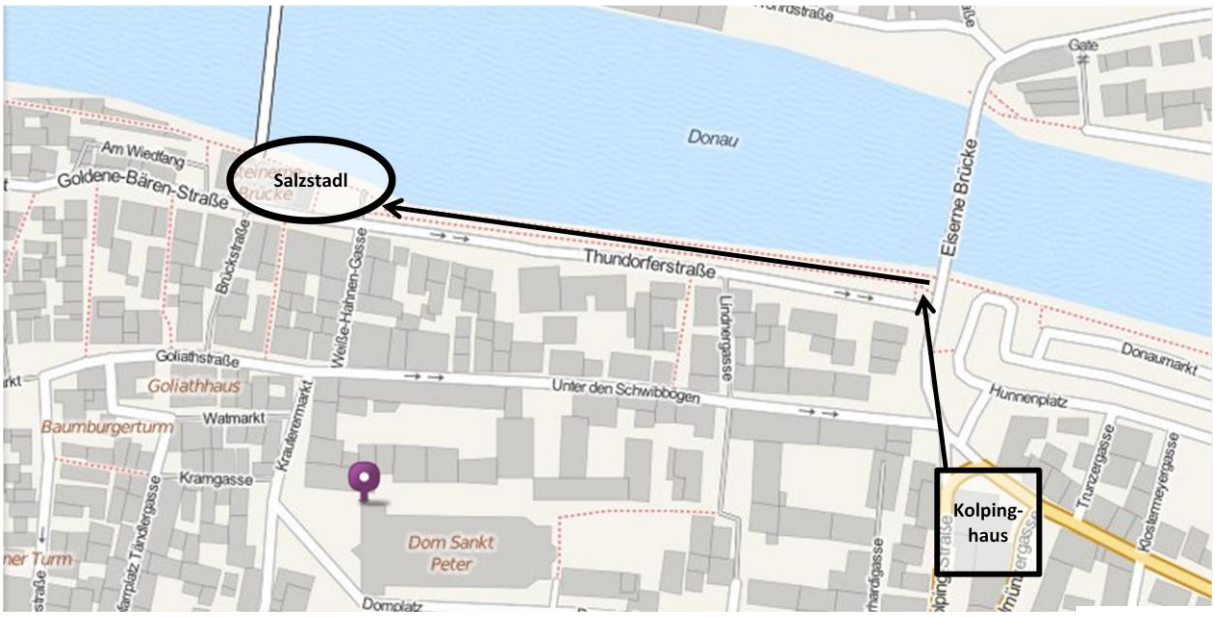
**Conference Dinner** Will take place at "*Der historische Salzstadl*" right next to the Stone Bridge in the city centre of Regensburg, Waffnergasse 6 - 8, on Saturday 13th, beginning at 19:30. We will be entertained by gentle harp music played by *Mrs. Eva König*, University of Regensburg.

**Saturday afternoon** Several options are offered (a small fee may be required), including

- a boat trip on the river Danube to the famous Walhalla
- a guided city tour in English
- bike trip in the surroundings
- walking tour to a traditional beer garden in the surroundings

Please ask at the Registration Desk for further information and to book/pay for your preferred tour (latest on Friday 12th 15.30).

## WALK FROM CONGRESS SITE *"KOLPINGHAUS"* TO CONFERENCE DINNER @ *"DER HISTORISCHE SALZSTADL"*




(c) Mapquest

## SCIENTIFIC PROGRAMME

## Thursday July 11th

16:00 – 20:00 **Registration *@ Kolpinghaus***

19:00 – 19:15 **Welcome Address**

19:15 – 20:00 **Plenary Lecture 1**
**PL-1 Alison Fleming**, University of Toronto, CA
Neuropsychology of mothering and effects of early experience
**Chair: Bob Bridges**, Tufts University, US

20:00 – 22:00 **Opening reception *@ Kolpinghaus***
Including music from the *Spitzweg Quartet* (former members of the famous *Domspatzen*)

## Friday July 12th

08:30 – 10:05 **Symposium S1: From animals to humans: Brain physiology of mothering**
**Chair: Colin Brown**, University of Otago, NZ

08:30 – 08:55 **S1-1 Arpád Dobolyi**, Semmelweis University Budapest, HU
A thalamic relay center affecting maternal physiology by peptidergic mechanisms

08:55 – 09:20 **S1-2 Danielle Stolzenberg**, UCDavis, US
Epigenetic mechanisms underlying experience induced improvements in maternal care

09:20 – 09:45 **S1-3 Eydie L. Moses-Kolko**, University of Pittsburgh, US
Interrelationships between postpartum mood symptoms, neural responses to emotional stimuli, and maternal caregiving

09:45 – 10:05 **S1-4 James Swain**, University of Michigan, US
Maternal Moods and Brain Physiology

10:05 – 10:30 **Coffee Break**

| | |
|---|---|
| 10:30 – 12:00 | **Symposium S2 Early-life adversity and outcome in adulthood**<br>**Chair: Paula Brunton**, University of Edinburgh, UK |
| 10:30 – 11:00 | **S2-1 Stefania Maccari**, University of Lille, FR<br>Grandma's curse of stress in the prenatal stress rat model |
| 11:00 – 11:30 | **S2-2 Harm Krugers**, University of Amsterdam, NL<br>Regulation of brain structure & function by variations in maternal care |
| 11:30 – 12:00 | **S2-3 Moishe Szyf**, McGill University Montreal, CA<br>The early-life social environment and DNA methylation |
| 12:00 – 13:30 | **Lunch Break** |
| 13:30 – 15:00 | **Symposium S3 Hot Topics I**<br>**Chair: Claire-Dominique Walker**, McGill University, CA |
| 13:30 – 13:45 | **Claire-Dominque Walker**, McGill University Montreal, CA (see **P99**) |
| 13:45 – 14:00 | **Clara Perani**, University of Regensburg, DE (see **P79**) |
| 14:00 – 14:15 | **Christina Ragan**, Michigan State University, US (see **P81**) |
| 14:15 – 14:30 | **Maria Zuluaga**, Universidad de la República, UY (see **P105**) |
| 14:30 – 14:45 | **Kumi Kuroda**, RIKEN Brain Science Institute, JP (see **P52**) |
| 14:45 – 15:00 | **Aniko Korosi**, University of Amsterdam, NL (see **P66**) |
| 15:00 – 15:30 | **Coffee Break** |
| 15:30 – 17:00 | **Symposium S4 Maternal Mood and Depression**<br>**- Alison Douglas Memorial Symposium -**<br>**Chair: Inga Neumann**, University of Regensburg, DE |
| 15:30 – 16:00 | **S4-1 Joe Lonstein**, Michigan State University, US<br>Stability of maternal anxiety across time: associations with mothering style, infant touch, and neurochemistry |
| 16:00 – 16:30 | **S4-2 Jamie Maguire**, Tufts University, US<br>Peripartum changes in GABAergic control of the hippocampus and HPA axis: implications for maternal mood |
| 16:30 – 17:00 | **S4-3 Gunther Meinlschmidt**, Ruhr-University Bochum, DE<br>Relation between oxytocin levels during pregnancy & postpartum depression |
| 17:00 – 19:00 | **Poster session 1**<br>Presentation of posters with odd numbers, with beer and brezel |

## Saturday July 13th

| | |
|---|---|
| 08:30 – 09:15 | **Plenary Lecture 2**<br>**PL-2 Tallie Z. Baram**, UC Irvine, US<br>How maternal signals 'rewire' baby's brain and influence cognitive and emotional outcomes<br>**Chair: C. Sue Carter**, RTI International, US |
| 09:15 – 10:45 | **Symposium S5 Early life factors affecting adult social behaviours & dysfunctions**<br>**Chair: Gordon Harold**, University of Leicester, UK |
| 09:15 – 09:45 | **S5-1 József Haller**, Hungarian Academy of Sciences, HU<br>Postweaning social isolation and aggression: behavior, emotions and neurobiology |
| 09:45 – 10:15 | **S5-2 Carmen Sandi**, EPFL Lausanne, CH<br>Neurobiological mechanisms linking early life stress to adult pathological aggression |
| 10:15 -10:45 | **S5-3 Gordon Harold**, University of Leicester, UK<br>Family relationship influences on children's psychopathology: unpacking nature from nurture |
| 10:45 – 13:00 | **Poster session II**<br>Presentation of posters with even numbers, including lunch |
| Free afternoon | Possibility to attend a guided tour of Regensburg, to go hiking or cycling, or to enjoy a boat tour on the river Danube (all tours can be booked and payed for onsite) |
| 19:30 – 00:00 | **Conference Dinner *@ Der historische Salzstadl***<br>Including harp music by *Eva König* |

## Sunday July 14th

| | |
|---|---|
| 08:30 – 10:00 | **Symposium S6 Paternal behaviour and physiology**<br>**Chair: Katharina Braun**, Otto-von-Guericke University, DE |
| 08:30 – 09:00 | **S6-1 Toni Ziegler**, University of Wisconsin, US<br>Social and hormone modulators of paternal care in New World marmosets and tamarins |
| 09:00 – 09:30 | **S6-2 Wendy Saltzman**, UC Riverside, US<br>Interactions between paternal care and fathers stress response |
| 09:30 – 10:00 | **S6-3 Frances Champagne**, Columbia University, US<br>Paternal-maternal interplay and offspring development |
| 10:00 – 10:45 | **Symposium S7 Hot Topics II**<br>**Chair: Frederic Lévy**, INRA-CNRS-Université de Tours, FR |
| 10:00 – 10:15 | **Alaine Keebaugh**, Emory University School of Medicine, US (see **P43**) |
| 10:15 – 10:30 | **Wibke Jonas**, University of Toronto, CA (see **P41**) |
| 10:30 – 10:45 | **Dominik Moser**, University of Geneva Hospitals, CH (see **P61**) |
| 10:45 – 11:15 | **Coffee Break** |
| 11:15 – 12:45 | **Symposium S8 Plasticity of the maternal brain during lactation**<br>**Chair: David Slattery**, University of Regensburg, DE |
| 11:15 – 11:45 | **S8-1 Hiroki Tsukamura**, Nagoya University, JP<br>Lactational anestrus and kisspeptin signaling |
| 11:45 – 12:15 | **S8-2 Liisa Galea**, University of British Columbia, CA<br>Stressed and Depressed: investigating the role of corticosterone during the postpartum on maternal hippocampal morphology |
| 12:15 – 12:45 | **S8-3 Benedetta Leuner**, Ohio State University, US<br>Hippocampal Neurogenesis during the postpartum period |
| 12:45 | **Closing remarks** |

# PLENARY AND SPEAKER ABSTRACTS

## PLENARY AND SPEAKER ABSTRACTS

## PL-1 - NEUROPSYCHOLOGY OF MOTHERING AND EFFECTS OF EARLY EXPERIENCE

Fleming AS, colleagues, and students

*University of Toronto (UTM), Mississauga, Ontario*

In most mammalian species, the female is not normally maternal until she herself gives birth. In rodents, inexperienced non-mothers withdraw from pups or in some cases even cannibalize them. However, at the end of pregnancy and at parturition the hormonal changes that occur result in a shift in the mother's approach-withdrawal tendencies and the new mother will approach young and develop an attraction to them; she then shows the full repertoire of species-characteristic maternal behaviors. Among humans as well, mothering motivation tends to increase after parturition and the quality of behavior depends on a shift in her appraisal of babies, an enhanced emotional sensitivity and alertness, and a change cognitive function. The present talk will discuss the role of these psychological systems in the regulation of mothering in rodent models and humans and how hypothalamic, limbic, and cortical systems within the brain are involved. It will also discuss how experiences acquired in early life and genetics may moderate the quality of later maternal care and its mediating behavioral and physiological mechanisms.

## PL-2 - HOW MATERNAL SIGNALS 'REWIRE' BABY'S BRAIN AND INFLUENCE COGNITIVE AND EMOTIONAL OUTCOME

Cope J, Korosi A, Regev L, Molet J, Baram TZ

*Depts. Pediatrics & Anatomy/Neurobiology UC-Irvine, Irvine, CA, USA*

Maternal sensory signals early in life play a crucial role in programming the structure and function of the developing brain, promoting vulnerability or resilience to emotional and cognitive disorders. Using rodent models, we found that predictable and consistent maternally-derived sensory signals reduced excitatory input to stress-sensitive hypothalamic neurons resulting in altered stress-sensitive gene expression and life-long resilience. In contrast, fragmented and unpredictable maternally-derived sensory signals provoked cognitive and emotional vulnerabilities that became apparent during adolescence. Ongoing studies examine if similar variability and inconsistency of human maternal signals during both gestation and early postnatal life influence development of emotional and cognitive functions, including those that underlie later depression and anxiety.

Supported by NIH grants MH73136, NS28912 and MH 096889

## S1-1 A THALAMIC RELAY CENTER AFFECTING MATERNAL PHYSIOLOGY BY PEPTIDERGIC MECHANISMS

Dobolyi A

*Department of Anatomy, Histology and Embrology, Semmelweis University, Budapest, Hungary*

While postpartum nursing affects mothers both physiologically and psychologically, our knowledge on the mechanisms how nursing affects the brain maternal centers is limited. We investigated how changing activity in ascending neuronal pathways affects postpartum lactation and maternal motivation in rats. Our focus is a cell group in the *posterior intralaminar complex* (PIL) of the thalamus that expresses the *tuberoinfundibular peptide 39* (TIP39). Experiments with retrograde and anterograde tracers showed that TIP39 neurons in the PIL both receive ascending information from the spinal cord and send information through projections to the preoptic area and the arcuate nucleus, two established maternal centers. We also demonstrated that suckling activates PIL TIP39 neurons, while pup exposure without physical contact does not. TIP39 mRNA levels increased markedly around parturition and remained elevated throughout lactation. We showed that injecting a virus that expresses an antagonist to the receptor of TIP39, the parathyroid hormone 2 receptor into the mediobasal hypothalamus markedly decreased the suckling-induced prolactin release. By contrast, injecting the same virus into the preoptic area had no effect on prolactin levels but dampened maternal motivation as judged by conditioned place-preference tests. This effect may be mediated by neurons expressing a recently identified maternal neuropeptide, amylin. Amylin is induced in mothers but its expression is restricted to neurons expressing Fos in response to pup exposure. Furthermore, amylin neurons were closely apposed by TIP39 terminals arising from the PIL and maternal amylin induction was reduced in mice lacking TIP39. In conclusion, TIP39 neurons in the posterior thalamus are ideally positioned to convey suckling information to hypothalamic maternal centers. Since we also showed that the TIP39 system is similar in rodents and human, the identified rodent anatomical pathways and neuropeptides represent an important step to understand the mechanisms underlying nursing effects on the maternal brain. Support: OTKA K100319.

## S1-2 EPIGENETIC MECHANISMS UNDERLYING EXPERIENCE INDUCED IMPROVEMENTS IN MATERNAL CARE

Stolzenberg DS

*University of California, Davis*

The initial experience of interacting with young forms an enduring mother-infant bond that ensures the mother will successfully handle the demands of motherhood and continue to provide maternal care. In most mammals, this bond is facilitated by pregnancy hormones, however can be formed between nonpregnant females and foster infants. A major theme in my research has been to understand the mechanisms through which maternal responsiveness occurs in the absence of pregnancy hormone stimulation. Activation of dopamine neural systems (both the mesolimic and incertohypothalamic) can substitute for

pregnancy hormone stimulation, and initiate and sustain high levels of maternal responsiveness. A downstream target of both estradiol and dopamine receptor stimulation, which is part of the transcriptional pathway that supports maternal responsiveness in both postpartum and virgin female mice, is cyclic AMP response element binding protein (CREB). Therefore, activation of the cyclic AMP-protein kinase A intracellular signaling pathway may be one route through which an initial interaction produces changes in gene expression and subsequent maternal behaviors. CREB-mediated gene transcription regulates experience-dependent behavioral modifications, in part, through acetylation of histone proteins via the recruitment of CREB binding protein (CBP). I hypothesized that interaction with infants might maintain maternal responding via epigenetic modifications that impact gene expression within the MPOA. In support of this hypothesis, manipulation of histone acetylation in nonpregnant female mice potentiates their maternal behavior and increases the expression of several genes, which are strikingly similar to changes noted in female mice just after they have given birth. Therefore, maternal experience may replicate or mimic the effects of pregnancy hormones on brain function.

## S1-3 INTERRELATIONSHIPS AMONG POSTPARTUM MOOD, NEURAL RESPONSES TO EMOTIONAL STIMULI, AND MATERNAL CAREGIVING

Moses-Kolko EL, Almeida JRC, Phillips ML, Zevallos CR, Hipwell AE

*Department of Psychiatry, University of Pittsburgh School Of Medicine; Western Psychiatric Institute and Clinic; Pittsburgh, Pennsylvania, USA*

**Background:** Neural processing of emotional faces is linked to affective disorders and mechanisms of social cognition and empathy. In postpartum mothers, clarifying relationships among emotion processing, affective symptoms and their risk factors, and infant behavior has the potential to inform mechanisms of maternal depression and its impact on infant outcomes. **Methods:** Women(n=36), age 19.7±0.65 and 4±1.1 months postpartum, identified from an ongoing prospective study of psychopathology, underwent functional magnetic resonance imaging with an implicit facial emotion processing task. Subjects identified a transparent color flash during a 1-sec movie of a face dynamically changing from neutral to sad or fearful. GLM modeling of BOLD response for each subject was entered into a random effects ANOVA with posthoc analysis of the sad(fearful) face minus shape contrast. **Results:** Regions most significantly activated to faces (z>3.00,whole brain) were ventromedial prefrontal cortex for sad (VMPFC;BA32, peak coordinate 4,46,-14) and right amygdala for fearful faces (peak coordinate 20,-4,-16). Extracted BOLD activity was significantly associated with 6.5 month depressive symptoms measured by EPDS (R=0.40,p=0.03) and 25-item Hamilton depression scale (R=0.52,p=0.003). More significant than prospective reports of affective disorders during childhood/adolescence was the relationship of harsh parenting received with maternal right amygdala activity to fearful faces (R=0.50,p=0.002). Maternal right amygdala activity was also associated with worse infant social referencing during free play (R=0.43,p=0.03). **Conclusions:** We found that increased VMPFC and amygdala activity to negative emotional faces in postpartum women may be markers both of early adversity and future postpartum depression. Furthermore, the relationship of faces-related amygdala activity with infant social referencing suggests that adversity-sensitive neural regions for

attending to emotional stimuli may be involved in mediating future depression and lower levels of mother-infant mutual engagement in daily infant interactions. Further exploration in a larger sample will further define biopsychosocial pathways for maternal depression and maternal sensitivity. **Acknowledgements:** R01HD067185.

## S1-4 MATERNAL MOODS AND BRAIN PHYSIOLOGY

Swain JE[1,2]

[1]*University of Michigan, Ann Arbor, United States,*
[2]*Yale Child Study Center, New Haven, CT*

**Introduction:** Human parenting constitutes evolutionarily conserved attachment behaviors and thoughts for caring responses to infants. Maternal sensitivity predicts brain responses to own baby-cry in reward and emotion regulation regions that may also be affected by mental health. In this functional magnetic resonance imaging study, we study whether: Mothers at risk for depression will have inhibited self-reflection/empathy brain responses in response to personalized messages about parenting. **Methods:** We studied 18 mothers of 2-7 year-old children with high risk (HR) associated with for previous mood disorder episodes and child abuse, including the working model of the child interview (WMCIP). Brain imaging involved tasks with baby-cry and personalized messages from their WMCI. **Results:** For the baby-cry task: Listening to "a baby-crying" vs. white noise activated salience-related extended amygdala and insula. Listening to "your baby-crying" vs. "a baby-crying" activated reward-related and salience regions of nucleus accumbens, and hippocampus. Listening to "you yourself as a baby-crying" vs. "a baby-crying" activated anxiety/stress-related regions of middle frontal gyrus, caudate, posterior insula, and habenula. Responses were proportional to cumulative psychopathological risk. For the interview task: personalized feedback vs. control activated self-reflection regions of dorsomedial-prefrontal-cortex, precuneus, posterior-cingulate-cortex (PCC), ACC and middle-temporal-gyrus (MTG). According psychopathoogical risk, responses were lower in PCC and precuneus with altered connectivity to MTG. **Conclusions:** Human parenting thoughts, behaviors and neural correlates are driven by key baby stimuli. Previous mood and anxiety alter parental brain responses, suggesting opportunities for intervention and improved child wellness.

**S2-1 "GRANDMOTHER" TRANSGENERATIONAL TRANSMISSION OF THE PRENATAL STRESS PHENOTYPE IN RATS**

Maccari S[1], Morley-Fletcher S[1], Mairesse J[1], Marrocco J[1], Leger H[2], Benecke A[2], Matrisciano F[3], Nicoletti F[4]

[1]*Neural Plasticity Team-UMR CNRS n° 8576 Structural and Functional Glycobiology Unit, North University of Lille, France*

[2] *Systems Epigenomics Group - Institut des Hautes Etudes Scientifiques/CNRS*

[3]*The Psychiatric Institute, Department of Psychiatry, College of Medicine, The University of Illinois at Chicago, USA*

[4]*I.R.C.C.S. Neuromed, Pozzilli, Italy*

Early life stress may program offspring susceptibility to lifelong health problems and there is increasing evidence that developmental programming by an altered intrauterine environment can be passed across generations. In rats, we have previously shown that prenatal restraint stress (PRS) induces long-lasting biochemical and behavioral changes, which result into expression of an anxious/depressive phenotype. In mice PRS increases expression of type-1 DNA methyl transferase in the frontal cortex and induces epigenetic changes in mGlu2/3 metabotropic glutamate receptors. Here we examined the transgenerational effect of PRS in rats by mating first-generation (F1) PRS females rats with naïve males. Remarkably, most of the behavioral and neurobiological alterations associated with PRS persisted in the second-generation (F2), despite the fact that these males were reared normally (i.e not directly exposed to stress *in utero*). We observed enhanced anxiety-like behavior, prolonged corticosterone response to stress, and increased BDNF and reduced mGlu2/3 receptor expression in the hippocampus in both F1 and F2 rats. In addition, we identified several genes stably regulated by PRS that were transmitted to F2 generation by a microarray analysis of the hippocampal transcriptome. Early life stress may program offspring susceptibility to lifelong health problems and there is increasing evidence that developmental programming by an altered intrauterine environment can be passed across generations. In rats, we have previously shown that prenatal restraint stress (PRS) induces long-lasting biochemical and behavioral changes, which result into expression of an anxious/depressive phenotype. In mice PRS increases expression of type-1 DNA methyl transferase in the frontal cortex and induces epigenetic changes in mGlu2/3 metabotropic glutamate receptors. Here we examined the transgenerational effect of PRS in rats by mating first-generation (F1) PRS females rats with naïve males. Remarkably, most of the behavioral and neurobiological alterations associated with PRS persisted in the second-generation (F2), despite the fact that these males were reared normally (i.e not directly exposed to stress *in utero*). We observed enhanced anxiety-like behavior, prolonged corticosterone response to stress, and increased BDNF and reduced mGlu2/3 receptor expression in the hippocampus in both F1 and F2 rats. In addition, we identified several genes stably regulated by PRS that were transmitted to F2 generation by a microarray analysis of the hippocampal transcriptome. Since vulnerability to stress-related disorders can be epigenetically programmed by maternal behavior we scored dams exposed to the repeated restraint stress during gestation (F0, grandmothers) as well as in their female offspring (F1, mothers). Gestational stress in grandmothers markedly reduced the amount of nursing and licking/grooming behavior, and enhanced anxiety during and after lactation.

Interestingly, PRS stress affected very mildly maternal behavior in F1 dams and had no effect on their anxiety-like profile. Our results show that the pathological programming induced by PRS in rats can be transmitted across generations and that transmission involves mechanisms independent of maternal behavior.

## S2-2 REGULATION OF BRAIN STRUCTURE AND FUNCTION BY VARIATIONS IN MATERNAL CARE

Krugers HJ[1], Van Hasselt FN[1], Joels M[2]

[1]*Swammerdam Institute for Life Sciences, Center for Neuroscience, University of Amsterdam, Science Park 904, 1098 XH Amsterdam, the Netherlands*
[2]*Rudolf Magnus Institute of Neuroscience, Department of Neuroscience and Pharmacology, University Medical Center Utrecht, 3508 AB Utrecht, the Netherlands*

Our primary research goal is to understand how regulation of synaptic function underlies memory formation and how these processes are regulated by the early life environment. I will present evidence that early postnatal maternal deprivation and low levels of maternal care hamper hippocampal synaptic plasticity, synaptic structure and spatial memory at adult age. Yet, these adverse early life conditions enhance synaptic plasticity and memory formation under stressful conditions. These studies suggest that individual differences in outcome of early experience depend on environmental context in later life. To investigate this in further detail we investigate the consequences of within-litter differences of maternal care on HPA-axis development, hippocampal morphology and function as well as cognitive performance at adult age.

## S2-3 THE EARLY-LIFE SOCIAL ENVIRONMENT AND DNA METHYLATION

Szyf M

*Department of Pharmacology and Therapeutics McGill University Montreal Canada*

Early life social adversity is known to have long-lasting impact on the phenotype of the offspring. What are the mechanisms that mediate between exposure to adversity during early life and long-term changes in the phenotype? Models of non-primate maternal social-ranking differences and maternal deprivation were previously examined (Suomi et al.,). We also examined the impact of maternal exposure to natural disaster (Quebec ice storm of 1998) on the methylome of the adult offspring (King et al.,). Since the brain is inaccessible in living humans we tested whether early adversity will affect the methylome in T cells which provide a noninvasive tissue source. Early life maternal separation in monkeys is associated with a DNA methylation signature that is seen at 14days. A large fraction of these differentially methylated regions remains to adulthood and there is gender specificity in the stability of the differentially methylated signatures associate with child adversity. We also identified several hundred differentially methylated regions in T cells of 15 year old that were associated with objective stress during their pregnancy as a result of random

differential exposure to the consequences of the ice storm of 1998. These data support the hypothesis that system wide DNA methylation changes early in life in response to social stress occur in both humans and animals in a genome wide and system wide manner. These are proposed to be “adaptive genomic” mechanisms that prepares life-long genome programming to the anticipated life-long environment based on stress signals received during gestation and early life. We will discuss the hypothesis that stress hormones might be mediating the genome wide and system wide response of the methylome to stress. Glucocorticoids might act as “integrators” that translate the social stress signals during gestation to genome wide methylation changes across multiple systems.

## S4-1 MATERNAL ANXIETY: INFLUENCE OF INFANT TOUCH, TIMING & CLASSICAL NEUROTRANSMITTERS

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The hormones of pregnancy and parturition have dramatic neurobehavioural consequences for female mammals. During the early postpartum period, these changes include a suppression of negative emotional reactivity, such as anxiety and its related behaviours. Using laboratory rats to study the sensory and neural factors influencing anxiety in new mothers, we have focused on the how non-suckling physical contact with offspring (suckling and lactation appear irrelevant) alters numerous classical neurotransmitter systems underlying anxiety-related behaviours. Some of our recent data indicate that females’ level of anxiety before mating predicts their postpartum anxiety and that litter contact does not invariably reduce anxiety behaviour, but instead modifies this “trait” anxiety to bring dams at both extremes to a more moderate level. Furthermore, this ability of litter contact to narrow the range of postpartum anxiety is associated with females’ capacity for noradrenaline synthesis in the brainstem. While these effects are found in inexperienced primiparous rats, it is important to acknowledge that approaching parturition with no prior history of caregiving is rare because most females naturally gain alloparental experience as juveniles while interacting with younger siblings or other neonates. We find that juvenile alloparenting produces a long-lasting phenotype characterized by low adult anxiety, high maternal responsiveness, and high midbrain serotonin synthesis. This phenotype mimics that seen after parturition in previously inexperienced female rats. Thus, interacting with offspring alters maternal neurochemistry to restrict anxiety within a range that may be optimal for mothering. Furthermore, early-life alloparenting primes females for these behaviors , thereby greatly reducing the importance of endocrine factors released during pregnancy and parturition. A lack of early parenting experience or inability to respond to infant touch with a recalibration of aminergic and other neurochemical systems may contribute to aberrations in anxiety and other emotional states during the postpartum period . Acknowledgements: Funded by NICHD R01HD057962

## S4-2 PERIPARTUM CHANGES IN GABAERGIC CONTROL OF THE HIPPOCAMPUS AND HPA AXIS: IMPLICATIONS FOR MATERNAL MOOD

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Alterations in $GABA_A$ receptor ($GABA_AR$) subunit expression have been previously demonstrated in the hippocampus of pregnant mice compared to postpartum and virgin mice. Decreased $GABA_AR$ δ subunit expression in the hippocampus is associated with deficits in tonic GABAergic inhibition and alterations in neuronal excitability of dentate gyrus granule cells. Our data suggests that these alterations are compensatory changes to offset the increase in neurosteroid levels during pregnancy, which can potentiate the effects of GABA on these receptors. Interestingly, the inability to regulate $GABA_AR$ δ subunit expression during pregnancy and the postpartum period in *Gabrd*$^{-/-}$ mice is associated with deficits in maternal behavior and depression-like behavior during the postpartum period. Recent data in our laboratory suggest that the behavioral deficits observed in *Gabrd*$^{-/-}$ mice during the postpartum period may be due to alterations in stress reactivity. We have identified a role for the $GABA_AR$ δ subunit in the regulation of the hypothalamic-pituitary-adrenal (HPA) axis. $GABA_AR$ δ subunit-containing receptors regulate the activity and neurosteroid sensitivity of corticotropin-releasing hormone (CRH) neurons in the paraventricular nucleus (PVN) of the hypothalamus, which are at the apex of HPA axis control. We observe alterations in the GABAergic control of CRH neurons and altered stress reactivity during pregnancy and the postpartum period, which likely plays a role in preventing elevations in stress hormone levels during this time. Our lab has uncovered a novel mechanism regulating HPA axis function during pregnancy and the postpartum period which may aide in the identification of potential therapeutic targets for the treatment of postpartum depression.

## S4-3 RELATION BETWEEN OXYTOCIN LEVELS DURING PREGNANCY AND POSTPARTUM DEPRESSION

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Postpartum depression (PPD) affects up to 19% of all women after parturition. The non-apeptide oxytocin (OXT) is involved in adjustment to pregnancy, maternal behavior, and bonding. Our aim was to examine the possible association between plasma OXT during pregnancy and the development of PPD symptoms. A total of 74 healthy, pregnant women were included in this prospective study. During the third trimester of pregnancy and within 2 weeks after parturition, PPD symptoms were assessed using the Edinburgh Postnatal Depression Scale (EPDS). Blood samples for plasma OXT assessment were collected in the third trimester. Following the literature, participants with postpartum EPDS scores of 10 or more were regarded as being at risk for PPD development (rPPD group). In a logistic regression analysis, plasma OXT was included as a potential predictor for being at risk for PPD. Results were controlled for prepartal EPDS score, sociodemographic and birth-outcome variables. Plasma OXT concentration in mid-pregnancy significantly predicted PPD symptoms at 2 weeks postpartum. Compared with the no-risk-for-PPD group, the rPPD group was characterized by lower plasma OXT concentrations. To our knowledge, this is the first study to show an association between prepartal plasma OXT concentration and postpartal symptoms of PPD in humans. Assuming a causal relationship, enhancing OXT release during pregnancy could serve as a potential target in prepartum PPD prevention, and help to minimize adverse effects of PPD on the mother–child relationship. **Acknowledgements:** This work was part of the NCCR sesam. The Swiss National Science Foundation (SNF) (project no. 51A240-104890), the University of Basel, the Hoffmann-La Roche Corp. and the Basel Scientific Society provided core support for the NCCR sesam. We are grateful to the Max Planck Institute of Psychiatry, Munich, Germany for the biochemical analyses. Further, we thank Andrea H Meyer, PhD, for his statistical support.

## S5-1 POSTWEANING SOCIAL ISOLATION AND AGGRESSION: BEHAVIOR, EMOTIONS AND NEUROBIOLOGY

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Post-weaning social isolation in rats is believed to model symptoms of early social neglect-induced externalizing problems including aggression-related problems. We showed earlier that rats reared in isolation from weaning show exacerbated autonomic and glucocorticoid responses to social challenges, abnormal features of aggressiveness as indicated by dramatically increased attacks counts (especially of those that are targeted onto the head, throat and belly of opponents), decreased intention signalling by social communication, and deficient social integration into newly formed groups. Extensive social experience ameliorated deficits in social integration, but abnormal forms of aggressiveness were resistant to such experience. A gross evaluation of aggression-related neuronal activation patterns by c-Fos staining indicated an increased activation of brain mechanisms that are known to control aggressiveness. Our recent findings show that in addition to such functional changes, the prefrontal cortex undergoes profound alterations during post-weaning social isolation. Such changes include a lateralized decrease in prefrontal volume, altered neuronal dendritic arborization, and glial plasticity. The dorsal endopiriform nucleus –a brain area that is at the junction of brainstem neuropeptide S and infralimbic afferents and which plays a role in anxiety– also appears to play a role in the behavioural effects of post-weaning social isolation. Taken together, these findings show that social contacts established during adolescence have an important role in neuronal development and the lack of such contacts results in a series of neuronal, emotional and behavioural abnormalities. The relevance of these findings for human development will be addressed

## S5-2 NEUROBIOLOGICAL MECHANISMS LINKING EARLY LIFE STRESS WITH ADULT PATHOLOGICAL AGGRESSION

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A major risk factor for violence perpetration is childhood exposure to violence, but the neurobiological mechanisms of these long-term effects remain uncertain. Using an animal model devoid of human cultural factors, we find that exposing peripubertal male rats to fear-inducing experiences produced pathological aggression both towards other male conspecifics and towards their female partners during adulthood. Importantly, their offspring also shows increased aggression towards females even without postnatal father-offspring interaction. In searching for key neurobiological mechanisms translating stress effects into increased aggression, we find alterations in amygdala-medial orbitofrontal circuit activity, the testosterone/corticosterone ratio, and the serotonergic system. We also find evidence for a programing role of glucocorticoids and for a link between altered polysialylation of the neural cell adhesion molecule during development and pathological

aggression. These findings will be discussed within a broader context reflecting on the societal implications of stress.

## S5-3 FAMILY RELATIONSHIP INFLUENCES ON CHILDREN'S PSYCHOPATHOLOGY: UNPACKING NATURE FROM NURTURE

Harold G

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New World monkeys, such as common marmosets (Callithrix jacchus) and cotton-top tamarins (Saguinus oedipus), are cooperative breeders that invest heavily in their offspring and their mate. Males of these species prepare for their paternal investment by showing pronounced physical alterations such as weight gain and hormonal responses to the mate's pregnancy. Fathers begin caring for their infants immediately following birth and frequently are in contact with their infants up to 80% of the day. Communication between fathers, mothers and infants relies on sensory stimuli and these cues are involved in the social bonding. We have shown in a series of studies that fathers will respond to the olfactory cues from their infants with a spontaneous decline in testosterone and elevated estrogens and this endocrine response is unique only to natal infants. Conversely, fathers are responsive to all infant distress cries regardless of familiarity. While variability does exist between fathers in their level of responsiveness to infants, motivation to parent exists solely with fathers. Males who have never been fathers show little to no interest in responding to infant stimuli even when hormonally stimulated (estradiol or testosterone) while males who are already fathers show high levels of responsiveness to infant stimuli which is further enhanced when hormonally stimulated by estradiol. Becoming a father and exhibiting hormonal and behavioral responses towards infants is not automatic but appears to require sensory interactions between the male, his pregnant mate and their infants. Funding of these studies has been provided by the National Institutes of Health grants: MH3215 to Charles T. Snowden, HD057684 to TEZ and the Wisconsin National Primate Research Center base grant RR000137.

## S6-1 SOCIAL & HORMONAL MODULATORS OF PATERNAL CARE IN NEW WORLD MARMOSETS AND TAMARINS

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A major risk factor for violence perpetration is childhood exposure to violence, but the neurobiological mechanisms of these long-term effects remain uncertain. Using an animal model devoid of human cultural factors, we find that exposing peripubertal male rats to fear-inducing experiences produced pathological aggression both towards other male conspecifics and towards their female partners during adulthood. Importantly, their offspring also shows increased aggression towards females even without postnatal father-offspring interaction. In searching for key neurobiological mechanisms translating stress effects into increased aggression, we find alterations in amygdala-medial orbitofrontal circuit activity, the testosterone/corticosterone ratio, and the serotonergic system. We also find evidence for a programing role of glucocorticoids and for a link between altered polysialylation of the neural cell adhesion molecule during development and pathological aggression. These findings will be discussed within a broader context reflecting on the societal implications of stress.

## S6-2 INTERACTIONS AMONG STRESS, ANXIETY AND PATERNAL BEHAVIOR IN CALIFORNIA MICE

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In several mammalian species, stress and glucocorticoids have been shown to disrupt maternal behavior. Correspondingly, lactating females have blunted hormonal, neural and behavioral responses to stress, which might buffer maternal care from stress-induced suppression. Virtually nothing is known, however, about interactions between stress and parenting in fathers. Therefore, we conducted a series of studies investigating possible effects of stress and glucocorticoids on paternal behavior, as well as effects of fatherhood on stress responsiveness, in the biparental California mouse (Peromyscus californicus). Fathers exposed to chronic variable stress showed reduced paternal care, as well as elevated circulating corticosterone (CORT) concentrations and vasopressin (AVP) mRNA expression in the paraventricular nucleus of the hypothalamus (PVN). In contrast, acute CORT treatment did not markedly affect paternal behavior. We found no evidence that fathers had altered baseline circulating CORT levels or CORT responses to acute or chronic stressors, as compared to nonbreeding males. Moreover, fatherhood did not alter males' behavioral responses to acute stressors, or expression of Fos, corticotropin-releasing hormone (CRH), or AVP in the PVN or the bed nucleus of the stria terminalis (BNST) under baseline or stressed

conditions. Among virgin males, however, paternal responsiveness to a pup was negatively correlated with behavioral and neural markers of anxiety. Finally, treatment of virgin males with conspecific placenta via oral gavage significantly enhanced paternal responsiveness and reduced Fos expression in the dorsolateral BNST, a region associated with stress and anxiety, following exposure to a pup. These findings suggest that in this biparental mammal, 1) chronic stress or anxiety, but not acute CORT elevations, can suppress paternal behavior; 2) fatherhood does not modulate stress-responsiveness; 3) individual differences in anxiety might contribute to individual differences in paternal responsiveness; and 4) placentophagia might reduce anxiety and therefore facilitate the onset of paternal care in new fathers. (Funded by NIH 1R21MH087806.)

## S6-3 PATERNAL-MATERNAL INTERPLAY AND OFFSPRING DEVELOPMENT

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Within biparental species, there is the opportunity for fathers to influence the development of their offspring through the provision of care. However, even amongst species in which the father has no postnatal contact with offspring, there is evidence for paternal effects on development. It an effort to determine the mechanism(s) through which paternal effects occur, we have explored the impact of paternal social experiences and nutrition on fathers, mothers, and offspring in laboratory mice. Males exposed to social/physical environmental enrichment were found to have decreased stress reactivity and changes in hippocampal gene expression. Females mated with these males were found to increase their level of postnatal maternal care toward offspring (particularly nursing and pup licking). Offspring of enriched fathers were found to benefit through increased weaning weight. These findings suggest that one mechanism through which fathers can alter offspring development is through paternally-induced effects on maternal care. Consistent with this finding, we determined that paternal food restriction leads to increased maternal food intake during pregnancy and increased frequency of nursing during the postpartum period. The phenomenon of altered maternal investment in offspring consequent to mating with fathers of variable “mate quality” has been demonstrated in many avian species and our findings suggest that the environmental experiences of fathers can act as a significant cue to mate quality. We discuss these findings in the context of two hypotheses regarding maternal-paternal interplay: 1) differential allocation (where females increase care of offspring sired by “preferred” mates and 2) compensation (where females increase investment of resources in offspring of males with compromised mate quality). Acknowledgements: This research was supported by Grant Number DP2OD001674-01 from the Office of the Director, National Institutes of Health

## S8-1 LACTATIONAL ANESTRUS AND KISSPEPTIN SIGNALING

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Follicular development and ovulation are profoundly suppressed during lactation in various mammalian species. It has been well known that the suppression is mainly due to the inhibition of pulsatile gonadotropin-releasing hormone (GnRH)/gonadotropin secretion. Kisspeptin, a peptide encoded by *Kiss1* gene, was discovered as an endogenous ligand for GPR54, a G protein-coupled receptor. Accumulating evidence suggests that central kisspeptin-GPR54 signaling plays a critical role in regulating GnRH and then gonadotropin release. The present paper focuses on the brain mechanism inhibiting GnRH and gonadotropin secretion via suppression of kisspeptin-GPR54 signaling by the suckling stimulus in lactating rats. Pulsatile luteinizing hormone (LH) secretion is strongly suppressed by the suckling stimulus in ovariectomized mother rats in the first half of lactating period, while the LH suppression was dependent on negative feedback levels of estrogen in the later half of lactation. In both early and later half of lactation, suckling-induced suppression of LH secretion was accompanied by strong inhibition of Kiss1/kisspeptin expressions in the hypothalamic arcuate nucleus (ARC), one of the kisspeptin neuronal populations, which is considered to be responsible for GnRH pulse generation. Central kisspeptin challenge immediately induced LH increase in lactating mothers, indicating that hypothalamic GPR54 functions normally during lactation. Thus, these results suggest that the lactational anestrus is mainly due to the inhibition of kisspeptin-GPR54 signaling in the ARC, leading to suppression of GnRH/LH pulse, follicular development/steroidgenesis, and ovulation. This work was supported in part by the Research Program on Innovative Technologies for Animal Breeding, Reproduction, and Vaccine Development.

## S8-2 STRESSED AND DEPRESSED: INVESTIGATING THE ROLE OF CORTICOSTERONE DURING THE POSTPARTUM ON MATERNAL HIPPOCAMPAL MORPHOLOGY

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Pregnancy and mothering is a time of dramatic change in brain and behaviour. The hippocampus is sensitive to steroid hormones that fluctuate during pregnancy and the postpartum and the integrity of the hippcoampus is implicated in cognitive and affective disorders. Reproductive experience (pregnancy and mothering) affects both hippocampus-dependent cognition and neurogenesis during lactation, after weaning and into middle age. Motherhood itself is associated with increased risk to develop a number of diseases including anxiety and depression. Indeed, the time of greatest risk to develop depression in a women's lifetime is during the postpartum period. We created an animal model of

postpartum depression by administering high corticosterone during the postpartum. Meta-analyses show that depressed patients have higher levels of cortisol and smaller hippocampal volume. Indeed, the hippocampus contains a high concentration of glucocorticoid receptors and is sensitive to stress.We found that high levels of CORT during the postpartum, but not during gestation, increased depressive-like behavior in the dams. Dams treated with high CORT during gestation or the postpartum also exhibited reduced cell proliferation at the time of weaning in the dentate gyrus compared to dams treated with vehicle. Further dams treated with high CORT postpartum exhibited reduced dendritic complexity in the basal region of CA3 pyramidal cells in the hippocampus.Perhaps paradoxically we found high CORT postpartum increased mushroom spines in both the apical and basal regions of CA3 pyramidal cells. Together these studies show that high CORT exposure during the postpartum alters hippocampal morphology; which may be linked to the expression of depressive-like behaviours. Future experiments will examine interventions to abrogate depressive-like endophenotypes in CORT-treated postpartum rats. Funding from CIHR and Coast Capital Depression Fund.

## S8-3 HIPPOCAMPAL NEUROGENESIS DURING THE POSTPARTUM PERIOD

Leuner B

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Motherhood is accompanied by alterations in numerous non-reproductive behaviors, including learning and memory, as well as anxiety and stress regulation. These functions have been linked to adult neurogenesis in the hippocampus, but the effects of maternal experience on this form of hippocampal plasticity have only recently been explored. This talk will discuss hippocampal neurogenesis during the postpartum period focusing on its regulation by steroid (corticosterone) and peptide (oxytocin) hormones associated with lactation. We propose that hormone-driven changes in neurogenesis during the postpartum period may be a potential mechanism underlying modifications in hippocampal function that occur during this critical period in a female's life. **Acknowledgements:** Supported by grants from NARSAD and the NIMH.

# POSTER ABSTRACTS

## POSTER ABSTRACTS

**P1 PUPS VS MALE CHOICE DURING POSTPARTUM ESTRUS: MODULATION BY A DOPAMINERGIC ANTAGONIST AND MOTHER-PUP INTERACTION**

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During the postpartum estrus (PPE), rats are maternal and sexual motivated however in a pups-male choice test they prefer the pups. As the dopaminergic (Da) system has been strongly implicated in the motivational aspects of maternal behavior, we hypothesized that its down-regulation will reduce pups' preference during the PPE. To probe this hypothesis we tested PPE rats in a Y-maze with three-choice chambers: two with reinforcing stimuli (eight pups or a sexually active male) and one neutral (empty), after the administration of the Da antagonist haloperidol (HAL: 0.0; 0.025 or 0.050 mg/kg, -60 min, n=10-11 per group). HAL-treated females decreased time spent in pups' chamber while increased the time spent in male's chamber, resulting in a lack of preference between both reinforcers. Although HAL may affect both motivations, this result indicates that it preferentially affected maternal over sexual motivation, and suggests that under control conditions the reinforcing value of pups prevents the expression of sexual motivation in PPE females. If this is the case, then the selective reduction of maternal motivation –by shortening the period of mother-pups interaction- will shift the choice from the pups to the male. With this aim, we tested PPE rats in the pups-male preference test after experiencing 10 or 2.5 hours of interaction with their litters after parturition ends (n=7-8 per group). As expected, PPE females continuously exposed to pups (10 hours) prefered them, while those dams that interacted with their litter 2.5 hours exhibited a marked preference for the male despite being maternal. Together, these results indicate that the strong incentive value that pups have for a PPE female prevents the expression of sexual motivation in this choice situation, and that the strength of maternal motivation during the PPE is built on previous mother-pup interaction. **Acknowledgements:** CSIC, SNI-ANII and PEDECIBA for financial support.

**P2 DECLINING SUCKLING-INDUCED FOS-ACTIVATION AND INCREASED IMMUNOREACTIVITY OF MELANIN-CONCENTRATING HORMONE (MCH) DURING LATE LACTATION**

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MCH has been largely implicated in the control of food intake, body weight and energy homeostasis. Moreover, lactation is an important physiological model to study hypothalamic integration to peripheral sensory signals, such as suckling stimulus and also those related to energy balance. Higher concentrations of MCH mRNA have been found during lactation in the medial preoptic area (MPOA) and in the anterior part of the paraventricular nucleus of

hypothalamus, especially around the 19th day of lactation when this hormone reveals its highest peak of mRNA expression, and decrease after weaning. The physiological significance of this phenomenon is unclear. In this sense, the aim of the present study was to contribute to the investigation of sensory and endocrine factors influencing in the expression of MCH and its relationship to neuroendocrine and behavioural changes involving the end of lactation, weaning and perpetuating reproductive cycle. Wistar female rats (n= 56), divided in subgroups of four animals, were sacrificed every day from 15th to 21st day of lactation, with (SS) or without (NS) suckling stimulus. MCH and *Fos* immunoreactivity (MCH-/*Fos*-ir) was evaluated in the lateral hypothalamic area (LHA), MPOA and incerto-hypothalamic area (IHy). The MPOA showed an inverse relationship existing in the *Fos*-ir and MCH-ir. Also, we observed an increase in the *Fos*-ir of the group SS, which was less intense on 18th day when compared to 15th day, while MCH-ir was increased. Besides, no colocalization between MCH-ir and *Fos*-ir was found. Our results suggest that suckling stimulus is able to influence the MCH-ir around the 19th day of lactation in LHA. Therefore, the areas were we found *Fos*-ir might have stimulated MCH-producing neurons. Hence, an indirect relationship between the areas of neuronal activation and MCH-ir during suckling stimulus seems likely. This study was supported by grants from the FAPESP (Nº. 2010/14469-2 and 2010/52068-0).

**P3 THE EFFECT OF DOPAMINE ON THE POSTERIOR DIVISION OF BED NUCLEUS OF STRIA TERMINALIS AFTER BEING FATHER**

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Male mice show the drastic changes of behavioral pattern for the pup exposure. Whereas the virgin male mice do not care but attack the pup, father mice retrieve the pup to their nest and care the pup. Recently, brain regions related to the transition of behavioral pattern were explored by using c-Fos expression as a neuronal activation marker. As a result, it was found that the numbers of c-Fos positive neurons in posterior division of bed nucleus of stria terminalis (pBNST) were significantly decreased after being father. To address the pharmacological property in pBNST, we performed ex vivo whole cell patch clamp recording from pBNST from the brain slice of virgin and father male mice. Current injection identified two types of firing pattern in pBNST neurons; regular and burst firing. In the presence of blockers of ionotropic glutamate receptors, we observed the evoked inhibitory postsynaptic current (eIPSC) by the stimulation of dorsal part of pBNST. Application of D1 receptor agonist SKF38393 decreased the eIPSC amplitude in regular firing neurons but not in burst firing neurons. Interestingly, the effect of SKF38393 was not observed in the slice from father mice. These data suggest that dopamine would induce disinhibition in pBNST and that the experience to be father reduced the effect of dopamine to maintained the inhibitory neurotransmission in pBNST. Acknowledgements; this work is supported by JSPS KAKENHI Grant Number 25713044

**P4 LONG LASTING EFFECTS OF EARLY VIOLENT ENVIRONMENT IN RATS: GESTATIONAL PARAMETERS AND LOW BIRTH WEIGHT**

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As part of the characterization of an animal model of early violent/aversive environment (EVE), we evaluate the long lasting effects of social stress during lactancy on offspring gestational parameters and the body weight of the second generation. Wistar rats were supplied by the Animal Breeding Center of our University. At the age of 11 weeks, on the evening of the proestrous, each female was caged with one male for breeding. On gestational day 19 pregnant females were isolated on new home-cages for parturition. The day of birth was considered post-natal day 0 (PND-0). On PND-1 all litters were set to 8±1 pups. For the EVE group, a male intruder (320-420g) was inserted in the home cage, on PND-3, 5, 7 and 9, between 3 and 4 hours after lights on, for 5min. Controls were left undisturbed. On PND-21 weaning was performed and females were allocated 4 per cage. On PND-80 evaluation of estrous cycle began. After three consecutive and regular estrous cycles, on the evening of proestrus, females were caged with a male for mating, considered gestational day 0 (GD-0). On gestational day 19 pregnant females were isolated on new home-cages for parturition. On PND-1 all litters were set to 8 pups. On PND-7 pup retrieval test was performed and recorded for 30min. EVE group showed increased gestational body weight gain between GD-0 and GD-19, but the litter weight was decreased in comparison to control group. There was no difference in the average number of pups/litter between groups. Gestational length was decreased on EVE group. No difference was found in the pups retrieval test. These preliminary results show that this animal model promotes long-lasting changes in reproductive parameters and second generation low birth weight, which is a risk factor for a number of negative outcomes.

## P5 THE DEVELOPMENT OF INFANT AND EARLY CHILDHOOD REGULATION AS AN OUTCOME OF PRENATAL DEPRESSION AND MULTIPLE SUSCEPTIBILITY GENES

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Genetic factors that might moderate prenatal programming and the development of limbic and cortical brain regions to predict regulation capacity in infancy and early childhood include polymorphisms in both dopamine and serotonin neurotransmission. The serotonin transporter polymorphism (5-HTTLPR) has been demonstrated to moderate the impact of early postnatal mother-child attachment on infant and preschool children' regulation (Kochanska, Philibert, & Barry, 2009). Dopamine polymorphisms DRD2, DAT and DRD4 have been demonstrated to moderate the impact of both positive and negative postnatal rearing environment on childhood externalizing symptoms (Bakermans-Kranenburg & van IJzendoorn, 2011). The present study sheds more light on the role of prenatal environment, and investigates how multiple susceptibility and risk genes in serotonin and dopamine transmission moderate prenatal depression to predict infant and early childhood regulation. *N* = 217 mother-infant dyads from the MAVAN cohort. The IBQ-R was reported by mothers at 3, 6, 18 and 36 months, and a measure of regulation was extracted at each time point. The CES-D was self-reported by mothers at 24-36 weeks gestation, and at 6, 12, 24 and 36 months postnatal to measure pre- and postnatal depression. Infant genotype was obtained with buccal swabs. We invested a graduated model of multiple susceptibility and risk genes, and considered the cumulative effects of 5-HTTLPR, DRD2, DRD4, DAT, COMT and BDNF as they interacted with prenatal depression to predict regulation. Selected results demonstrate that early childhood regulation was significantly associated with 5-HTTLPR, DRD4 and COMT at 36months, as an outcome of prenatal depression. Results will be discussed in more detail. Overall, the pattern of results demonstrates that prenatal depression appears to be moderated by a host of susceptibility and risk genes in the prediction of early childhood regulation at 3 years of age, and within a model of differential susceptibility

**P6 ENERGETIC AND NEURAL EFFECTS OF MALE PARENTING**

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While the energetic effects of female parenting are well-studied, particularly in rodents, the energetic effects of male parenting, and their relationship to neural mechanisms involved in feeding and weight maintenance, are not as well understood. We examined the effects of male parenting in a series of studies in prairie voles (*Microtus ochrogaster*) and titi monkeys (*Callicebus cupreus*), both socially monogamous species in which males contribute large amounts of time to infant care. In prairie voles, fathers exhibited significant losses in body weight ($F_4$=3.15, p=0.026), losses of subcutaneous fat ($F_2$=3.84, p=0.036), and drops in leptin ($F_4$=21.31, p<0.0001), coincident with a reduction in feeding behavior. Father's pre-pairing weights tended to be positively correlated with the time they later spent in contact with their pups (FDR adjusted p-value = 0.08). Fathers had significantly lower insulin values than non-fathers after caring for pups ($t_{17}$ = 2.525, p = 0.019). CART (cocaine and amphetamine-related transcript) levels in the arcuate nucleus were significantly different between fathers, males housed with their brothers, and recently mated males ($F_{2,24}$ = 2.89, one-sided p =0.044). In titi monkey males, which also contribute heavily to infant care, weight losses across infant care were not significant. The energetic effects of male parenting are likely to be species and environment-specific but can sometimes be substantial. Funding: NIH MH073022 and HD053555, NSF 0437523, Office of Research Infrastructure Programs grant P51OD011107, and the Good Nature Institute.

**P7 SYMPATHETIC NERVES ACTIVATION DURING GESTATION IMPAIRS FOLLICULAR RECRUITMENT IN THE OVARY OF FEMALE OFFSPRING**

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Stress is particularly harmful when exposure occurs during gestation. In adult rats we found that chronic cold stress activates ovarian sympathetic innervation and develops polycystic ovary (PCO) condition. PCO syndrome is the most frequent ovarian pathology during reproductive years in women and most of the characteristic cases of PCOS originate during early development in human and are expressed either before or during puberty, suggesting a condition derived from *in utero* exposure to neural or metabolic derived insults. The objective of this work was to study the effect of gestational sympathetic stress in the development of ovary function and in the onset of puberty. Timely pregnant rats were exposed to a 4°C cold stress 3h/daily (from 10:00-13:00hrs) during all pregnancy. Ovary development of the female progeny was studied at 2 days old (neonatal) and at 30 days old

(pre-pubertal). The age of puberty and steroids plasma levels were studied in another group of rats. Neonatal rats exposed to sympathetic stress during gestation presented a lower number of ovarian primary follicles and a lower transition between primary to secondary follicles. The expression of FSH receptor and its response to FSH was decreased. The response to FSH-induced secondary follicles development was decreased. Estradiol plasma level before puberty was decreased and the puberty onset (as seen by vaginal opening) was delayed. The amount of ovarian norepinephrine was significantly reduced in stressed rats. Thus we conclude that gestational stress not only decreases the early follicular development of the progeny but also the responsiveness to gonadotropins and thus delaying puberty. On the other hand the fact that ovarian NE was decreased could mean that increased NE levels during gestation might induce a compensatory response in the progeny by decreasing the development of sympathetic nerves of the ovary. Supported by Fondecyt 1130049 and DFG-PIA-Conicyt grant

**P8 OXYTOCIN SIGNALING STIMULATED BY PARENTAL TOUCH MAY MODULATE SUSCEPTIBILITY TO DISRUPTIONS IN PARENTAL NURTURING**

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Tactile stimulation from the caregiver may be the salient factor affecting offspring responses to parental nurturing, including modulating adult social behavior. We examined the role of oxytocin (OT) in mediating long-term responses to maternal nurturing in monogamous prairie voles. A 5 min tactile stimulation with a paintbrush elicited immediate early gene (IEG) activity in PVN OT neurons in neonatal female ($p<0.02$), but not in male prairie voles. AVP neurons were not activated in either sex. We then investigated the effects of social isolation during the postnatal period on adult attachment. Between PND1-14, experimental pups underwent daily 3hr isolations while controls remained with the parents. In adulthood, isolated females as a group did not display a partner preference after 48hr cohabitation with a male while controls did ($p=0.033$). Early social isolation did not alter oxytocin receptor (OTR) density in the nucleus accumbens (NAcc), a region involved in partner preference formation. However, isolated females with low densities of NAcc OTR did not display a preference for their mated partner, while those with high OTR densities did ($p=0.012$). This suggests that OT signaling in the NAcc may buffer against the negative impact of social isolation, and that females with low OTR levels in the NAcc are particularly susceptible to disrupted parental nurturing. We then chronically administered 10 mg/kg melanotan-II (MTII), a melanocortin-4 receptor agonist that induces IEG expression in hypothalamic OT neurons, for the first week of the 2 week isolation. MTII-treated females displayed a partner preference after an abbreviated 6hr cohabitation ($p=0.001$), while saline-injected controls did not. These data suggest that neonatal accumbal OT signaling, which may be stimulated by parental tactile stimulation, can have long lasting effects on the neural circuits involved in the formation of social relationships. Supported by NIH MH096983 to LJY.

## P9 EXPRESSION AND IMMUNOREACTIVITY OF MCHR1 IN MAMMARY GLAND OF THE RAT DURING LACTATION

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**Introduction:** The melanin-concentrating hormone (MCH) mRNA, as well as the MCH, are located predominantly in hypothalamic nuclei. Novel sites of MCH mRNA expression and immunoreactivity during lactation final period have been identified in other hypothalamic nuclei, such as the ventral part of medial preoptic area (MPOAv). The MCH receptor 1 (MCHR1) is an orphan G protein-coupled receptor detected in many regions of the rat brain, but there are no descriptions of MCHR1 expression in the mammary glands of non-lactating or lactating dams. **Objective:** this project was designed to detect MCHR1 mRNA expression and immunorreactivity in the mammary glands of lactating and non-lactating rats, correlating MCH mRNA expression in the MPOAv with the consequent MCHR1 mRNA expression in the mammary gland, thereby, increasing the knowledge regarding the control of maternal behavior (MB). **Material and methods:** We used in situ hybridization and immunohistochemistry to detect MCHR1 in mammary gland tissue from four groups of rats : virgins; dams of lactation day 5; dams of lactation day 12; and dams of lactation day 19. **Results:** We detected MCHR1 mRNA in the mammary glands of dams, in the lactation days 12 and 19, a comparable expression in the controls, in the stroma; a differential expression was found in the glandular tissue of dams of lactation day 12 compared with day 19. By immunohistochemistry, we found MCHR1-ir cells in hair follicle in skin. In glandular tissue we found cells MCHR1-ir bordering the acini, compatible with mRNA expression of MCHR1 seen in lactation day 12, but not in the day 19. **Conclusion:** Once that there is a differential expression of MCHR1 mRNA and MCHR1-ir cells in different parts of the mammary gland during the lactation days, this data suggests that MCHR1 is involved at the end of the lactation process. **Acknowledgements:** FAPESP, CAPES and CNPq.

## P10 VASOPRESSIN V1B RECEPTORS MEDIATE MATERNAL CARE AND AGGRESSION IN OPPOSING DIRECTIONS IN LACTATING RATS

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Maternal behaviour in rodents is mediated by brain vasopressin and V1a-receptors. However, nothing is known about an involvement of the V1b-receptor subtype (V1bR). Here, we aimed to investigate the role of V1bR in maternal behaviour following acute treatment with a specific V1bR agonist (d[Leu4,Lys8]VP; V1bR-ago) or antagonist (SSR149415; V1bR-A). On pregnancy day 18, female Wistar rats were fitted with a guide cannula targeting the

lateral ventricle. After parturition, dams received daily one acute treatment injection followed by observations of maternal care (lactation day (LD) 1), maternal motivation in the pup retrieval test (LD 2), and maternal aggression against a virgin female intruder in the maternal defence test subsequently followed by maternal care (LD4). V1bR-A decreased the time the mothers spent on nursing and overall maternal care ($p < 0.01$, each), while V1bR-ago had no effect. Maternal care after maternal aggression revealed that exposure to maternal defence decreased nursing in all groups ($p < 0.05$). In addition, such a decrease was found for overall maternal care in the V1bR-A mothers ($p < 0.05$). Neither treatment altered maternal motivation. Regarding maternal aggression, V1bR-A mothers showed more often keep down- and lateral threat-positions ($p < 0.05$, each), and tended towards increased offensive upright-positions ($p=0.06$) and number of attacks ($p = 0.07$) compared to the VEH group. Furthermore, during maternal aggression both vehicle as well as V1bR-A mothers showed less social versus non-social behaviours ($p < 0.01$), while V1bR-ago mothers displayed both behaviours equally. In conclusion, blocking V1bR decreased maternal care but increased maternal aggression, whereas activating V1bR had no behavioural effects under basal conditions. However, V1bR activation facilitated social behaviour during maternal aggression. The V1bR agonist and antagonist were generously provided by M. Manning (University of Toledo) and C. Serradeil-Le Gal (Sanofi-Aventis).Supported by DFG BO1958/6-1 to OJB

## P11 NO MODERATING EFFECT OF 5-HTTLPR ON ASSOCIATIONS BETWEEN ANTENATAL ANXIETY AND INFANT BEHAVIOR

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**Objective:** Maternal antenatal anxiety is associated with an increased risk of behavioral disturbances in offspring. Recent work has suggested that the effect of maternal antenatal anxiety on infant temperament at 6 months is moderated by the serotonin transporter polymorphism 5-HTTLPR, with carriers of the short allele more susceptible to the adverse behavioral outcomes of maternal antenatal anxiety. These findings, however, are yet to be replicated and extended beyond infancy. The aim of the current study was to assess this same potential moderator (5-HTTLPR) in a large population-based cohort study, and to determine whether or not the effects persist into childhood and early adolescence. **Method:** Data from the Avon Longitudinal Study of Children and Parents (ALSPAC) cohort (N 1⁄4 3,946) were used to assess whether the 5-HTTLPR genotype moderated the association between self-reported maternal antenatal anxiety (Crown Crisp Index) in pregnancy, and child temperament at 6 months (Infant Temperament Questionnaire), and also later behavioral and emotional problems on the Strengths and Difficulties Questionnaire from age

4 to 13 years. **Results:** We found no evidence to suggest that the 5-HTTLPR polymorphism moderated the effects of maternal antenatal anxiety on infant temperament at 6 months or infant behavioral and emotional problems from childhood through to adolescence. **Conclusion:** Our results, based on a large prospective community sample that assessed children from infancy to early adolescence, provide a thorough test of, but no evidence for, a genetic moderation of the effects of maternal antenatal anxiety by 5-HTTLPR.

## P12 DAD MATTERS, TOO! PATERNAL DEPRIVATION DELAYS/ SUPPRESSES THE DEVELOPMENT OF CATECHOLAMINERGIC INNERVATION IN PREFRONTO-LIMBIC CIRCUITS IN AN AGE- AND REGION-SPECIFIC MANNER

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Background: Modern societies are increasingly concerned that fatherless children are at dramatically greater risk of drug and alcohol abuse, poor educational performance and criminality. Since these behavioral dysfunctions are assumed to be caused by impaired catecholaminergic neurotransmission, the aim of this study in the biparental rodent *Octodon degus* was to test the hypothesis that paternal care is critically involved in the development of catecholaminergic fiber innervation of cortical and limbic brain regions. Results: Using immunocytochemical staining against tyrosine hydroxylase (TH) to label catecholaminergic fibers two age (juvenile/P21, adult/P90) and rearing groups: 1) degus reared without father and 2) degus reared by both parents, were compared for immunoreactive fiber densities in the somatosensory cortex, orbitofrontal and prelimbic cortex, nucleus accumbens, hippocampus and the amygdala. Juvenile father-deprived animals showed significantly elevated densities of TH-immunreactive fibers in all analyzed regions, except in the orbitofrontal cortex, compared to biparentally reared animals. In the prelimbic, infralimbic and somatosensory cortices the difference between the two rearing groups was still significant in adulthood. In contrast, in the subregions of the hippocampal formation and central amygdala the elevated TH-stained fiber density observed in the juvenile father-deprived animals “normalized” until adulthood. Interestingly, the elevated TH fiber density in both nucleus accumbens subregions was reversed in adulthood, i.e. adult father-deprived animals showed strongly reduced TH fiber densities compared to biparentally reared animals. Conclusion: This study is the first to show that paternal care is critically involved in the development of catecholaminergic innervation (dopamine, noradrenaline) in the brain of the offspring. Supported by grants from the BMBF (UBICA, TRANSGEN), the German-Israeli Foundation (GIF 101/2011), the Center of Brain and Behavioral Sciences (CBBS) and the European Regional Development Fund (ERDF).

**P13 CORTICOSTERONE DURING THE POSTPARTUM PERIOD: LONG TERM IMPACT ON DAM BEHAVIOR AND CONSEQUENCES FOR THE OFFSPRING.**

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Postpartum depression (PPD) affects about 15% of new mothers, however, not much is known about the etiology of PPD or how it affects the outcome of the offspring. In the current study we used a corticosterone (CORT)-induced rodent model of PPD, which is based on the strong association between elevated cortisol levels and depression in humans, to investigate: 1) whether the effects of CORT treatment in the dam's first postpartum period would alter maternal care and depressive-like behaviors in a subsequent (second) postpartum period; and 2) whether offspring exposed to CORT during the postpartum period may be more vulnerable to adolescent stress compared to non-exposed offspring. Dams received either sesame oil (control) or CORT (40mg/kg) during their first postpartum period. Shortly after weaning, dams were mated again and their maternal care and FST-behavior was tested during their second postpartum period during which they did not receive any treatment. The CORT- or oil-exposed offspring were exposed to restraint stress for 1hr/d every other day from postnatal day 30-52 ('stressed group') or were left undisturbed ('non-stressed group'). All offspring were tested in a serious of behavioral tests in adulthood and neurogenesis levels were evaluated in the hippocampus of young adult offspring. Surprisingly, CORT-treated dams gave birth to smaller litters and spent less time immobile at the end of the second postpartum period relative to oil dams. For the offspring, results revealed that early corticosterone exposure and adolescent stress affected adult male and female offspring differently but being exposed to both stressors did not necessarily have a cumulative effect. In summary, elevated stress hormone levels during the postpartum period have a substantial influence on subsequent postpartum behavior in the dams as well as long lasting and sex-dependent consequences for the offspring.

**P14 SEX-DEPENDENT OVERWRITING OF PRENATALLY PROGRAMMED STRESS RESPONSES IN RATS WITH NEUROACTIVE STEROIDS**

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Maternal social stress exposure during pregnancy results in enhanced hypothalamo-pituitary-adrenal (HPA) axis responses to stress in the male and female adult offspring. Here we tested whether the 5α-reduced (5αR) metabolites of progesterone (allopregnanolone) and testosterone (androstandiol) can normalise HPA responses in prenatally stressed (PNS) rats. Allopregnanolone normalised ACTH responses to interleukin-1β (IL-1β; a potent activator of the HPA axis) in PNS females, but not PNS males. However, androstandiol reversed the hyperactive HPA response in PNS males. Next we measured central allopregnanolone levels as an indicator of central 5αR activity. Allopregnanolone levels were significantly lower in hypothalamic, midbrain and whole brain homogenates from male PNS rats compared with controls; however this effect was not observed in PNS females. To further examine a role for reduced capacity for central neurosteroid production in PNS rats we quantified 5αR mRNA expression by *in situ* hybridisation. In males, PNS was associated with reduced expression of 5αR mRNA in brain regions that provide excitatory drive to the HPA axis (PVN and nucleus tractus solitarii; NTS). Conversely, 5αR mRNA was significantly increased in PNS males in limbic areas that exert an inhibitory influence over HPA axis activity (medial prefrontal cortex and the dorsal part of the lateral septum). In PNS females, 5αR mRNA expression was significantly reduced compared with controls only in the NTS.

**P15 INTERACTIONS WITH THE YOUNG DECREASE OLFACTORY NEUROGENESIS AND ENHANCE MATURATION OF NEUROBLASTS IN SHEEP MOTHERS**

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Motherhood induces profound behavioral changes in mammals. In species in which neonates are mature (ungulates), maternal behavior is characterized by the establishment of

an exclusive bonding based on the learning of the young olfactory signature. This study is aimed at understanding whether olfactory neurogenesis, a supply of brain plasticity, could be a mechanism by which olfaction contribute to this learning. We addressed this question by investigating the influence of parturition and interactions with the young on neurogenesis in sheep mothers. Using bromodeoxyuridine, a marker of cell division, in combination with markers of neuronal maturation the percentage of neuroblasts and new mature neurons in the olfactory bulb (OB) was compared between groups of parturient ewes which interact or not with their lamb and virgins. The dentate gyrus (DG) was also studied as a control neurogenic structure. We observed that the post-partum period was associated with a decrease in olfactory and hippocampal neurogenesis. In the OB, the suppressive effect on neuroblasts was dependent on interactions with the young, whereas in the DG, the decrease in new mature neurons was associated with parturition. In addition, a morphological analysis measuring the dendritic arbor of neuroblasts showed that maturation of newly born neurons was enhanced by interactions with the lamb in the OB but not in the DG. Because interactions with the young involved learning of the olfactory signature of the lamb, we propose that this learning is associated with a down-regulation in olfactory neurogenesis and an enhancement of neuroblast maturation**.** Our hypothesis is that fewer new neurons decrease cell competition and enhance maturation of those new neurons selected to participate in the learning of the young odor. **Acknowledgements:** "Programme transversal INRA/Institut Pasteur N° 319", INRA/Région Centre for the grant to M. Brus and ANR Programme Blanc 2012 PLASMATBEHAV.

## P16 TEMPORAL POLAR AND ANTERIOR CINGULATE CORTICAL THINNING IN VIOLENT PSYCHOPATH OFFENDERS

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The biological and environmental factors responsible for the development and maintenance of antisocial behaviour and psychopathy constitute the purpose of study of several researches. Psychopathy is formed by a confluence of personality characteristics including manipulation, shallow affect, callousness and lack of remorse, irresponsibility, impulsivity, aggression and loss of empathy. The aim of this research was to determine whether brain regions involved in emotional processing and behavioral show structural alterations in violent psychopathic criminals. Corticometric Iterative Vertex- based Estimation of Thickness (CIVET) was used for processing structural imaging Nuclear Magnetic Resonance T1, to

detect associations between the thick cortical gray matter and total score psychopathy scale (PCL-R) on a full analysis of the cortex, in 97 violent offenders (29 classified as psychopaths and 68 classified as non psychopaths). It was found that psychopathy is associated with a highly significant decrease (FDR = 0,01) cortical thickness in the dorsal anterior cingulate cortex and the temporal pole, both cerebral regions located of the left hemisphere. These findings are consistent with different studies These results are consistent with other studies showing abnormal functioning in frontal and temporal regions in psychopathic subjects and support the hypothesis that outlines that impairments in brain regions as anterior cingulate regions and the temporal pole, could be contribute to poor empathic and emotional processing associated with psychopathic behaviour.

**P17 CHILD AGGRESSIVE BEHAVIOR, MAOA POLYMORPHISMS AND ADVERSE CAREGIVING IN THE CONTEXT OF INTERPERSONAL VIOLENCE**

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Interpersonal violence (IPV) is a serious societal problem with a high prevalence among members of the same family and across generations. Understanding how IPV can be transmitted from one generation to the next is crucial for designing interventions to prevent intergenerational transmission of violence. Strong evidence suggests that activity of the *monoamine oxidase A (MAOA)* gene modulates aggressive behavior. Interestingly, studies have shown that the low activity variant of the *MAOA-uVNTR* polymorphism (*MAOA-L)* increases the risk of antisocial behavior given early adversity. Since women exposed to IPV are likely to suffer from psychiatric disorders with subsequent impairment in parenting and their children might experience adverse caregiving we hypothesize that toddler carriers of *MAOA-L* will present high scores in externalizing behaviors —particularly those of aggressive/impulsive behaviors- if their mothers suffered IPV-related posttraumatic stress disorder (IPV-PTSD). Here, we report preliminary results from an ongoing study that involves maternal and child psychiatric assessment, parent-child interaction assessment, parent-child cortisol response to stress, and maternal fMRI. Mother-child dyads participated in a laboratory session where maternal sensitivity and child difficulty were scored during mother-child play interaction of 3-5 min (Crintenden, CARE-Index). *MAOA-u VNTR* genotyping was performed on salivary DNA collected from mothers and toddlers during the session. We found that IPV-PTSD mothers displayed less sensitive behavior and their children showed higher rates of difficult behavior. Strikingly, toddler carriers of *MAOA-L* presented high scores in externalizing behaviors only if theirs mothers suffered IPV-PTSD, while the opposite was true for toddlers' carriers of the high activity variant of *MAOA*. Our preliminary findings emphasize the relevance of GxE studies and *MAOA* genotype as a possibly useful predictor of an aggressive/impulsive endophenotype in toddlers of IPV-exposed mothers with PTSD. Work supported by grants from the SNSF NCCR-SYNAPSY, Gertrude von Meissner Foundation, Prim'Enfance, and Research Development Fund of Geneva Hospitals University

**P18 PROGESTERONE PRETREATEMENT REVEALS INHIBITORY EFFECTS OF OPIOIDS ON BEHAVIOUR IN LACTATING RATS**

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Changes in plasma progesterone levels during late pregnancy are a determining factor in the expression of maternal behaviour during lactation. Previous studies showed that mild opioidergic stimulation during late pregnancy makes lactating females more sensitive to opioidergic-induced inhibition of maternal behaviour and more willing to display hunting behaviour. Such previous behaviourally meaningful opioidergic stimulation also selectively increased serum progesterone levels. The present study tested whether progesterone treatment during late pregnancy interferes with the display of maternal behaviour and behavioural selection during lactation. In Experiment 1, rats were treated with progesterone (400 and 500 μg per day) from the 17th to 22nd day of pregnancy. The lowest progesterone dose did not interfere with pregnancy or parturition, and this dose was used in Experiments 2 and 3, in which the rats were treated with progesterone (P; subcutaneous [s.c.]) or peanut oil (O) for 5 days beginning on pregnancy day 17. On day 5 of lactation, dams were challenged with morphine (M; 1.5 mg/kg, s.c.) to yield the OM and PM groups or saline (S; s.c.) to yield the OS and PS groups. Dams were then tested for maternal care (Experiment 2) or behavioural selection with pups and cockroaches (Experiment 3). Animals treated with progesterone during late pregnancy and challenged with morphine during lactation exhibited significantly decrease in maternal behaviour in both Experiments 2 and 3. Predatory hunting was not modified by previous progesterone treatment. These results indicate that sensitivity to opioidergic-mediated inhibition of maternal behaviour is enhanced by prepartum progesterone administration. Acknowledgement: FAPESP for financial support.

**P19 MATERNAL MOTIVATION AND LACTATION ARE AFFECTED BY THE THALAMIC NEUROPEPTIDE TIP39**

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Extensive maternal caring is critically important for the survival of a newborn offspring. Still, not all components of the regulatory circuits are established yet. In this study, we describe novel neuronal pathways containing a thalamic neuropeptide that are involved in the regulation of maternal responses. We examined the activation of TIP39 neurons in the

posterior intralaminar complex of the thalamus (PIL) in mother rats with or without close contact with their pups and showed that suckling but not olfactory, visual and auditory input from pups activated TIP39 neurons in the PIL. Neurons in the PIL receive ascending information from the spinal cord and project to maternal brain centers including the preoptic area and the arcuate nucleus as shown by retrograde and anterograde tracer studies. Double labeling indicated that the thalamo-hypothalamic pathways contained TIP39. For functional analysis of the pathways, genetically modified lentivirus expressing an antagonist of the receptor of TIP39, the parathyroid hormone 2 receptor (PTH2R) was injected into the mediobasal hypothalamus of female rats, which infected cells around the injection site and made them release the PTH2R antagonist HYWY-TIP39. Plasma prolactin concentrations were measured in virus injected mothers on postpartum day 10. We observed a lower basal prolactin level and a significant reduction in suckling-induced prolactin levels in the PTH2R antagonist expressing dams. The same virus was injected into the preoptic area and conditioned place preference test was performed in virus injected mothers. The results indicated that PTH2R antagonist expressing mothers showed no preference for pup-associated chamber as did control virus injected dams suggesting reduced maternal motivation following blockade of endogenous TIP39 action. In conclusion, TIP39 neurons are ideally positioned in the PIL to convey suckling information towards maternal brain centers to regulate different maternal responses in the postpartum period. Support: OTKA K100319, Bolyai Award of the HAS.

**P20 EARLY-LIFE ENVIRONMENTAL INTERVENTION ALTERS THE MORPHOLOGY OF THE OLFACTORY BULB IN RATS**

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Neonatal handling alters maternal behavior and mother-pup relationship inducing physiological and behavioral changes. The interactions and social bonds are very important for development and odor has an essential role in different behaviors. The present study aimed to analyze the effects of neonatal handling on the number of neurons and GFAP-positive astrocytes in the olfactory bulb (OB) of male and female rats at 90 days-old. Pregnant Wistar rats were divided into: nonhandled, animals were not touched during the first 10 postnatal days; handled, animals were separated from mother and handled 1 min per day for the first 10 postnatal days. At 90 day-old rats were anesthetized and perfused. The brains were removed and processed for NeuN and GFAP immunohistochemistry. There were six animals in each group. The results were compared by a two-way ANOVA. Results showed that repeated brief mother-infant separation followed by handling decreases the NeuN-positive neurons at the glomerular [$F_{(1,20)}$=9.68], mitral [$F_{(1,20)}$=8.96] and granular layer [$F_{(1,20)}$=19.73] on the OB of female. The number of NeuN-positive neurons is not altered in

males. Handling did not alter the regional and cellular GFAP density on males and females. Neonatal handling induces long-lasting stable structural changes, reducing the number of neurons in the OB of females rats. Previous works showed that neonatal handling reduces the preference for maternal odor and, later in life, sexual behavior on female rats. Since the OB is a crucial structure for mother-pups attachment and social behaviors, the alteration in the morphology of the OB induced by the handling procedure, could be a factor for the behavioral changes observed in these animals.

## P21 RESPONSES TO CHRONIC VARIABLE STRESS IN MALE CALIFORNIA MICE (PEROMYSCUS CALIFORNICUS): INTERACTIONS WITH PATERNAL STATE

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Lactating females are hyporesponsive to stress, presumably to prevent corticosterone (CORT)-induced disruption of maternal care. Male California mice (*Peromyscus californicus*) show high levels of paternal care, especially in the week following the birth of their litter. We hypothesize that California mouse fathers show reduced physiological and endocrine responses to chronic stress in order to prevent possible detrimental effects of increased allostatic load on paternal care and, consequentially, pup development. Therefore, new California mouse fathers (NF, housed with a female cage mate and their first newborn litter) underwent a 7-day chronic variable stress paradigm (CVS, n=7), or remained in the home cage as controls (CON, n=7). Pair-bonded males (PBM, housed with a tubally ligated female) and virgin males (VM, housed with a male) served as housing controls in both CVS and CON conditions (n=6-8/group). CVS caused weight loss, increased basal plasma CORT concentrations, and increased basal expression of arginine vasopressin (AVP) mRNA in the paraventricular nucleus of the hypothalamus (PVN) in NF, PBM and VM alike. CVS did not alter novel-stressor-induced CORT release, spleen or testis mass, or basal expression of corticotropin-releasing hormone (CRH) mRNA in the PVN in any housing condition. NF had lower adrenal masses and higher thymus masses than PBM and VM under CON but not CVS conditions, suggesting that NF were less sensitive to mild “control stress” (repeated weighing and blood sampling) but not to CVS. CVS impaired paternal behavior on day 6 of the 7-day paradigm, but pups from CVS and CON fathers did not differ in weight gain, timing of developmental milestones, or basal or stress-induced CORT levels. Taken together, these results suggest that CVS affected physiological and endocrine parameters in male California mice independent of paternal state, and mildly impaired paternal care but not offspring survival or development. (Funded by NIH grant 1R21MH087806.)

## P22 PATERNAL EXPERIENCE INCREASES AROMATASE ACTIVITY IN THE MOUSE LIMBIC SYSTEM

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The neural bases of maternal care in rodents are rather well-studied while brain mechanisms of paternal care are, in general, poorly understood. In house mice, paternal care needs experience with pups [1]. Naïve males often kill or ignore pups and only become paternal after several days of exposure to pups. Estrogen injection helps to become paternal [1] and experience with pups increases estrogen receptor content in limbic brain areas [2]. Here we ask, whether aromatase activity, converting testosterone to estrogen locally in brain areas, may contribute to establish paternal behavior in mice. We used immunocytochemistry to stain and quantify aromatase-positive cells in limbic brain areas of three male groups in which paternal care was quantified via pup retrieval: naïve males (M0, no sexual experience, no pup contact), fathers co-caring for their first litter together with the mother for 5 days (M1ex5, 5 days pup exposure), fathers co-caring for their first litter until weaning and their second litter for another 5 days (M2ex5; ~27 days pup exposure). Only males with pup experience retrieved pups (0% in M0; 83% in M1ex5; 92% in M2ex5). Aromatase-positive cells increased in number in M2ex5 (partly in M1ex5) relative to M0 in the lateral septum, amygdala, piriform cortex, and ventromedial hypothalamus. No significant changes occurred in nuclei associated with maternal care, i.e., medial preoptic area, bed nucleus of stria terminalis, nucleus accumbens, however, in these areas aromatase activity was higher in the left compared to the right brain hemisphere. Increased paternal performance correlates with increased aromatase activity in brain areas regulating emotional/motivational sensory processing and learning. This suggests local estrogen to be involved in paternal brain networks different from those regulating maternal instinct (supported by the DFG EH53/19). [1] Ehret G, Koch M (1989) Ethology 80, 81-93. [2] Ehret G et al. (1993) NeuroReport 4, 1247-1250.

## P23 MODE OF DELIVERY EFFECT ON MATERNAL MOOD AND BREASTFEEDING

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As a part of a larger study to investigate the effects mode of delivery has on several aspects of attachment behaviors and mental health in Spanish women a prospective study approved by Local Ethical Committee was carried out. Women were requested to participate in the study upon arrival at the delivery room and asked to sign a consent form if they agreed to participate. 127 mothers were included: 85 had given birth vaginally (VB) and 42 by elective

caesarean section (CS). All had singleton, healthy pregnancies and new-borns were placed in skin-to-skin contact with the mother after delivery. Wish to breastfed, Apgar 5m>7 and correct understanding of language were other inclusion criteria. Patients were excluded if caesarean section was made after study inclusion or new-born was admitted in NICU. Three months after the birth mothers were contacted by telephone. Data regarding breastfeeding, maternal mood (EPDS) and trauma symptoms (Perinatal PTSD Questionnaire translated to Spanish) TEPT were collected by a midwife. 85,9% responded at three months; (n=110 mothers 73 from the VB and 37 from the CS group). **Results**: 13 women scored above the screening point of EPDS (12,0%) , 8 from the VB (11,3%) and 5 from the CS (13,5%) (p= ns). Of the 107 women who completed the Perinatal PTSD questionnaire only 2 (1,9%) scored above cut off PTSD, both in the CS group 5,4% (vs 0, % in the VB group) p=ns At three months 60,9% of mothers were exclusively breastfeeding, 23,6 % were supplemented and 15,5% were solely formula feeding. Highest rates of women were breastfeeding exclusively in the VB group (67,1%) than in the CS-group(48,6%). **Conclusions**: Maternal mood was not significantly affected by type of delivery. High rates of women breastfeeding fully or partially at three months may be related to the Baby Friendly politics of this hospital.

## P24 MELANIN CONCENTRATING HORMONE IN THE MEDIAL PREOPTIC AREA REDUCES ACTIVE COMPONENTS OF MATERNAL BEHAVIOR DURING EARLY POSTPARTUM

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The melanin-concentrating hormone (MCH) is expressed only during lactation in the medial preoptic area (mPOA), a key region in the control of maternal behavior, and this expression increases in late postpartum inversely paralleling the natural decline in maternal behavior. Therefore, MCH, acting in mPOA, could possibly modulate the maternal behavior across the postpartum period. To test this idea we evaluated maternal behavior following a bilateral infusion into the mPOA of either MCH (50 and 100 ng in 0.2 µl/side) or the same volume of vehicle during early (PPD5-6) and late (PPD14-15) postpartum, in a counterbalanced design. Early postpartum females, receiving MCH infusion into the mPOA, exhibited significant deficits in their active maternal behaviors compared to those treated with saline. In contrast, the same treatment during late postpartum did not affect maternal behavior. In addition, MCH did not affect nursing behaviors either during early or during late postpartum period. This is the first evidence showing that MCH, acting through mPOA, controls the active maternal behaviors during early but not late lactation supporting the idea that mPOA exhibits a functional change across the postpartum period. This study was supported by "Proyecto Fondo Clemente Estable" FCE_3_2011_1_5970, Agencia Nacional de Investigación e Innovación (ANII) and by the "Programa de Desarrollo de Ciencias Básicas" (PEDECIBA), Uruguay.

**P25 DISRUPTANCE OF MOTHER-PUP INTERACTION AFFECTS MATERNAL BEHAVIOUR INDEPENDENTLY OF THE SEPARATION PERIOD DURATION**

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Maternal care is essential for mammal development and maternal separation has been widely used as a model of social stress, with different outcomes in adulthood depending on the amount of time pups are separated from mothers. This differential effect may either result directly from the procedure of handling the pups, or indirectly, by influencing the mother, affecting the pattern of maternal care. In this study, we investigated the effect of neonatal interventions on maternal behaviour, in rats. 27 litters were randomly assigned to the treatments, from PDN1 to PND10: non-handled (NH) - left undisturbed with their dams; briefly handled (H) - pups were placed inside an incubator at 32° C, 10 minutes; and maternal separation (MS) – pups were placed inside an incubator at 32° C, 3 hours. Observations were performed for 1:15 h, every 3 minutes, from PND1 to PND10, twice in the dark and thrice in the light phase. The frequency of licking, nursing (high crouching, low crouching and supine posture) and mother off nest was computed. We found that both H and MS increased the licking frequency in the period after the pups are returned to their nests, but the increase in MS was stronger (MS=4.1±0.3;H=3.3±0,2;F=5.872,p=0.000). MS also increased high-crouch nursing in the two observation periods after the intervention (F=7.433,p=0.000), while nursing in general decreased in both intervention groups in first light period. In this same period, MS mothers were found to be off nest more frequently (MS=9.7±4.1;NH=4.4±3.0,F=4.325,p=0.000) and H mothers showed a similar tendency (7.1±2,2). Our data confirms that removing pups from their nests increases and changes the temporal pattern of subsequent maternal care, but suggests that differences observed in adult handled and separated rats result directly of the time the pups spend apart from their mother and are not due to differentiated effects on maternal care.

**P26 EFFECTS OF EARLY REARING ENVIRONNEMENT ON AFFILIATIVE BEHAVIOURS AND NEONATAL PHYSIOLOGY IN SHEEP**

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Attachment to the mother plays a key role in the psychobiological development of the young. Studies in primates have demonstrated that isolation- and peer-rearing in infancy results in behavioural and neuroendocrine disturbance, by contrast very little is known in non-primate species. In this study we investigated the behavioural and endocrine development of mother-reared (M), peer-reared (P), and object-reared (O) infants in sheep, known for establishing a strong mother-young bond. Observation of the general activity revealed that motherless lambs were less active than M lambs. Basal cortisol levels appeared

to be highest in O lambs and lowest in M lambs in the first two weeks after birth but differences did not reach statistical significance. When separated from the familiar partner or object in their home-pen at one week of age, M lambs were much more agitated and vocal than those from the other groups; O lambs were not reactive. After reunion, a soothing effect was recorded in M and P lambs. Similar behavioural outcomes were obtained at one month of age except that P lambs expressed a stronger distress response after separation than at one week. When tested in a novel environment with two partners or objects (familiar and alien) of the same category (ewe for Ms; lamb for Ps; object for Os), lambs spent more time near their familiar than near the alien stimulus. In all groups lambs reacted with increased vocal and locomotor activity when the familiar stimulus was removed and brought back while the alien was present. No reaction was recorded when the alien stimulus was taken away. This study suggests that i) attachment develops more rapidly with the mother than with a peer, ii) the preference for an inanimate object may not reflect affiliative behaviour, and iii) like primate infants, motherless lambs express behavioural and endocrine disturbances.

## P27 THE EFFECTS OF LITTER SIZE ON PHYSICAL, REFLEXIVE AND SEXUAL DEVELOPMENT OF WISTAR RAT PUPS

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Pups from Small litter (SL: 3 pups/dam)) and Normal litter (NL:12pups/dam) were observed daily from postnatal day (PND) 1 to 21 in order to evaluate physical, sexual and reflexive development. Body weight control was performed every 3 days and measurements of the naso-anal length (NAL) and anogenital distance index (ADI) were done on days 1, 10 and 21 of life. Eye opening, hair appearance, pinna unfolding and incisor eruption were observed in pups. The reflexes evaluated were righting, negative geotaxis, palmar grasp, auditory startle, vibrissa placing and visual placing. Testis descent and vaginal opening were evaluated following weaning. Pups from SL showed greater weight gain and increased NAL than pups from NL. ADI did not differ between groups. Pinna unfolding, hair growth and eye opening were significantly advanced in offspring from SL rats. There was no difference in time of incisor eruption between NL and SL pups. Pups from SL presented righting and negative geotaxis before the animals from NL. Palmar grasp, evaluated at ages by which this response had waned, was also advanced in SL rats. Auditory startle and vibrissa placing were first demonstrated in animals from overfed group. Only the appearance of visual placing was not significantly different between groups. As for sexual development, male offspring demonstrated the testis descent earlier, whereas females showed no differences in the day of vaginal opening. It is possible that the increased supply of breast milk accelerates physical development and the appearance of reflexes in pups due to changes in neurohormonal regulation. The mechanisms by which early overfeeding determine a permanent change in body weight regulation and lead to changes in neurohormonal regulation are not still fully elucidated and need to be further researched. **Acknowledgements:** We would like to thank CAPES and FAPEMIG for financial support.

## P28 MOUSE PUP ULTRASOUNDS ACTIVATE AUDITORY CORTICAL FIELDS DIFFERENTLY ACCORDING TO THEIR "MEANING"

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In mother mice recognition of pups is present right after having given birth, evident e.g. by selective phonotaxis to pup ultrasounds. Virgin females need more than 1 day of experience with pups to show selective phonotaxis, i.e. the discrimination of the acoustic quality of ultrasounds and preference of adequate models of pup calls [1]. On that background of perceptual data, we studied the activation of the auditory cortical fields in mothers and virgins with 1 or 5 days of pup-experience while they evaluated and responded with maternal behavior to adequate or inadequate models of pup ultrasounds. Neural activation was shown via c-FOS immunocytochemistry and quantified by counting strongly labeled cells [2] separately in 5 auditory cortical fields in the left and right brain hemisphere. We aimed to answer the following question: Does auditory cortical activation reflect the perception of the biological significance ("meaning") of pup sounds and if so, does it discriminate between instinctive (mothers) and learned (virgins) perception? We found "meaning" not to be represented in the three primary fields of the auditory cortex. The labeling pattern in the higher-order field AII (second auditory field) discriminated between instinctive and learned perception, and "meaning" was represented as a left-hemisphere dominant labeling in the higher-order field DP (dorsoposterior field) which also reflected the level of motivation to respond. We conclude, that activation in primary fields of the auditory cortex mainly reflects the acoustic properties of sounds. Activation in higher-order fields depends on "who perceives the sound", i.e. on the experience with the sounds and with the behavioral context as the basis for an adequate maternal response (supported by the DFG, EH 53/20). [1] Ehret G, Buckenmaier J (1994) J. Physiol. (Paris) 88, 315-329. [2] Geissler DB, Schmidt HS, Ehret G (2013) J. Physiol. (Paris) 107, 62-71.

## P29 MATERNAL ANTIDEPRESSANT USE ALTERS BRAIN AND BEHAVIOUR OF MALE AND FEMALE OFFSPRING

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Postpartum depression is a severe mental illness that disrupts healthy maternal care and consequently promotes early life adversity for offspring. Moreover, male offspring appear to be more sensitive to maternal distress than females. Postpartum depression can be treated with antidepressants such as fluoxetine, a selective serotonin reuptake inhibitor. However, fluoxetine can remain active in breast milk, raising serious concern in depressed mothers who breastfeed their children. Unfortunately, little is known regarding long-term developmental consequences of postpartum fluoxetine exposure. Further, it remains unknown if postpartum fluoxetine differentially affects male and female offspring. In this

study, we utilize a rodent model of postpartum depression in which dams were treated with high levels of corticosterone (CORT), to induce a depressive-like phenotype, as well as fluoxetine or saline and examined brain and behaviour alterations in adolescent and adult offspring. Specifically, we examined anxiety-like and depressive-like behaviour as well as immature neuron production in juvenile, adolescent, and adult offspring in both dorsal and ventral hippocampus. Preliminary findings indicate that maternal CORT postpartum increased anxiety-like behaviour in the elevated plus maze and that maternal fluoxetine mitigated this effect. However, maternal fluoxetine induced novelty-suppressed hypophagia in adult male, but not female, offspring. We hypothesize that male and female offspring of CORT-treated dams will exhibit a reduced number of immature neuron production throughout the developmental lifespan that will be altered with concurrent maternal fluoxetine exposure. This study will provide a better understanding of maternal depression and the consequences of its treatment as well as highlight possible sex differences in hippocampal neurogenesis and anxiety-like behaviour. Our findings will shed light on developmental trajectory of differential vulnerability between the sexes to develop neuropsychiatric illness due to maternal adversity.

**P30 PATERNAL DEPRIVATION ALTERS CORTICOTROPIN RELEASING FACTOR (CRF)- AND CALBINDIN-D28K (CABPD28K)-EXPRESSING NEURONS IN THE BED NUCLEUS OF THE STRIA TERMINALIS OF THE BIPARENTAL OCTODON DEGUS**

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While the critical role of maternal care on the development of brain and behavior of the offspring has been extensively studied, our knowledge about the importance of paternal care for brain development of his offspring is still comparatively scarce. We analyzed the impact of paternal care on the development of corticotropin-releasing factor (CRF)-expressing neurons in the bed nucleus of the stria terminalis of the biparental caviomorph rodent *Octodon degus*. CRF is a polypeptidergic hormone, which is expressed and released by a neuronal subpopulation in the brain and is essential not only for regulating stress and emotionality, but also is critically involved in cognitive functions. We found that at P21 paternal deprivation resulted in a decreased density of CRF-containing neurons in the medial but not in the lateral BNST. These deprivation-induced changes were still prominent in adulthood. The central amygdala, characterized by dense clusters of CRF-immunopositive neuropil, was not affected by paternal deprivation. The density of CaBPD28k-expressing neurons was specifically increased in the medial but not lateral BNST in three-week old father-deprived animals, similar effects were observed in the basolateral and central amygdala. In adulthood the father-deprived animals show significantly decreased density of CaBPD28k-expressing neurons in the lateral but not medial BNST. Taken together, this is the first evidence that paternal care is essentially involved in the developmental expression

pattern of an emotional and cognitive modulator system. *Supported by grants from the BMBF (UBICA, TRANSGEN), the German-Israeli Foundation (GIF 101/2011), the Center of Brain and Behavioral Sciences (CBBS) and the European Regional Development Fund (ERDF).*

## P31 ACUTE STRESS MODIFIES SOCIAL MEMORY DEFICITS IN PRENATALLY STRESSED RATS

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Prenatal stress (PNS) exposure negatively affects cognition and emotionality in rodents. PNS rats show impaired memory in object recognition and spatial learning tasks, however, to date it is not known whether PNS affects social memory. We used an ethologically relevant prenatal social stress model to investigate the effect of PNS on social memory in adult male and female rat offspring. Social memory was assessed by the rats ability to discriminate between familiar and novel same-sex juveniles: if the rat remembers encountering the familiar juvenile it will spend more time investigating the novel juvenile. There were no differences in social discrimination between control and PNS males, however, social discrimination was significantly impaired in PNS females compared with control females. This was not a result of reduced sociability in the PNS females, since control and PNS rats of both sexes showed similar behaviour in a social preference test. Moreover, impaired social memory in the PNS females seems to result from the prenatal stress exposure rather than from a variation in post-natal maternal care, as we found no differences in the maternal behaviour of stressed dams compared with controls. Next we investigated the effect of acute stress (30 min restraint) immediately prior to the social discrimination task. Following acute stress, control females were no longer able to discriminate between familiar and novel juveniles. In contrast, acute stress significantly enhanced social discrimination in the PNS females. In conclusion, prenatal stress induces social memory impairment in female PNS rats under basal conditions, whereas under acute stress conditions, social memory performance is enhanced in PNS females. This adaptation may aid PNS rats to cope under stressful conditions, however it may prove maladpative when there is a mismatch between the predicted and the actual post-natal environment. The underlying neural mechanisms remain to be elucidated.[Funding: BBSRC/BSN]

## P32 FINNBRAIN COHORT: OXYTOCIN SYSTEM, MOTHER-CHILD ATTACHMENT AND CHILD'S STRESS REACTIVITY IN THE DEVELOPING BRAIN

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**Introduction:** Altered functioning of the stress regulatory systems (e.g. HPA-axis) is one of the mechanisms through which life events and environmental factors are suggested to

associate with increased risk of later psychiatric and cardiovascular disorders. Attachment patterns, the quality of nurture, and social support are significant mediators of stress regulation. Oxytocin system of the brain may mediate the interactions between parental care, attachment and stress responses. FinnBrain Birth Cohort studies among other things the biological mechanisms that mediate the facilitative effects of mother-child attachment to the stress reactions of the child. **Objectives:** 1) Study the functioning and quality of mother's oxytocin system using the activation of the mentalisation capacity e.g. reflective functioning during pregnancy. 2) Study the development of the HPA-axis responses of the child to the physical stress during the first year of life. **Hypothesis:** Functioning of the oxytocin system of the mother during pregnancy is associated with the quality of her mentalisation capacity, which in turn may modulate the child's HPA-axis stress reactivity. **Methods:** FinnBrain Birth Cohort aiming at 5000 families includes a Focus Cohort of 500 mothers with experienced stress during pregnancy, their 500 healthy controls and 1000 children. From this group we; 1) Measure mother's oxytocin response in blood to a fetal 4D-ultrasonography with a reflective function activation during a pregnancy weeks 29-31. 2) Measure children's cortisol response patterns to a stress test with 5 saliva samples using a venipuncture as a stressor at the age of 10 weeks, 6 monts and 14 months. We are comparing the responses of the cases and controls. Study is in progress. **Acknowledgements:** FinnBrain research group for the recruitment of the families and data collecting. **Financial support:** Finnish Graduate School of Neuroscience, Finnish Cultural Foundation - Varsinais-Suomi Regional Fund, Turku University Foundation, Oy H. Lundbeck Ab and Academy of Finland.

## P33 DAD MATTERS, TOO! PATERNAL DEPRIVATION DELAYS/ SUPPRESSES DENDRITIC AND SYNAPTIC DEVELOPMENT IN THE ORBITOFRONTAL AND SOMATOSENSORY CORTEX

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Modern societies are increasingly concerned that fatherless children are at dramatically greater risk of drug and alcohol abuse, poor educational performance and criminality. The aim of this study in the biparental rodent Octodon degus was to assess the impact of paternal deprivation on neuronal and synaptic development in the orbitofrontal cortex, a prefrontal region which is essential for emotional and cognitive function. On the behavioral level the quantitative comparison of parental behaviors in biparental and single- mother families revealed that (i) degu fathers significantly participate in parental care and (ii) single-mothers do not increase their maternal care to compensate the lack of paternal care. On the brain structural level we show in three-weekold father-deprived animals that layer II/III pyramidal neurons in the orbitofrontal cortex displayed significantly lower spine densities on apical and basal dendrites. Whereas biparentally raised animals have reached adult spine density values at postnatal day 21, fatherless animals seem "to catch up" by a delayed increase of spine density until reaching similar values as biparentally raised animals in adulthood. However, in adulthood reduced apical spine numbers together with shorter

apical dendrites were observed in father-deprived animals, which indicates that dendritic growth and synapse formation (seen in biparental animals between postnatal day 21 and adulthood) were significantly suppressed. These results demonstrate that paternal deprivation delays and partly suppresses the development of orbitofrontal circuits. The retarded dendritic and synaptic development of the apical dendrites of layer II/III pyramidal neurons in the orbitofrontal cortex of adult fatherless animals may reflect a reduced excitatory connectivity of this cortical subregion. *Supported by grants from the BMBF (UBICA, TRANSGEN), the German-Israeli Foundation (GIF 101/2011), the Center of Brain and Behavioral Sciences (CBBS) and the European Regional Development Fund (ERDF).*

**P34 INFLUENCES OF AN EARLY ADVERSE SOCIAL ENVIRONMENT UPON INFANT RAT ATTACHMENT, OLFACTORY BULB AND PLASMA OXYTOCIN**

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Infant rats are sensitive to environmental events, such as maternal care and stress. Rat pups develop strong attachment to the mother, rapidly learning to identify and approach the dam through olfactory cues. We investigated the effects of the Social Instigation paradigm (SI) on pup's nest odor preference (NOP), monoamine activity in olfactory bulb (OB) and plasma oxytocin. At postpartum days 2 and 5, Wistar dams with their litters were submitted to the SI: an adult male inside a perforated tube was placed in the dam's cage with its pups for 5min. After a 5min interval, another male was introduced into the home-cage for 10min. The control group (C) was left undisturbed. At postpartum day 7, male and female pups were tested for NOP in a two-odor choice between the areas with nest or fresh bedding. The siblings had their motor skills evaluated. Immediately after the NOP, pups were decapitated to collect the OBs and trunk blood. Serotonin, dopamine, noradrenaline and their metabolites were analyzed by HPLC-ED; plasma oxytocin was analyzed by ELISA. Results showed no difference among the groups on NOP; however, SI pups spent less time in contact with nest bedding compared to C. There were no differences on motor skills among the groups as well as no differences on monoamine activity in OBs. SI pups showed decreased plasma oxytocin levels, and females showed lower levels compared to males. Our results showed that SI has not altered the odor preference or OB function. However, regardless of motor development, SI pups crawled less to reach the nest bedding, spending less time in contact with it, which may be associated to the decreased plasma oxytocin - hormone related to affiliation and attachment. We suggest that SI pups may have impairment in systems related to the motivation and reward of pup-mother approach.

**P35 INVOLVEMENT OF THE INFRALIMBIC MEDIAL PREFRONTAL CORTEX IN THE REGULATION OF STRESS RESPONSIVENESS DURING EARLY LACTATION**

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The prelimbic and infralimbic (IL) portion of the medial prefrontal cortex (mPFC) are differentially involved in the regulation of the HPA axis response to psychogenic stressors and maternal responsiveness to pups in early (EL) versus late lactation. Although, the mPFC IL seems to be actively engaged in maternal behaviour particularly in EL, its involvement in the processing of stressor salience and HPA responses during EL is still unclear. Here, we investigated the role of mPFC IL activation in the regulation of the stress response to salient emotional stimuli in EL. Pregnant and virgin rats were equipped with a bilateral guide cannula aimed at the mPFC IL on gestation day 15 and a jugular vein catheter on lactation day (LD) 2 (equivalent in virgins). On LD4, pups either stayed with (+) or were removed from the dam (-) during the testing period. Females were left undisturbed for 90min before taking a basal blood sample prior to intra IL injection of saline or the local anesthetic bupivacaine (BUP) (0.75%; 0.5µl/side/2min). Ten min later, all rats were subjected to a 30min exposure to ferret odor. Additional blood samples were taken 15, 30, 60 and 90min after stress onset and analysed for ACTH and CORT. Whereas saline treated EL(+) animals produced a similar ACTH response to virgins after the pup-threatening stressor, BUP treatment significantly reduced this response in both groups. In EL (-) animals CORT response to ferret odor was blunted and BUP treatment had no effect on CORT secretion, suggesting a lack of engagement of the mPFC IL in this stressor when the pups were absent and salience of the stimulus was reduced. These findings indicate that the mPFC IL plays an important role in the appropriate processing of emotional information and stimulus salience in virgins and EL(+) mothers, but that removal of pups during testing might disengage this structure and reduce HPA activation in EL females. Supported by CIHR grant to CDW and BW

**P36 REPRODUCTIVE STATE AFFECTS SHORT-TERM CELL SURVIVAL AND SEROTONERGIC CAPACITY IN SUBREGIONS OF THE DORSAL RAPHE**

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The peripartum brain undergoes profound neural modifications that underlie postpartum socioemotional behaviours. Postpartum rats show increased maternal caregiving behaviours, increased aggression, and reduced anxiety-related behaviours compared to nulliparous females. We hypothesize that peripartum modifications in the dorsal raphe (DR), the main source of serotonin in the brain, help promote these changes. To begin investigating this, we here determined the influence of reproductive state on: 1) the numbers of proliferating and short-term surviving cells in the DR and 2) optical densities of cells in the DR containing immunoreactivity for serotonin and for tryptophan hydroxylase 2 (TPH2, the rate-limiting enzyme for serotonin synthesis). We found that reproductive state

affects cell survival in the dorsal raphe in a subregion-specific manner and independently of proliferation. New cells in the lateral wings of the DR were less likely to survive if they were born during the early postpartum period than if they were born at the end of pregnancy. Because neurons of the lateral wings inhibit serotonergic output of the DR as a whole, this reduction in cell survival could promote the increased serotonergic function seen in postpartum females. If so, changes in serotonin and TPH2 immunoreactivity would also be subregion specific. Indeed, preliminary data reveal that while immunoreactivity for serotonin and TPH2 is higher for postpartum than virgin rats in the dorsal subregion of the DR, there is no such difference in the lateral wings. Given the DR's extensive efferents, peripartum plasticity involving survival of new cells and changes in serotonergic activity could contribute to the physiological and behavioral changes accompanying motherhood.

**P37 MUSICAL ENVIRONMENTAL ENRICHMENT – EFFECTS IN NEWBORN RATS DEVELOPMENT**

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The positive effects of enriched environment in neurorehabilitation are well-known. Among others, enrichment reduces the extent of ischemic and traumatic injuries. Previously, we have shown that exposing rats to environmental enrichment can reduce the extent of retinal toxic or ischemic damage. The effects of musical enrichment are much less known and there are no data about the effects of musical enrichment on early neurobehavioral development. Therefore, our aim was to investigate whether musical enriched environment has any effects on the neurobehavioral development of newborn rats. We used two types of musical enrichment: classic and heavy-metal music from 6PM till 6AM daily. Animals were tested daily for their neurobehavioral development: eye opening, incisor eruption, negative geotaxis, and some reflex performances: placing, grasping, crossed extensor, sensory reflexes. Our results show that musical enriched environment has slight effects on the normal development. We found slight differences between the two music groups: the heavy-metal group showed appearance of some reflexes earlier than the classic one. This finding could show that metal music could be a stress factor, accelerating somatic and reflex development. However, as shown with other stressors, this accelerated development has harmful consequences on brain morphology and biochemistry. In our preliminary histological examination of the brain we found differences in myelination and number of oligodendrocytes of the corpus callosum. These results show that musical environmental factors only slightly influence the early somatic and reflex development. Our preliminary results show that it can affect the myelination of the brain. We plan to make further examination with CNS injuries to investigate whether it has similar positive effects we previously found in complex enriched environment after CNS injury. We hope that our results could be bridge between the rehabilitation, clinical practice and basic science in the future.

**P38 RAISING PUPS REDUCES ANXIETY AND DEPRESSIVE-LIKE BEHAVIORS WHILE INCREASING OBJECT MEMORY IN MALE CALIFORNIA MICE (*PEROMYSCUS CALIFORNICUS*)**

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Paternal care of offspring is seen in relatively few mammalian species. One such species is the California mouse (*Peromyscus californicus*), which participates in almost every aspect of parenting, except nursing young. Little is understood about how paternal experiences shape the brain, specifically the hippocampus, which mediates behaviors important for parental care (ex. anxiety-like, object recognition, depressive-like behaviors). Paternal experience reduces adult hippocampal neurogenesis in the California mouse (Glasper et al., 2011); however, the effects of reduced adult neurogenesis on hippocampal-related behaviors are unclear and should be further explored. Given this, we investigated the effects of varied paternal experience on dentate-gyrus mediated behaviors (object recognition and emotional regulation) in this species. A behavioral battery of tests (open field, novel object recognition, elevated plus maze, and the Porsolt forced swim task) was employed after the birth of pups in two groups 1) fathers that participated in raising their offspring (intact), and 2) fathers that were permanently separated from offspring on postnatal day 1 (P1; separated). Our results suggest that California mouse fathers who were separated from their offspring on P1 display more anxiety-like behavior in the open field (decreased central tendency) and during the elevated plus maze (increased closed arm duration) compared to intact fathers. Separated fathers also demonstrated reduced object recognition (equal familiar and novel object exploration) compared to intact fathers. Finally, separated fathers exhibited more depressive-like symptoms during the forced swim task (shorter latency to first immobility, longer durations of immobility) compared to intact fathers. Despite a reduction in hippocampal adult neurogenesis, paternal experience in California mice may exert positive, or protective, effects on dentate-gyrus mediated behaviors. This raises the question of whether other forms of experience-induced plasticity may be altered in California mouse fathers. **Acknowledgments:** We thank Robyn Harper for her contributions in behavioral testing.

**P39 DETERMINATION OF RECEPTORS EXPRESSED IN GONADOTROPIN-RELEASING HORMONE AND KNDY (KISSPEPTIN/NEUROKININ B/DYNORPHIN) NEURONS IN RAT**

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Kisspeptin is considered as a principal regulator of animal reproduction via stimulation of gonadotropin-releasing hormone (GnRH) secretion. Accumulating evidence suggests that kisspeptin neurons in the anteroventral periventricular nucleus (AVPV) are responsible for

GnRH surge generation, while kisspeptin neurons in the arcuate nucleus (ARC) is involved in GnRH pulse generation. ARC kisspeptin neurons are referred to as KNDy (kisspeptin/neurokinin B/dynorphin) neurons, in which neurokinin B (NKB) and dynorphin (Dyn) may play a stimulatory and inhibitory role in the GnRH pulse generation. The present study aims to determine possible action sites of the NKB, Dyn and kisspeptin by determining their receptor expressions in GnRH, KNDy and AVPV kisspeptin neurons. GnRH neurons were collected from adult GnRH-GFP transgenic rats. ARC and AVPV kisspeptin neurons were collected from Kiss1-tdTomato knock-in rats. Expressions of mRNA of *Gnrh, Gpr54 (kisspeptin receptor gene), Tacr3 (NKB receptor gene), Oprk1 (Dyn receptor Gene), Kiss1, Tac2 (NKB gene)* and *Pdyn (Dyn gene)* were determined in GnRH and kisspeptin neurons by RT-PCR. GnRH neurons expressed *Gnrh* and *Gpr54* mRNA, but not *Tacr3* or *Oprk1*. ARC kisspeptin (KNDy) neurons showed *Kiss1, Tac2, Pdyn* and *Tacr3* expressions, but not *Gpr54* nor *Oprk1*. AVPV kisspeptin neurons expressed only *kiss1* gene among the genes determined. All the genes were expressed in the whole hypothalamic tissue. These results suggest the following mechanism regulating GnRH release. NKB produced in KNDy neurons directly acts on the neurons themselves. Dyn acts on adjacent non-KNDy neurons. The two neuropeptides orchestrate KNDy neuron activity to generate GnRH pulses. Kisspeptin released from ARC KNDy neurons and/or AVPV kisspeptin neurons is a final output, which directly stimulates GnRH release through GPR54 on GnRH neurons. This study was supported in part by Research Program on Innovative Technologies for Animal Breeding, Reproduction and Vaccine Development (to H.T).

**P40 EFFECTS OF CAFETERIA DIET ON MATERNAL BEHAVIOR OF WISTAR RATS**

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In rats, alterations in mother behavioral patterns can lead negative effects on neuroendocrine and behavioral pup development. The present study aimed to evaluate the effects of cafeteria diet on Wistar females maternal behavior responses. Wistar rats newly weaned (n=30) were divided into Control (free access to standard chow and water) and Cafeteria groups (free access to water, soft drink, and standard chow plus palatable hypercaloric food). After 10 weeks, each female were fertilized by sexually active males. Their respective diets were maintained during pregnancy and lactation. The number of pups was culled to 8 per dam and maternal behavior registering were performed daily, 4 times a day (3 in light cycle and 1 in dark one) from 1-10 days after pups birth, when were obtained the frequencies of nursing, nest building, licking pup's body and permanency at the nest. After pups weaning the dams had evaluated their body weight, visceral fat content and serum insulin and leptin levels were measured by ELISA. For all evaluations was performed t test, significance level of $P<0,05$ and results were expressed as mean ± SEM. Cafeteria group mothers showed increased visceral fat weight (8.1 ± 1.1g N=9 vs 4.6 ± 0,6g N=10) and increased serum levels of insulin and leptin (5.9 ± 0,5ng/mL N= 7 vs 2,7 ± 0,5ng/mL N= 8 and 253.4 ±18.5pg/mL N=7 vs 154±13.9 N=8, respectively). Cafeteria group also showed increased frequencies of permanency at the nest and licking (682.3 ± 27.7 N=9 vs 593.9 ± 25.3 N=10 and 117.1 ± 5.8 N=9 vs 81.3 ±4.4 N=10, respectively). In conclusion, a hypercaloric diet before and during pregnancy and lactation results in changes on maternal behavior

patterns in association to increased visceral fat content, insulin and leptin serum levels. Acknowledgements: We would like to thank the CNPq for financial support.

## P41 VARIATION IN THE OXYTOCIN GENE POLYMORPHISM RS 2740210 INTERACTS WITH EARLY ADVERSITY TO PREDICT BREASTFEEDING DURATION AND DEPRESSION

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Breastfeeding and lactation are central components of caregiving in all mammalian species. Large variation in the duration of breastfeeding exists; these individual differences are affected by maternal mood, individual differences in the functioning of relevant neurotransmitter systems and the genetic makeup. Little is known about the roles of oxytocin genes, specifically the oxytocin peptide gene (*OXT*) and the *OXT* receptor gene (*OXTR*), in breastfeeding. We studied single nucleotide polymorphisms (SNPs) in *OXT* (*rs2740210* and *rs4813627*) and *OXTR* (*rs237885*) in 280 mothers. *OXT rs2740210* was significantly associated with exclusive breastfeeding at 3 and 6 months and any breastfeeding at 12 months postpartum. Larger proportions of mothers with the *AA/AC* genotypes than mothers with the *CC* genotype engaged in breastfeeding at these time points. This SNP also interacted with early life adversity (measured by the Childhood Trauma Questionnaire) to predict variation in weeks of breastfeeding and depression (measured by the Center for Epidemiologic Studies Depression Scale) throughout 12 months postpartum. A full mediation model showed that depression mediates the effect of early life adversity on breastfeeding duration; a subsequent moderated mediation model showed that this mediation occurred only in women possessing the *CC* genotype of the *OXT rs2740210* SNP, but not in women with the *AA/AC* genotype. There were no effects of genetic variation in *OXT rs4813627* and *OXTR rs237885*. The findings show that the extent to which mothers' early adversity affects their postpartum mood and breastfeeding behavior depends on the variation at *OXT* rs2740210. Acknowledgements: We would like to thank Patricia Szymkow, Carmen MacPherson and the entire Hamilton team, and also Natalie Freeman, Maria Tampakeras and their team for assistance with genotyping. We also would like to thank Melissa Rourke for her initial work on this topic.

## P42 PRENATAL STRESS AND INFANT BRAIN EMOTION SYSTEM MATURATION – THE FINNBRAIN BIRTH COHORT STUDY

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**Background:** Early life stress influences child neurodevelopment. Less is known about the mechanisms of how the environment shapes the brain and how neurodevelopmental trajectories are linked with child health outcomes. We will investigate the effects of parental prenatal stress on the infant brain emotion processing systems and the role of immune activation in the process. **Hypotheses:** We expect that maternal prenatal stress is associated with 1. Maternal and infant immune activation, 2. Infant brain morphology in cortico-limbic networks, and 3. Infant responses to negative auditory emotional stimuli. 4. Paternal prenatal stress affects the infant outcomes both independently and via maternal stress. **Method:** *The study population* is from a Focus Cohort (aim n=500 + 500 families) within the FinnBrain Birth Cohort Study (www.finnbrain.fi), a multidisciplinary neurodevelopmental general population longitudinal study (aim N=6000 families). Consecutive pregnant women and their spouses are personally recruited by a research nurse at their first trimester ultra sound (gestational week, gwk 12). Questionnaires and DNA blood sample are included. *The case-control-based Focus Cohort* is identified from self-report questionnaires on pregnancy-related anxiety (PRAQ-R) and depression (EPDS). *Brain imaging* is performed for 200 + 200 infants by using 3.0T magnetic resonance imaging (MRI) including diffusion tensor imaging (DTI) sequences at the age of 4 weeks. Near-infrared spectroscopy (NIRS) is performed in response to emotional auditory stimuli at the age of 8 weeks. *Immune activation* is measured from repeated cytokine profile assessments of parental pre- and postnatal blood samples and infant (< 12months) blood samples. Gut microbiota analyses are conducted from repeated feces samples of mothers and infants (< 12 months). **Results:** Pilot data shows that the study protocol is feasible to be carried out. Individual methods have been tested and validated. Baseline subject recruitment is ongoing and will be taking place until the end of the year 2014.

**P43 NUCLEUS ACCUMBENS OXYTOCIN RECEPTOR REGULATES PARENTAL BEHAVIOR IN MALE AND FEMALE PRAIRIE VOLES WHICH IMPACTS THE DEVELOPMENT OF ADULT SOCIAL ATTACHMENT IN THE OFFSPRING: A GENE MANIPULATION STUDY**

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Psychiatric disorders result from an interaction of genetic and environmental factors. Oxytocin signaling plays a critical role in the regulation of parental nurturing and parent-infant bonding. Parental nurturing and mother-infant bonding may be important contributing factors in the development of emotional and social behaviors in the offspring. We used both shRNA knockdown and natural variation in striatal oxytocin receptor (OXTR) expression to explore (1) the role of OXTR on the expression of parental behavior in the socially monogamous prairie vole and (2) the impact of variation in parenting on later-life social attachments in the offspring. OXTR was decreased in the nucleus accumbens (NAcc) of 21 day old male and female prairie voles using a viral vector expressing a shRNA targeting Oxtr mRNA. At 60 days of age experimental animals were paired with an unmanipulated mate. Dams and sires with OXTR knockdown were assessed for parental behavior and offspring were evaluated for their ability to form a social attachment in adulthood. Animals receiving shRNA displayed less parental care (females: licking and grooming $p=0.026$, retrieving $p=0.037$; males: licking and grooming, $p=0.695$, retrieving $p=0.008$) than scrambled injected controls. Further, we found that adult female offspring with naturally low OXTR binding in the NAcc born to OXTR knockdown dams did not display mating-induced partner preferences in adulthood ($p=0.249$) while female offspring with naturally high OXTR binding in the NAcc did ($p=0.007$) following a 24hr cohabitation with a partner. This phenomenon was not observed in male offspring who were not affected by parental treatment. This suggests that females with low OXTR binding in the NAcc are vulnerable to variation in maternal nurturing behavior while high OXTR binding in the NAcc buffers against variation in early nurturing experience. These findings parallel human studies suggesting that a polymorphism in OXTR confers susceptibility for females to develop depression and anxiety but only if the genotype is associated with early life adversity.

**P44 LACK OF SEX STEROID HORMONES, BUT NOT SOCIAL ISOLATION, DURING PUBERTY AFFECTS MATERNAL BEHAVIOR IN ADULT FEMALE MICE**

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At the time of birth, female rodents ensure the survival of their offspring with the display of maternal behaviors (pup retrieval, licking, nursing). Nulliparous rats and mice can also show

maternal behavior when presented with pups. Unlike rats, female mice of many strains show faster spontaneous maternal responses to pups, suggesting that the expression of maternal behavior in mice is less dependent on hormonal mediation than in rats. The presence or absence of gonads in adulthood has previously been shown to make little difference in the absolute expression of parental behavior in mice of both sexes, although gonadectomy can increase pup-retrieving behavior. Housing conditions also represents an important environmental variable, especially as mice are naturally social animals. Social stress can profoundly and persistently affects brain development, which results in altered behavioral responses in adulthood. In the present study, the influences of sex steroid hormones and social stress during adolescent period on maternal behavior in adult female mice were assessed. C57BL/6J mice were divided into four groups: socially isolated or group housed, ovariectomized before (on day 25) or after puberty (on day 60). After day 75, mice were tested for maternal behavior to assess the influence of sex steroid hormones and social isolation during puberty. Results show that ovarian hormones during puberty are important for the expression of maternal behavior in adult female mice. Mice ovariectomized after puberty showed better maternal behavior (latency to pick up pups, the number of retrieved pups, latency to retrieve single/all pups into the nest, crouching over pups) than those ovariectomized before puberty. However, social isolation during puberty did not affect maternal behavior in adult females regardless of the time of gonadectomy. The results suggest that exposure to gonadal hormones during puberty is important for the expression of maternal behavior in inexperienced nulliparous female mice. *Keywords:* female mice; puberty, ovariectomy; social stress, social isolation; maternal behavior.

**P45 EFFECTS OF CHRONICLE CENTRAL INSULIN INFUSION DURING LACTATION ON MATERNAL FOOD INTAKE AND PUP GROWTH**

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The postpartum period represents perhaps the most energetically demanding stage of the life of a female mammal. Several metabolic and neural changes take place on the mother during pregnancy and lactation that allows the successfully rearing of the young. Research on functions and signaling pathways of insulin during pregnancy and lactation has traditionally focused on peripheral tissues. Since the discovery more than 30 years ago of insulin receptor on the CNS, a substantial number of studies have been conducted to explore insulin effects on the brain. However, despite the large amount of data reporting the effects of maternity on the brain, whether changes on insulin brain content and/or signalling plays a role on maternal physiological and behavioral adaptations to pregnancy and lactation it remains a question. Therefore, the present study aimed to investigate the effects of chronicle central insulin infusion during lactation on maternal food intake and pup growth.

Female Wistar rats were mated. Around pregnancy day 22, rats delivered naturally. One day after parturition (postnatal day-PND1) rats underwent surgery for cannula placement in the lateral ventricle. Osmotic pumps delivered either saline (Control group, n=10) or 10mU of insulin (Insulin group, n=10) per day at a rate of 0.5µl/hour from PND 1 to 14. Maternal BW and and food intake and litter BW were recorded daily during lactation. Rats were submitted to glucose and insulin tolerance test during lactation. There was a trend towards reduced maternal food intake during lactation on Insulin rats. Offspring from Insulin rats gained less weight during lactation than offspring of Controls. There were no differences regarding maternal body weight change during lactation or insulin and glucose tolerance tests. In conclusion, chronicle central insulin infusion during lactation reduced maternal food intake during lactation resulting in reduced growth rate of the offspring.

## P46 GENE X ENVIRONMENT INTERACTION AND EPIGENETICS IN CDH13 KO MICE, A MOUSE MODEL FOR ANXIETY AND DEPRESSION

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Our body and brain is not only responding to stressful events, but they are also adapting in order to survive in harsh and highly dangerous environments. An early life predictor of future adversities is the amount and quality of maternal care received during rearing. As a part of the adaptation during this period, long term changes in neuronal connectivity, survival and molecular composition are made within the brain. An interesting new genetic factor we would like to investigate in this context is CDH13, a member of a the calcium dependent cell adhesion protein family, which has been shown to be up regulated due to chronic stress in rodent models. Cadherins are important molecules for tissue formation, proper cell adhesion and neuronal growth. With this project, we hope to get a better insight into the function of CDH13 in the development of early life stress related disorders and vulnerabilities. On a molecular level, we will investigate methylation, RNA and protein expression changes.

## P47 REDUCED CRF RECEPTOR ACTIVATION IN THE POSTERIOR BNST IS CRUCIAL FOR APPROPRIATE EXPRESSION OF MATERNAL BEHAVIOUR IN LACTATING RATS

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The bed nucleus of the stria terminalis (BNST) contains various neuropeptidergic systems that regulate complex social behaviours, e.g. maternal behaviour. Here, we aimed to

characterize the involvement of the local corticotropin-releasing factor (CRF) system in maternal behaviour and anxiety in lactating rats. We assessed CRF receptor (CRF-R) mRNA distribution in virgin versus lactating rats. Further, we manipulated CRF-R1 and -R2 within the posterior BNST (pBNST) by local injection of specifics agonists or antagonists, and measured maternal care in the homecage, maternal aggression in the maternal defence test, and anxiety-related behaviour on the elevated plus-maze. Finally, repeated blood samples were taken under basal conditions to assess any possible effects on the hypothalamo-pituitary-adrenal axis. CRF-R1 or -R2 mRNA expression did not differ between virgin and lactating rats. However, CRF-R2 mRNA was more abundant in the pBNST than the medial BNST. Intra-pBNST injection of both CRF-R1 and -R2 agonists impaired maternal care. The antagonists had no effect under basal conditions. Following a strong psycho-social stressor, i.e. the maternal defence test, maternal care was impaired in the vehicle and agonist-treated dams while both antagonists prevented this stress-induced decrease. Moreover, the CRF-R2 antagonist increased arched back nursing after stress. During maternal defence, the CRF-R2 agonist and antagonist abolished and increased maternal aggression, respectively. Regarding anxiety, the CRF-R1 agonist was anxiogenic whereas both antagonists were anxiolytic, which could be extended to virgin females. Neither CRF-R2 manipulation in the pBNST altered basal plasma levels of ACTH or corticosterone. In conclusion, CRF-R activation (e.g. following stressor exposure) impairs maternal behaviour. In the pBNST of lactating rats, these detrimental effects are dominantly mediated via CRF-R2. Moreover, CRF-R1 and, contrary to findings in males, also CRF-R2 regulate anxiety in females independent of their reproductive status.

## P48 MATERNAL HIGH FAT NUTRITION: IMPACT ON MATERNAL BEHAVIOUR AND OFFSPRING DEVELOPMENT

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The present study aimed to evaluate the impact of maternal high fat nutrition on maternal behaviour and offspring physical and sexual development. Pregnant female Wistar rats were assigned either to: high fat group (HF, 45% fat diet from day 0 of pregnancy to day 21 of lactation; n=4) or control group (standard diet - 4% fat, during the same period; n=7). Maternal behavior was analyzed on postnatal day (PND) 5 and 10. On the test day, all pups were removed from the home cage and the nest was destroyed. After 30 minutes, the pups were returned to the cage and mother-pup interaction was recorded for 30 min. Pup retrieval latencies, pup grooming, self grooming, total time of crouching, total time off pups, and nest building were observed. Rats were scored as fully maternal if they retrieved all pups to the nest and nursed them for 3 consecutive minutes. Maternal food intake and body weight were followed througth pregnancy and lactation. Offspring physical and sexual

development and body weight were observed daily. Body length and anogenital distance were obtained on PND 1 and 21. HF mothers spent more time off the nest, more time on self grooming and had more pup contacts than controls. As expected, there was a significant effect of time on both maternal food intake and body weight gain during pregnancy and lactation but there were no differences between groups. Body weight was increased on offpsring of HF rats during lactation. Vaginal oppening was delayed on HF female offspring. Body length and anogenital distance increased over time on both groups. In conclusion, maternal high fat diet increased offspring body weight and delayed puberty on female offspring. Although maternal high fat nutrition altered some aspects of maternal behaviour, it did not compromise overall maternal care. **Support:** FAPESP (2012/07378-6).

## P49 THE CORTISOL AWAKENING RESPONSE, RESTING BLOOD PRESSURE AND QUANTITATIVE DNA METHYLATION OF GENES (*OXTR, BDNF*) ASSOCIATED WITH BONDING

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Epigenetic marks are considered indicators for a connection between environmental stimuli as early bonding experiences and stress related diseases. To investigate if quantitative DNA methylation in genes related to stress-protection and parenting (i.e. the oxytocin receptor (*OXTR*) and brain-derived neurotrophic factor (*BDNF*)) is associated with other biomarkers of stress load, we examined correlations with the cortisol awakening response (CAR) and resting blood pressure. The cross sectional study took place at the Division of Clinical and Physiological Psychology, University of Trier, Germany. We included 83 participants (aged 61–67 years), from which 76 participants completed the full study protocol, including measures of blood pressure as well as blood and saliva sampling to assess DNA methylation, the CAR, and effects of dexamethasone on the CAR. We assessed quantitative DNA methylation of whole-blood cells using Sequenom EpiTYPER. DNA methylation of the *OXTR* was negatively associated with the CAR and positively with resting blood pressure. There were no constant associations with DNA methylation of *BDNF*. The results suggest that DNA methylation of genes as *OXTR*, known to be involved in social interaction and especially parenting, are related to physiological indicators of stress load. The findings may contribute to a better understanding of the relation between environmental experiences and stress protection and stress vulnerability.

**P50 INFLUENCE OF NEONATAL INTERVENTION ON THE PROCESS OF MEMORY EXTINCTION IN ADULT ANIMALS**

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Sensory experiences in early life can affect neural development and behavior of an adult animal. Both the handling and the separation are considered neonatal stressful stimuli. Neonatal handling in rats is the "manipulation" of the pups for a few minutes in the first two weeks of life, when the pups are separated from their mothers during the day, while the separation is the separation of offspring from the mother for longer periods. Memories are modulated by emotions, being difficult to acquire memories without a minimum state of alert. Thus, stress shows up as an important regulator of memory processes, having different actions in acute and chronic activity. The aim of this study was to determine whether the handling and maternal separation in the neonatal period alters the persistence of extinction of an aversive and an appetitive memory. Three months after the neonatal intervention, behavioral tests were performed to observe the memory in rats, using the task of contextual fear conditioning, as aversive stimulus, and social transmission of food preference, as appetitive stimulus. We observe from the tasks performed in this work that the control group showed a similar and an expected behavior in both types of task. They expressed significant learning on both tasks, efficient extinction and spontaneous recovery of the original memory after two weeks. The manipulated expressed learning in both tasks, and a very efficient extinction, as there was no spontaneous recovery in both, the aversive and the appetitive tasks. The separate behaved similarly to the control in the aversive task, also demonstrated learning, extinguishing efficiently and presenting spontaneous recovery. They also learned the appetitive task, however, the extinction process was not efficient as the controls. Neonatal interventions, such as neonatal handling and separation, can influence the persistence of extinction of aversive and appetitive memories in adult animals.

**P51 PATERNAL DEPRIVATION INDUCES ELEVATED ANXIETY IN THE PRECOCIAL RODENT OCTODON DEGUS**

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Human studies revealed that the absence of the father in the family results in socio-emotional impairments in the developing child. *Octodon Degus* provide an ideal animal model to systematically investigate the impact of paternal care on the development of brain and behavior. Degus live in complex family structures, in which degu fathers significantly invest in the upbringing of their offspring. We have shown that after the removal of her “husband” single degu mothers do not compensate for the absent father by increasing maternal care, thus, a fatherless family represents a socio-emotional impoverished environment, which allows to study brain structural alterations as well as the emergence of

behavioral dysfunctions. The questions addressed in the current study are: can the father be substituted by another female caregiver and thereby "protect" the offspring from behavioral and brain functional alterations and are there sex-specific effects in response to paternal deprivation? The emotionality was compared in three experimental groups: degus raised (1) by a single mother, (2) by mother and father and (3) by their mother and a foster mother ("aunt"). Adolescent degus of both sexes raised without father or with a foster mother displayed elevated anxiety. These data indicate, that a foster mother cannot replace the father and thus cannot not "protect" the offspring from behavioral changes. *Supported by grants from the BMBF (UBICA, TRANSGEN), the German-Israeli Foundation (GIF 101/2011), the Center of Brain and Behavioral Sciences (CBBS) and the European Regional Development Fund (ERDF)*

**P52 COOPERATIVE INFANT CALMING RESPONSE DURING MATERNAL CARRYING**

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Mother-infant relationship is critical for well being and development of mammalian infants. To promote this bond, infants have innate behaviours to seek maternal proximity and protest upon separation. However, the physiological mechanisms regulating these infant behaviour require further investigations. Here we present a novel infant cooperative response during maternal carrying. Infants under six months of age carried by a walking mother immediately stop voluntary movement and distress vocalization, compared with holding by a sitting mother, and infant heart rate rapidly decreased after the mother started walking. Furthermore, a strikingly similar response has been found in mouse preweaning pups, defined by immobility and diminished ultrasonic vocalizations and heart rate. Using pharmacologic and genetic interventions in mouse pups, we identified the upstream and downstream neural systems regulating the calming response. Somatosensory and proprioceptive input signalling are required for induction, and parasympathetic and cerebellar functions mediate cardiac and motor output, respectively. The loss of calming response hindered the maternal rescue of distressed pups, suggesting a functional significance for the identified calming response. These results demonstrate that the infant calming response to maternal carrying is a coordinated set of central, motor and cardiac regulations, and is a conserved component of mammalian mother-infant interactions. The possible clinical applications will be discussed, including (i) using the carrying test to assess the infants' autonomic nerve responsivity, which may contribute to early diagnosis and prognosis of perinatal brain damage; (ii) screening for abnormal sensory integration as an early biomarker of autism spectrum disorders. These findings may also impact current parenting theory and practice, since unsoothable crying is the major risk factor for child abuse.

**P53 EXPOSURE TO PRENATAL SMOKING AND THE EARLY REFLEX AND MOTOR DEVELOPMENT OF RAT PUPS**

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**Aims**: Maternal smoking can affect the developing fetus, which results in delayed cognitive and motor development, retarded locomotor behavior. An increase in the incidence of psychological abnormalities has also been reported. Our aim was to investigate the influence of maternal smoking during pregnancy on early neurobehavioral development of newborn rat pups. **Methods**: Wistar rats were exposed to whole-body smoke exposure for 40 minutes daily from the mating until delivery, except for the control group. After delivery, animals were divided into 4 groups: gestational smoker rat mothers (M+) with pups who were exposed to smoke prenatally (P+) and control pups (P-); gestational non-smoker rat mothers (M-) with pups who were exposed to smoke prenatally (P+) and control pups (P-). The offspring were tested for somatic and neurobehavioral development daily for 21 days. On the 4th and 5th weeks a motor-coordination (footfault) test was carried out. Data were compared to that of the control group by using ANOVA test. **Results**: Our results showed significant differences between the data of group P+ vs. P-, independently of the raising mother. Some parameters like eye-opening, ear unfold, incisor eruption, ear twitch, acoustic startle reflex appeared earlier in P+ than P-. On the other hand, we observed a delay in the development of some other reflexes, like crossed extensor reflex, air righting and hind limb placing. In the motor-coordination test there were no differences between the groups. **Conclusion**: We have previously described dramatic delays in the neurobehavioral development of severe perinatal conditions, like asphyxia and neonatal hypoxia. Based on the present findings, maternal smoking during pregnancy does not lead to such marked changes in the neurological maturation of rat pups. However, to determine whether it has long-term vulnerability in certain lesions awaits further investigation. **Acknowledgement**: OTKA K104984, TAMOP (4.2.1.B-10/2/KONV-2010-002, 4.2.2.B-10/1-2010-0029, 4.2.2.A-11/1/KONV-2012-0024), Arimura Foundation, PTE-MTA “Lendület” Program.

**P54 MEDIATORS AND MODERATORS OF THE ASSOCIATION BETWEEN PATERNAL DEPRESSION IN THE POSTNATAL PERIOD AND CHILD DEVELOPMENT**

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**AIMS:** We investigate whether the association between depression in fathers during the postnatal period and subsequent children behaviour may be mediated or moderated by different factors. **METHODS: Subjects:** The Avon Longitudinal Study of Parents and Children

(ALSPAC) is a longitudinal cohort study on a large population sample of children and their parents from early pregnancy through childhood. Questionnaires were sent to mothers and fathers at regular points during and after pregnancy. **Measures:** Edinburgh postnatal *depression* scale (EPDS) was used to assess fathers at 8 weeks after the birth; scores of more than 12 identify likely major depressive disorder. Child outcomes were assessed when the child was aged 42 months using the Rutter revised preschool scales. Individual items combine to form 4 scales (*emotional problems, conduct problems, hyperactivity* and *prosocial* behaviour) and all problem behaviours combine to give a total problems scale. Mediators: maternal depression, marital conflict, paternal involvement. Moderators: trouble with police, suspension from school, paternal education, consumption of alcohol and cannabis. **Statistical analysis:** A series of regression analyses were performed to evaluate moderator and mediator effects. **RESULTS:** The association of paternal depression with increased scores on the child behavioural scales was not moderated by any of the hypothesised factors. The strength of the association of paternal depression with increased scores on the child behavioural scales dropped 34% after adjusting by maternal depression, 44% by marital conflict and 15.5% by paternal involvement. **CONCLUSIONS:** These findings suggest that the association between paternal postnatal depression and children behaviour problems is mediated by marital conflict, maternal depression and, to a lesser extent, paternal involvement. History of antisocial behaviour in fathers did not affect this association. These results highlight the importance of paternal depression and familiar environment in children´s development, although the influence of paternal antisocial traits cannot be excluded.

## P55 EARLY HANDLING INCREASES $NA^+K^+$ATPASE ACTIVITY, SYNAPTOPHYSIN, TIROSINE HYDROXILASE AND IMPULSIVITY IN ADULT RATS

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Early handling (EH) in rats is an important model to observe lasting early life environmental influences on adult physiology and behavior. The aim of this work was to analyze, in adult rats, the effect of EH on the impulsive behavior and on some neurochemical parameters in the frontal cortex. Female pregnant Wistar rats were used, and the litters were divided into two groups: (1) early handled (EH), in which pups were separated from their mothers in the first 10 days of life, 10 minutes per day, and put in an incubator at 32ºC; (2) not-handled (NH), in which pups were maintained with their mothers until weaning at the 21st day. At 60th day of age, male rats were isolated and maintained in a restricted diet (RD) (15-20g per day) for one week in the home cage. After the RD period the animals were trained to obtain a small-but-immediate reward or a large-but-delayed reward, accessible 15 and 30 seconds later in the test sessions. At 90th day of age, the animals were sacrificed and biochemical analyses were carried out. In the test sessions, the EH group showed a reduction in choices of the large-but-delayed reward relative to the NH group (repeated measures ANOVA,

p=0.0035). No difference was found in the pre-training sessions without delay and the training session with a 15-s delay (p>0.10). The synaptophysin and tirosine hydroxilase content was increased in the EH group (Student's t test; p=0,024 and p=0,043, respectively), but not that of the $D_2$ receptor (p= 0,309). $Na^+K^+$ATPase activity also increased in the EH group relative to the NH group (p=0,012). Taken together, these results suggest that EH increases, in adult life, the impulsive behavior and the content of neurochemical markers in the frontal cortex, an important cortical region responsible for controlling executive processes. Acknowledgments: CNPq

**P56 HOW DO DIFFERENT TYPES OF CRANIOFACIAL ABNORMALITY IMPACT ON AESTHETIC JUDGMENTS OF INFANT FACES?**

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Yamamoto et al (2009) and Parsons et al (2012) found that infants with facial abnormalities receive significantly lower ratings of attractiveness than those without abnormalities. Because attractiveness (and cuteness) ratings of infant faces correlate with ratings of care-giving motivation and influence behavioural judgments, it is vital to know the magnitude to which different types of craniofacial abnormalities impact on aesthetic ratings so that adequate parental support can be provided. Do all abnormalities cause an equal reduction in attractiveness and cuteness ratings, or, do some cause a greater reduction than others? To answer this question, 4 versions of 48 different infant faces were created using Photoshop; one with a Cleft lip, one with a Haemangioma, one with Strabismus and the original un-manipulated image. These images were subdivided in to four different sets, each containing one version of each face. The participants were each presented with one set and rated either how attractive, or how cute, they thought each face was on a 7-point scale. There was a significant effect of abnormality type and participant gender on rating levels, but no significant difference between the cuteness and attractiveness ratings for each face category. Male participants gave lower ratings than female participants to infants with abnormalities, but not the un-manipulated images. Both genders gave images with a haemangioma significantly lower ratings than the un-manipulated images, and images with strabismus and a cleft palate significantly lower ratings than those with a haemangioma. These findings suggest a gender difference in aesthetic judgments of faces with abnormalities, and that abnormalities affecting the core features of the face cause a greater level of disruption to aesthetic ratings than those in the peripheral regions. Fathers and parents of infants with abnormalities affecting the core features may benefit the most from community support.

## P57 THE EFFECTS OF PRENATAL STRESS ON THE EARLY NEUROBEHAVIORAL DEVELOPMENT OF RAT PUPS

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**Introduction:** Pre- and perinatal periods are the most important periods of ontogeny, during which the developing fetus may be exposed to several harmful stimuli. Evidences from epidemiological and clinical studies indicate that these stimuli have short and long-term effects on the newborns. The aim of the present study was to investigate the influence of maternal stress during different terms of pregnancy on the early physical and neurological development of the rat pups. **Methods:** Pregnant Wistar rats were exposed to restrain stress for 1 hour per day in different periods of pregnancy (1, 2. and 3. term) by restricting them in moving. After delivery, the offspring were tested for somatic and neurobehavioral development daily for the first 3 weeks. Data were compared to those of the control group - made up of pups from the same age group– by using ANOVA as the statistical method. **Results:** Our results showed that maternal stress during the second term of pregnancy retarded the development of several somatic signs and neurological reflexes (incisor eruption, ear unfolding, ear twitch, forelimb placing, acustic startle, air righting). We also observed a delay in the development of maturation signs of the pups whose mother had been stressed in the first term of pregnancy (ear unfolding, ear twitch, eyelid reflex, forelimb placing and grasp, auditory startle). In contrast, third-term maternal stress did not have a marked influence on the development of the newborns. **Conclusion:** These data suggest that exposure to stress in the early and middle term of pregnancy may impair the somatic and neurological development of the rat pups. On the other hand, third-term maternal stress had no marked effects on the examined parameters. Our findings may help to reveal the later, adulthood effects of fetal stress. **Acknowledgements:** OTKA K104984, TAMOP (4.2.1.B-10/2/KONV-2010-002, 4.2.2.B-10/1-2010-0029, 4.2.2.A-11/1/KONV-2012-0024), Arimura Foundation, PTE-MTA “Lendület” Program.

**P58 WHEN MALES BECOME THE ENEMY: MATERNAL AGGRESSION IS INDUCED BY THE ATTRACTIVE MALE SEXUAL PHEROMONE DARCIN, IN MICE**

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In rodents maternal behaviour consist of pup-directed components (pup retrieval and licking, arched back position and nursing) and non-pup directed ones including maternal aggression. In mice, virgin females show spontaneous pup care whereas aggression to intruders is only displayed by dams in the first week of lactation (declining during the second week). Maternal aggression depends on vomeronasal stimuli since both, null mutations of the vomeronasal function ($G\alpha_o$-/-; trpc2-/-) and vomeronasal ablation impair this behaviour. This work explores the hypothesis that pheromones of the male intruder trigger or enhance aggression in lactating females. If so, maternal aggression to castrated males would be reduced. To test this hypothesis we performed aggression tests towards male intruders in three groups of FEMALES: dams, sensitized virgin females (sisters of the dams sharing pup care) and virgins having no contact with pups. Each female was tested against two MALE intruders: intact and castrated (order counterbalanced). There was a significant effect of FEMALES on the latency to attack, with dams showing shorter latency. Moreover, attack time to intact males differs significantly among females, dams attacking more and in longer bouts. In contrast, aggression to castrated males is low and similar among females. The lack of aggressiveness of sensitized females suggests that continuous interaction with pups (at least three days), is not enough to promote aggression, which would likely depend on endocrine/physiological changes related to parturition and lactation.We then tested whether the urine-borne attractive male sexual pheromone also induces maternal aggression. To do so, we performed aggression tests towards castrated males swabbed with either urine of intact males, the recombinant sexual pheromone r-darcin (Roberts et al., BMC Biol. 2010 8:75; doi: 10.1186/1741-7007-8-75) or saline solution. Preliminary results indicate that both, urine and r-darcin, promote high level of aggressiveness towards swabbed-castrated males. Funded by the MICINN-FEDER (BFU2010-16656)

## P59 CUMULATIVE PREGNANCY ANXIETY AND PRETERM BIRTH: THE ROLE OF RESILIENCY FACTORS

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Maternal mental health, including anxiety and depression may adversely influence birth outcomes (e.g. preterm birth; PTB) and parenting. Children born to mothers with poor mental health are at risk of developmental delay, potentially as a consequence of poor attachment, poor birth outcomes and/or suboptimal parenting. The objective of this study was to investigate the relationship between cumulative pregnancy anxiety (CPA) and the risk of early preterm (EP; <34 weeks) and late preterm (LP; 34-36 weeks) compared to term delivery (≥37 weeks), and to examine the buffering effect of social support and optimism. Methods: Data was analyzed from the All Our Babies study, a prospective community-based pregnancy cohort in Alberta, Canada (n=3388). CPA included excessive symptoms of anxiety in pregnancy, a history of poor mental health or abuse, and negative feelings about the pregnancy. Multinomial logistic regression examined the effect of CPA on PTB after controlling for demographics and medical risk. Results: CPA was an independent risk factor for LP birth (OR 1.72; 95% CI: 1.06, 2.79), but not for EP birth (OR 2.45; 95% CI: 0.96, 6.38) after adjustment. CPA was not a risk factor for PTB among women with high social support or high optimism. Conclusions: External and internal resiliency factors mitigate the influence of CPA on risk of PTB. Social support is a coping mechanism related to resiliency, while optimism is related to a sense of mastery over life and each reduce the influence of CPA on the risk of PTB. Our findings suggest that stress-related emotions are related to adverse pregnancy outcomes, each of which may influence parenting ability (to be examined in future analysis). Programs that enhance social support may improve birth outcomes and facilitate optimal parenting. Women with CPA and who experience PTB may benefit from enhanced parenting supports to encourage attachment and optimal developmental outcomes.

**P60 OXYTOCIN, A POTENT ANTI-STRESS IN PRENATALLY STRESSED RATS, AN ANIMAL MODEL OF DEPRESSION**

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Oxytocin (OXT) plays a key role in parturition, lactation, and mother/infant interaction. However, OXT has also an anti-stress action in adulthood by reducing the activation of the HPA axis. Prenatal restraint stress (PRS) in rat programs the offspring to develop an anxious-like phenotype characterized by a prolonged HPA response to stress. PRS rats represent a valuable model of programmed anxious/depressive-like symptoms. This perinatal programming is induced by both prenatal overexposure to maternal glucocorticoids and a reduced maternal behavior received during the early postnatal life. To our knowledge, little is known about the involvement of the mother/pup OXT systems in the programming of the adult PRS phenotype. We examined (i) the effect of a treatment with the OXT receptor agonist, carbetocin (1mg/kg, i.p.), to stressed and control mothers during the first *post-partum* week (lactation period), first on maternal behavior, then its consequences on the adult PRS phenotype (anxiety and HPA response to stress); and (ii) the effect of chronic carbetocin administration in control and PRS rats during adulthood on the HPA response to stress, on anxious/depressive-like but also social behaviors and on the expression of some stress-related genes in the hippocampus. In each case, carbetocin normalized plasma corticosterone levels seen in adult PRS rats exposed to stress. In addition, carbetocin administration to lactating mothers increased maternal care and reduced the anxiety-like behavior of male adult PRS rats, whereas in the adult life it reinforces social memory and also reduces anxious/depressive-like symptoms in PRS rats. Moreover, carbetocin treatment in adults up-regulated the expression of type-I and type-II glucocorticoid receptors (MR and GR) in the hippocampus. We conclude that the OXT system in the early life plays a protective role against the programming effect of adverse experiences. The OXT system could be considered as a novel potential therapeutic target for stress-related disorders.

**P61 AN MRI STUDY: THE RELATIONSHIP BETWEEN OBSERVED MATERNAL SENSITIVITY AND EXPERIENCE OF INTERPERSONAL VIOLENCE**

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**Background:** This study investigated the relationship between maternal sensitivity and interpersonal violence-related Posttraumatic Stress Disorder (IPV-PTSD) with respect to gray matter density and brain activation when IPV-PTSD mothers versus non-PTSD controls were exposed to scenes of male-female interaction of differing emotional valence and arousal. **Methods:** Mothers of 37 children, 12-42 months of age, participated: Twenty mothers with symptoms of IPV-PTSD and 17 non-PTSD controls. Well-validated clinical measures (CAPS and PCL-S) were used to assess PTSD diagnosis and severity. During MRI, mothers watched a validated stimulus-protocol of 23 different 20-second silent epochs of male-female interaction, which were either neutral (neutral valence/low arousal), menacing (negative valence/high arousal) or positive (positive valence/medium to high arousal). Maternal sensitivity was assessed by naive rating of videos of mother-child interaction acquired prior to MRI, using the CARE-Index. **Results:** While both groups deactivated the anterior cingulate (ACC) when viewing menacing scenes, only IPV-PTSD mothers deactivated it during positive ones. IPV-PTSD mothers showed greater dorsomedial prefrontal activation (dmPFC) only in response to menacing scenes. IPV-PTSD mothers showed greater activation of the dorsal ACC, dorso-lateral PFC and dmPFC in response to menacing vs. positive scenes. Activation in the ACC was significantly negatively correlated to maternal sensitivity. The density of gray matter in bilateral insulae was correlated negatively with maternal sensitivity. **Conclusions:** IPV-PTSD mothers showed less cortico-limbic regulation than HC in response to a newly validated paradigm making use of menacing vs. other feature film scenes. This is consistent with the fMRI literature involving adults with IPV-PTSD. IPV-PTSD mothers compared to controls tended to deactivate the ACC during all emotional scenes. This failure to deactivate the ACC was also related to observed maternal sensitivity, suggesting that neural processes used for emotion regulation with adults are also used in maternal interaction with the subject's own child.

**P62 ANALISYS OF THE PARTICIPATION OF ROSTRODORSAL PORTION OF THE PERIAQUEDUCTAL GRAY IN MATERNAL BEHAVIOR INHIBITION AFTER CAT EXPOSURE**

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Behavioral inhibition is considered a defense response and may be a critical strategy for survival of animals in the natural environment and maintenance of their own species. Recently, a functional study of maternal behavior inhibition in lactating rats exposed to cat odor showed that this behavior was clearly inhibited favoring specific defensive responses such as freezing and risk assessment. In this study, we observed a clear Fos expression in the dorsolateral column of periaqueductal gray (PAG) correlated with maternal behavior inhibition in response to cat odor. In addition, the bilateral NMDA lesion in this particular area of the PAG was able to prevent the switching from taking care of offspring and the defensive response to predatory threat. These studies confirmed the classic role of the dorsolateral column of PAG as a critical site for neural expression of defense responses. However, the present study provides the first evidence of involvement of the dorsolateral column of PAG in behavioral inhibition. Therefore, it is important to evaluate the defense response and the maternal behavior inhibition in lactating rats separately. For this investigation, we established a behavioral protocol in which maternal behavior response was evaluated immediately after ten minutes of cat exposure. The behavioral analysis showed a clear maternal behavior inhibition for one hour after exposure to the cat. Next, we tested the rostrodorsal PAG involvement in this behavioral inhibition. Our results showed that bilateral NMDA lesions in the rostrodorsal PAG, but not in other parts of the PAG as the caudal lateral portion, produced inhibition of defensive responses and restored the maternal behavior in these lactating female rats exposed to the natural predator. Overall, the present findings provide further evidence to support the view that the PAG acts as a critical influence on motivational drive to select proper adaptive behavioral responses.

**P63 ANALYSIS OF GENES EXPRESSION IN THE BRAIN OF LACTATING RATS WHICH DISPLAY DIFFERENT PATTERNS OF MATERNAL BEHAVIOR**

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**Introduction:** In rats, variations in the levels of neuromodulatory molecules and in the expression of their receptors are observed during pregnancy and postpartum. These changes may contribute to the development and management of maternal behavior. The frequency of licking the pups is used to evaluate maternal care, having mothers with low licking (LL) and high licking (HL) frequencies. Our objective was to analyze the expression of the receptors for serotonin (HTR1a, HTR1b), estrogen (Erα, Erβ), dopamine (D1a); and of BDNF, in the hippocampus (HP), striatum (ST), prefrontal cortex (PFC), and olfactory bulb (OB), from LL and HL. **Methods:** Lactating *Wistar* rats were divided according to the behavior of licking their pups: LL (n=8), HL (n=8); and virgin female (diestrus=D; n=6) were used as controls. Maternal behavior was studied from the $1^{st}$-$7^{th}$ postpartum days. In the $8^{th}$ day, brain parts were removed, RNA was extracted and followed by qPCR. Expression levels for constitutive genes (β-actin, cyclophilin-A, ubiquitin-C) were evaluated, as internal control. The fold change was measured by the formula $2^{-\Delta CT}$. **Results:** There were differences in the expression of the receptors Erα, D1a, HTR1a and HTR1b in the OB, with greater expression in HL rats (fold change: Erα=3.05; D1a=5.17; HTR1a=2.30; HTR1b=3.80). In the HP, these genes were differently expressed only when comparing HL with D, or LL with D. On the other hand, expression of these genes was similar in the ST and in the PFC. No differences in BDNF and Erβ were found. **Conclusion:** Results suggest that the differences in the levels of gene expression in the OB, are related to licking behavior, thereafter contributing for a better understanding of the molecular mechanisms involved in the different patterns of maternal behavior developed by mothers living under the same conditions and environment. **Financial support:** PROAP/UFCSPA, FAPERGS.

## P64 SELECTING STABLE HOUSEKEEPING GENES FOR EVALUATION OF TRANSCRIPTIONAL EXPRESSION LEVELS IN RAT BEHAVIORAL MODELS

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**Introduction:** A growing number of recently published articles relate the expression of specific genes with the different patterns of behavior in rats. The quantification of mRNA in these studies is made by RT-PCR, normalized by an internal control or reference gene (housekeeping gene). **Methods:** In the present study we used *Wistar* rats (virgin females; n = 6) in the diestrus period. They were decapitated, the brains were quickly removed and the following regions were collected: olfactory bulb (OB), hippocampus (HP), striatum (ST) and prefrontal cortex (PFC). Total RNA was extracted and cDNA was produced by semi-quantitative RT-PCR. Amplification was performed by real-time qPCR (SYBR Green) using primers for the reference genes most commonly used in the literature: β-actin (ActB), cyclophilin A (CypA) and ubiquitin C (UbC); their stability was determined using NormFinder. **Results:** Results show that in the HP and ST the most stable housekeeping gene was ActB. Yet, in the PFC it was CypA, and UbC in the OB. **Conclusion:** Using our pattern of samples and having the gene selected for each brain region, further studies relating the expression of target genes with the animal behavior can be accomplished with the security of using a stable control gene. **Financial support:** PROAP/UFCSPA, CAPES, FAPERGS.

## P65 KISS1 GENE IS REQUIRED FOR ABOLISHMENT OF LORDOSIS BEHAVIOR AND ESTABLISHMENT OF MALE SEXUAL BEHAVIORS IN RATS

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Kisspeptin, encoded by *Kiss1* gene, is considered to be a key regulator for gonadotropin-releasing hormone (GnRH) secretion. On the other hand, little is known about roles of kisspeptin in sexual behaviors. The present study examined the role of kisspeptin in regulating sexual behaviors with *Kiss1* knockout (KO)/tdTomato knockin rats. Female and male sexual behaviors were tested both in *Kiss1* KO and wild-type rats. Briefly, 9-13 weeks old female and male rats were used for behavior tests and were gonadectomized and

implanted with estradiol or testosterone 5 or 7 days before behavior tests. Behavior tests were carried out between 16:00 and 19:00. *Kiss1* KO males, primed with estradiol, showed robust female sexual behaviors with the LQ not being significantly different from females. Wild-type male rats displayed mounts, intromissions and ejaculation, while *Kiss1* KO male rats, albeit they were primed with testosterone, did not show male sexual behaviors. Surprisingly, *Kiss1* KO males showed a high plasma testosterone level at embryonic day 18 and postnatal day 0 as wild-type males did. Taken together, the present study showed that Kiss1 gene is required to abolish lordosis behavior and establish male sexual behaviors. Kisspeptin might be responsible for the downstream of perinatal androgen surge for the defeminization or masculinization of neuronal mechanism controlling sexual behaviors in rats. **Acknowledgements:** This work was supported in part by the Research Program on Innovative Technologies for Animal Breeding, Reproduction, and Vaccine Development.

## P66 EARLY-LIFE STRESS PERSISTENTLY AFFECTS BRAIN STRUCTURE AND FUNCTION VIA NUTRITIONAL AND EPIGENETIC PROGRAMMING

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Early-life stress (ES) has lasting effects on mental health and cognition, associated with altered hippocampal plasticity. The underlying mechanisms are yet unknown. Deficits in elements of the parent-offspring relationship (e.g. sensory, nutritional) are potent early-life stressors, but the role of nutrition has been largely ignored so far. Regarding the molecular mechanisms, epigenetic programming is suggested to be involved. Importantly, the epigenetic machinery requires specific micronutrients (e.g. folate, vitamin $B_6$, $B_{12}$). Here we study if ES alters micronutrient levels and we study ES-induced changes in hippocampal neurogenesis and epigenetic modifications. Chronic ES was induced in C57Bl/6 mice by limiting nesting material during postnatal day (P)2-9. Micronutrient levels were measured in milk, plasma and brain samples of dams and pups by liquid chromatography/mass spectrometry. Levels of neurogenesis in the hippocampal dentate gyrus (DG) were assessed using immunohistochemical markers (Ki67, NeuroD1, Calretinin, BrdU) at P9 and at P150. Cognitive function was examined from P150 onwards via standard behavioral tests. ES dams show erratic maternal care and reduced bodyweight gain. This induces chronic ES in the pups that show reduced bodyweight gain and elevated basal plasma corticosterone levels at P9. ES decreased stomach milk levels of folic acid and vitamin $B_6$ at P9, suggesting a role of these micronutrients in mediating the effects of ES. ES exposure increased postnatal proliferation ($Ki67^+$) and differentiation ($Calretinin^+$) in the DG at P9. These early-onset structural changes are associated with cognitive impairments at P150. Studies addressing the role of epigenetic regulation and the effects of ES on adult neurogenesis are ongoing. Identifying a causal relation between early environmental exposure, nutrition, epigenetics and brain structure and function might provide new opportunities to treat the lasting effects of ES by nutritional intervention.

## P67 ANTENATAL DEPRESSION & INFANT SLEEP, EXAMINING THE MODERATING EFFECTS OF 5-HTTLPR & TEMPERAMENT

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Antenatal depression predicts a range of adverse child outcomes, including disturbed infant sleep (O'Connor et al., 2007). Recent GxE studies, using this specific polymorphism, suggest that (5-HTTLPR) may moderate the effect of negative early life events on a number of phenotypic outcomes. Reactive temperament has also been shown to be a moderator of the effects of a range of negative life events on developmental outcomes. Infant sleep is identified as an important marker of early bio-behavioural development. Serotonin has been extensively linked to the study of sleep and is implicated in both sleep and wake promoting processes. This study examined two moderators, 5-HTTLPR and infant reactive temperament. **Methods:** We examined whether the association of antenatal depression at 32 weeks gestation and infant disturbed sleep at 18 and 30 months would be moderated a) by the polymorphism in the serotonin transporter promoter gene area 5HTTLPR and b) by mother-rated reactive temperament, in a large population cohort (the Avon Longitudinal Study of Parents And Children, n=5,402). We hypothesized that the association between maternal mood disturbance and infant sleep a) would be stronger in those infants with low activity alleles of 5-HTTLPR compared to those with high activity alleles b) would be stronger in infants with reactive temperament. Infants with more reactive temperament would be more susceptible to the effects of antenatal depression and would exhibit more disturbed sleep. **Results:** Regression models did not show evidence of a moderating effect of 5-HTTLPR x depression. Reactivity however was found to be a moderator of sleep problems and nighttime awakenings at 18 and 30 months of age. **Conclusion:** These findings suggest different developmental trajectories for individuals with different temperamental characteristics. They further support that high reactivity is associated with differential vulnerability to negative life events, such as antenatal maternal depression, even during very early development.

## P68 THE IMPACT OF EARLY LIFE STRESS ON *IN VITRO* GAMMA OSCILLATIONS

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Early life adversity in the form of abuse, neglect or parental loss during early development is associated with an increased risk of many neuropsychological disorders in adulthood. These include depression, post-traumatic-stress disorder, panic disorder, attention deficit disorder [1] as well as psychosis and schizophrenia [2]. Stress exposure in early life is also linked to deficits in cognitive function, including impaired spatial learning and memory [3]. A well-established rodent model of early life stress is 24 hour maternal deprivation at postnatal day 9 [4]. Maternally deprived (MD) adults display a range of behavioural impairments, many of which are commonly described in neuropsychiatric disease. MD rodents show alterations in

the stress response system, hippocampal morphology and specific NMDA receptor expression. However, little information exists concerning the impact of early life stress on neuronal function, including the ability of cortical networks to generate persistent rhythmic activity of cognitive relevance. Gamma oscillations (30-80Hz) are crucial for the coordination of neural activity across many brain areas simultaneously and are involved in many cognitive functions. We examined these oscillations in MD adult male Wistar and control rats, which remained with the dam until weaning at postnatal day 21. Extracellular LFP recordings were taken in the medial entorhinal cortex and the CA3 subfield of the hippocampus, in combined EC-hippocampal brain slices (450µm) prepared from MD and control adult rats. Gamma oscillations were induced by bath application of kainate (100nM and 200nM). Results will potentially reveal a difference in gamma frequency and power between MD and control groups, and we hypothesize that disruptions of cortical interneuronal function underlie any deficiencies.

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**P69 OXYTOCIN AND THE DEVELOPMENT OF A PREFERENCE FOR THE MOTHER IN LAMBS**

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During the peripartum period oxytocin (OT) plays a key role in the expression of maternal behaviour in several species including sheep, yet its relevance in infants when interacting with their mother still remains to be demonstrated. Because early mother-young interactions have profound psychodevelopmental effects on the young, we examined the link between suckling, the oxytocinergic system, and the development of attachment in lambs. Our data showed that: a) in a two-choice test opposing two maternal ewes, control lambs displayed a preference for their mother within 12 h; such affiliative behaviour was delayed when suckling was prevented for 6 h after birth by covering the ewes' udder. b) OT levels increased in the plasma during nutritive and non-nutritive contact with the mother but the rise was much higher in the first case. OT also increased in the cerebrospinal fluid (CSF) following suckling. c) when the oxytocin antagonist L368,899 was administrated orally at birth, 2h and 4h post-partum, whilst control lambs developed a preference for their mother at 12 h, those receiving the antagonist were slightly (low dose) or severely (high dose) impaired. Finally, we examined the distribution of OT receptors binding sites on sections (20 µm) of fresh frozen lamb brains incubated with $^{125}$IOTA. The selectivity of the radioligand to OT receptors was successfully tested on sections of rat brains and sheep uterus. By contrast no binding could be seen on lamb brains although OT neurons were identified and OT detected in the CSF. These data suggest that the oxytocinergic system is activated during

early interactions with the mother, participates in the development of filial attachment, but OT receptors cannot be revealed in the brain with $^{125}$IOTA. Additional studies are on their way to understand the lack of binding which contrasts with immunohistochemistry data previously obtained in the ewe at parturition.

**P70 RELATIONSHIP OF AGE AND SEX DIFFERENCES IN PARENTAL AND INFANTICIDAL BEHAVIOUR WITH BRAIN OXYTOCIN RECEPTORS IN MICE**

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Naïve mice show significant variability in their behavioural response toward newborns (rapidly-induced maternal or infanticidal behaviour). Oxytocin (OXT) facilitates maternal behaviour in many species. However, knock out mice studies for OXT receptor (OXTR) and OXT genes have been controversial. While some studies found no behavioural differences, others concluded that OXT facilitated maternal and inhibited infanticidal behaviour. In the first experiment, the development of infanticidal and parental behaviour was investigated in CB57BL6 naïve mice. The results showed that adult, but not juvenile (20-22 days of age), females were rapidly induced to display maternal behaviour. Besides, adult males were infanticidal more often than juveniles or adult females. The second experiment investigated if adult males had lower OXTR than juveniles or adult females in areas associated with maternal behaviour (cingulated cortex, medial preoptic area, olfactory bulb, septum, among others). If adult females (highly maternal towards newborns) had higher brain OXTR than juveniles or adult males was also investigated. Results revealed that juveniles (males or females) had higher or similar OXTRs, compared to adults (males and females) in areas of the brain associated with maternal behaviour. Therefore, a decline in brain OXTR density was associated with increased parental and infanticidal responses in females and males respectively. There was no sex difference in the density of OXTR in juveniles. We are currently analysing sex differences in OXTR density in estrous/proestrus females and adult males. The present study suggests that mouse behavioural development and OXT mediation of parental behaviour differ significantly from that described in rats and voles. I hypothesize that natural variations in brain OXTR density are not sufficient to explain differences in the incidence of parental or infanticidal behaviour in mice. Other OXT-independent mechanisms are likely critical for the development of rapidly induced parental or infanticidal responses in this species. Funding: CSIC I+D (UdelaR)

## P71 MODE OF DELIVERY EFFECT ON ATTACHMENT BEHAVIOR DURING MATERNAL INFANT SEPARATION

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**Introduction** Maternal-infant separation (MIS) is a highly stressing situation for the neonate. Our previous pilot study revealed that neonatal crying following minimal maternal separation was influenced by the mode of delivery (1). Neonates born by a planned C-Section cried much less on maternal separation. The objective of this bigger study is to assess whether the mode of delivery influences maternal behavior during MIS or infant crying after restoration of skin contact within the first 48 hrs of life. **Material and Methods** 127 mothers and their new-borns were included: 85 were born vaginally (VB) and 42 by elective caesarean section (CS). Gestational age was 39,4 wks VB vs 38,9 wks EC group. A brief maternal-infant separation situation was videotaped, to observe the reactions of mothers and newborns within the first 12-48 hrs of life and then coded. One blind observer coded maternal and newborn behaviour watching videotapes. **Results** Mean GA was 39.4±1.2w in the vaginal delivery (VD) group and 38.9±0.9w in the caesarean group (CS). 67 new-borns were females (44 VB, 23 CS) and 60 were males (41 VB, 19 CS). Maternal behaviours previous to separation were higher in the CS group (58,4% VB vs 75,26% CS; p = .015) while there were no significant differences in maternal behaviour post separation (60,9% VB vs 70,3% CS; p=.19). Non significant differences on new-born time to calm down after separation were found, contrary to our previous finding (VBt=27,3sec+_49,8DE VB vs CSt=14, sec + 37,9DE; p=.087) **Conclusions** Mothers who gave birth by planned caesarean showed more maternal behaviours previous to the MIS than mothers who have delivered vaginally. There were no differences on maternal behaviour post-separation. Infants born vaginally tended to cry more after restoring contact, although the differences were non-significant. REFERENCES: Olza Fernández I, Marin Gabriel MA, Garcia-Murillo L, Malalana Martinez A, Costarelli V, Millan Santos I. Mode of delivery may influence neonatal responsiveness to maternal separation. Early Human Development, Volume 89, Issue 5, May 2013, Pages 339-342, ISSN 0378-3782, 10.1016/j.earlhumdev.2012.11.005. Research supported by grant number: PI10/00791 from the Spanish Ministry of Science.

**P72 INCREASED HIPPOCAMPAL GENE EXPRESSION IS ASSOCIATED WITH LOW BIRTH WEIGHT IN FEMALE NON-HUMAN PRIMATE NEONATES**

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Low birth weight is associated with reduced hippocampal volume and impaired cognitive abilities. Increased *in utero* exposure to glucocorticoids defines the endocrine conditions associated with low birth weight and compromised neural development. However, little is known about the differences in gene expression in late fetal or early postnatal development which might mediate these effects. The aim of this study was to identify changes in hippocampal gene expression early in development which are associated with low birth weight. We compared the relative mRNA expression of genes involved in glucocorticoid signaling in the hippocampus of non-human primate neonates (*Macaca fascicularis*) of naturally occurring normal and low birth weights by qPCR and Western-blotting. We then used microarray expression profiling to conduct an open search for genes regulated by birth weight. We detected a decreased mineralocorticoid receptor/glucocorticoid receptor (MR/GR) ratio in the hippocampus of low birth weight animals on the transcriptional as well as on protein level suggesting a key role for these receptors in hippocampal brain development. No significant differences were detected for the glucocorticoid and mineralocorticoid receptors individually. Analysis of our microarray data revealed an almost complete separation of hippocampal samples according to birth weight based on individual gene expression signatures derived from 24,154 probe sets. Gene ontology and pathway analysis suggests increased transcriptional activity as well as enhanced cellular outgrowth and synapse formation in the hippocampus of low-birth weight animals. Disease-related GO terms indicate an up-regulation of numerous genes associated with mental disorders (e.g., ANK3, SAP97, TCF4). Our data suggest that impaired fetal growth associates with altered hippocampal transcription of genes linked to multiple forms of psychopathology. Acknowledgement: This study was supported by the Agency of Science, Technology and Research (A*STAR), Singapore.

**P73 ARE OVARIAN HORMONES RESPONSIBLE FOR HIPPOCAMPAL NEUROPROTECTION DURING LACTATION?**

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Lactation has been shown to protect the hippocampus of the mother against excitotoxic action of kainic acid (KA). The lactational phase is associated with increased levels of progesterone, glucocorticoids, prolactin, and oxytocin, which are maintained by suckling

stimulation and reinforced by external signals from the litter. Neuroprotection of the hippocampus during lactation can involve actions of any one, or a combination of these hormones. Here we investigated whether ovarian hormones participate in the lactational neuroprotection of the dorsal hippocampus. Ovariectomised- (OVx) or SHAM-lactating rats were injected with a single dose of 7.5 mg/kg b.w. of KA or vehicle at day 15-18 pp. They were perfused 48 h after KA injection, and cell damage was assessed in CA1, CA3, and the hilus of the dentate gyrus by NISSL stain. KA-induced cell loss was higher in OVx-lactating than in SHAM-lactating rats. OVx or SHAM groups injected with saline either showed no differences in cell number in the hippocampal fields analysed. However, the magnitude of damage induced by KA in the OVx group (20-30% vs. corresponding control) was shorter than in virgin-dioestrous rats (30-50% vs. corresponding control). In conclusion, our data demonstrate that the lack of ovaries made the hippocampus of the lactating female more sensitive to the damaging action of KA, thus ovarian hormones are part of the hormone mix contributing to the neuroprotection of this brain region during lactation. Financial support: PAPIIT DGAPA-UNAM, Mexico IN202812 y CONACYT of Mexican Goverment 128090.

**P74 THE DOPAMINERGIC SYSTEM AND THE NEUROENDOCRINE RESPONSE IN A RAT MODEL OF PRENATAL STRESS**

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We have previously demonstrated that prenatal stress (PS) exerts an impairment of midbrain dopaminergic system (DA) metabolism especially after puberty, suggesting a particular sensitivity of DA system to variations in gonadal hormones peaks. Additionally we demonstrated that PS alters the reproductive hormone profile and testis development of the rat male offspring. We employed a commonly use paradigm of prenatal stress in rats which consisted on restraining the dams three times per day from the 14th day of pregnancy until birth. Evaluation of D2 dopamine (D2R) and sexual hormones receptor levels on prefrontal cortex (PFC), hippocampus (HPC) and ventral tegmental area (VTA) were performed on prepubertal and adult male offspring. Additionally, evaluation of dendritic arborization in PFC and HPC were measured by quantifying the immunoexpresion of MAP2. Our results show that PS affected estrogen receptor alpha (ER$\alpha$) expression: mRNA Er1s levels and ER$\alpha$ protein expression were decreased on PFC and HPC of brain adult offspring. Moreover, PS reduced D2R protein levels in HPC of prepubertal rats, whereas its levels were increased in VTA. Morphological studies revealed that both prepubertal and adult PS males presented a decrease in the number of MAP2 immunoreactive neurons in both areas suggesting that PS reduces dendritic arborizations. Our findings suggest that PS exerts long-term effects both in the HPT axis and DA system by altering the normal conectivity between areas, and by

modulating the expression of D2R and ERα in an age-related pattern. Since the developing forebrain DA system was shown to be influenced by androgen exposure, and PS was shown to disrupt perinatal testosterone surges, our results suggest that prenatal insults might be affecting the organizational role of androgens and differentially modulate their activational role on brain development.

**P75 MINOR STRUCTURAL ABNORMALITIES IN THE BABY FACE DISRUPT BRAIN PROCESSING: A UNIQUE WINDOW INTO CAREGIVING RESPONSES**

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Both Darwin and Lorenz argued that infant faces play an important role in eliciting responsive care from parents. Infant faces have been shown to elicit early, specific activity in the orbitofrontal cortex (OFC), a key cortical region for reward and affective processing. A causal test of the relationship between infant facial configuration and early OFC activity is provided by naturally-occurring changes to the infant facial structure. One such change is cleft lip, which represents a relatively limited, localised abnormality, associated with disruption to early parenting. We investigated brain activity in response to briefly presented (300ms) infant faces with cleft lip and typical infant and adult faces using magnetoencephalography. Source reconstruction revealed the previously-described OFC activity at 140msec in response to infant faces, but reduced activity to adult faces and infant faces with cleft lip. In addition, the face-selective M170, localised to the fusiform face area, was similar for adult and healthy infant faces, but was substantially attenuated for infant faces with cleft lip. This is the first evidence that a minor change to the otherwise unaffected facial structure can disrupt the robust neural activity usually seen in response to infant faces. This may have implications for caregiving, at least before surgical repair of the cleft lip. Acknowledgements: This work was supported by the TrygFonden Charitable Foundation, the Barclay Foundation and the Medical Research Council, UK.

## P76 THE NORMALISATION OF DISRUPTED ATTENTIONAL PROCESSING OF INFANT DISTRESS IN DEPRESSED PREGNANT WOMEN FOLLOWING CBT

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**Background:** Perinatal depression is associated with disrupted mother-infant interactions and poor infant outcomes. Antenatal depression may play a key role in this cycle by disrupting the initial development of infant responsive cognitive processing. We have previously demonstrated that depressed pregnant women fail to show the attentional bias towards infant distress that develops across pregnancy in non-depressed women and which is positively associated with reported mother-infant relationships after birth. In the current study we investigated whether Cognitive Behavioural Therapy (CBT) normalises depressed pregnant women's abnormal attentional processing of infant distress. **Method:** Depressed pregnant women participating in a randomised control trial completed a measure of attentional bias towards infant distress before and after intervention. Between their first and last trimesters of pregnancy, women received either 12 sessions of CBT (n=11) or treatment as usual TAU (n=12). Reaction times to disengage attention from distressed as compared to non-distressed infant faces provided an index of women's attentional bias towards infant distress. **Results:** At baseline depressed women in both the CBT and TAU arm of the trial showed a diminished attentional bias towards infant distress as compared to a comparison group of non-depressed pregnant women (n=56). However, following treatment, the attentional biases of women who received CBT **increased** on average by 60ms (95% CI, 20 to 100) whereas the attentional biases of women who received TAU **decreased** on average by -31ms (95% CI,-118 to 57). There was evidence for a time by intervention interaction (β= -102, 95% CI -184 to -20, p=0.02). Following treatment, the attentional biases of women who received CBT were comparable to non-depressed pregnant women. **Implications:**This suggests that CBT during pregnancy may improve mothers' cognitive processing of infant distress. Further investigation is required to disentangle whether this effect is a consequence of improvements in depression or of the intervention itself.

## P77 THE IMPACT OF DEPRESSION AND OF ALCOHOL USE DURING PREGNANCY ON MATERNAL REPSONSES AFTER BIRTH

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Work in animals has shown that prenatal stress affects maternal behaviour toward their offspring. Less is known about the effects of prenatal stress on parenting behaviour in humans. There is evidence to suggest that neurocogntive preparations for parenting can be impaired in pregnant women who experience depression. Interuption of reward pathways may be an explanation for this. Using longitudinal data from over 900 mother‐infant pairs in a longitudinal study starting in pregnancy (ALSPAC), we found that women with high depressive symptom scores during mid pregnancy, had a 30% increased risk of low observed maternal responsiveness when the infant was 12 months compared to women with consistently low depression scores. There was no risk of low maternal sensitivity for women depressed at 8 months postnatally. We also investigte the effect of alcohol use during pregnancy and found use in mid pregnancy but not late pregnancy was associated with reduced maternal sensitivity at one year. These data provide evidence that disruption to maternal prenatal neurocogntive preparations for responding sensitively to their infants postnatal programming may explain the link between prenatal stress exposure of various types and adverse outcomes for children. Acknowledgements: We are extremely grateful to all the families who took part, the midwives for help in recruiting them, and the whole ALSPAC team, which includes interviewers, computer and laboratory technicians, clerical workers, research scientists, volunteers, managers, receptionists, and nurses. The United Kingdom Medical Research Council, the Wellcome Trust, and the University of Bristol provide core support for ALSPAC. The project was supported by an ESRC small grant RES-000-22-4175.

## P78 NOVEL INSIGHT INTO PITUITARY AND ADRENAL MECHANISMS UNDERLYING PERIPARTUM HYPERCORTICISM IN THE MOUSE

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During pregnancy and lactation the maternal organism undergoes behavioural and physiological changes that are important for the developing offspring and her well-being. Prominent alterations include basal hypercorticism and a reduced HPA axis response to stress exposure. However, despite the increased basal plasma corticosterone there is no

change in basal adrenocorticortopic hormone levels. Taken together these findings suggest that both glucocorticoid negative feed-back and adrenal gland functionality may adapt peripartum. However, such mechanisms are poorly studied, especially in the mouse. Therefore, the aim of the present study was to investigate whether pituitary glucocorticoid receptor expression and nuclear translocation, and adrenal cholesterol delivery pathways, are altered by lactation. We determined that, despite the elevated circulating corticosterone levels, neither pituitary glucocorticoid receptor expression nor nuclear translocation is altered in lactating mice. In contrast, substantial plasticity of adrenal cholesterol delivery pathways was observed. In detail, low density lipoprotein receptor and scavenger receptor B1 protein levels were both up-regulated in lactating compared with virgins. Our findings suggest that mechanisms beyond pituitary glucocorticoid receptors may explain unaffected adrenocorticotropic hormone secretion. Moreover, the increase in adrenal lipoprotein receptors in early lactation, concurrent with maternal plasma hyperlipidemia, indicates that plasma lipoproteins may serve as primary cholesterol source for steroidogenesis. While the pituitary gland seems to be insensitive to increased circulating corticosterone, the adrenal glands actively adapt to drive higher steroidogenesis during lactation in the mouse.

**P79 NOVEL INSIGHT INTO MECHANISMS UNDERLYING PERIPARTUM HYPERCORTICISM: INVOLVEMENT OF THE ADRENAL CHOLESTEROL DELIVERY PATHWAYS**

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During the peripartum period the maternal organism undergoes behavioural, metabolic and physiological changes, including a basal hypercorticism, stress hyporesponsiveness and hyperlipidemia, to promote effective pregnancy and lactation. Despite increased basal plasma corticosterone there are no changes in adrenocorticortopic hormone levels suggesting that the adrenal glands also adapt. However, no studies have investigated adrenal glands peripartum plasticity and the potential maladaptive effects of feeding a high fat diet on maternal hypothalamus-pituitary-adrenal axis peripartum physiology. Therefore, the aim of the present study was to investigate whether adrenal cholesterol delivery adapts during lactation in the rat and whether feeding a high fat diet may interfere with lactation-associated adrenal plasticity compromising the maternal basal hypercorticism and stress hyporesponsiveness. We determined that adrenal lipid vesicles are depleted beginning at mid-pregnancy and lasting until mid-lactation. In contrast, expression of hormone sensitive lipase and Acyl CoA: Cholesterol O-acyl transferases were unchanged. The receptors responsible for lipids uptake, adrenal low-density lipoprotein receptor and scavenger receptor B1 were both upregulated – but only at mid-lactation. Finally, we could show a lactation-induced decrease in the adrenal expression of 3-hydroxy-3-methylglutaryl coenzyme A (HMG Co-A) reductase. Interestingly, maternal high fat diet prevented most of the lactation-induced changes in adrenal cholesterol delivery. Moreover, intake of a high-fat diet was able to block basal hypercorticism *in vitro* and *in vivo* and lactation-associated anxiolysis. Finally, will the high-fat diet did not affect the hyporessponsiveness of the HPA axis to 60s swim stress it did restore the corticosterone response to an ACTH injection *in*

*vivo*. These findings reveal that all cholesterol delivery pathways within the adrenal gland are altered across the peripartum period. The adrenal lipid stores depletion together with the increase in lipoprotein receptors at mid-lactation, also the time of maternal plasma hyperlipidemia, suggest that plasma lipoproteins may represent an important cholesterol source to sustain basal hypercorticism. Feeding a high fat diet blocked most of the adrenal changes in cholesterol delivery pathways. Lactation-associated hypercorticism and stress hyporesponsiveness were also prevented suggesting that adrenal glands adaptations together with balanced hyperlipidemia are key regulators for maternal hypothalamus-pituitary-adrenal axis physiology.

**P80 CHANGES IN NUCLEUS ACCUMBENS DOPAMINE RELEASE DURING MOTHER-PUP INTERACTIONS AT EARLY AND LATE POSTPARTUM STAGES**

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Nucleus accumbens dopamine (DA) plays a critical role in modulating different aspects of goal-directed behaviors. Considerable evidence supports an important facilitatory role of accumbens DA in maternal behavior, and studies employing in vivo neurochemical monitoring techniques report that extracellular levels of accumbens DA are elevated during maternal interaction with pups. The majority of this evidence, however, has only focused on the early postpartum period, and consequently, virtually nothing is known about the specific contribution of DA release dynamics in the accumbens to late postpartum maternal behavior. Accordingly, the present study employed a novel approach that combines analysis of maternal responding toward pups with concurrent rapid, in vivo microdialysis sampling (5 min interval) of accumbens DA in female rats at both early and late postpartum stages. During early postpartum, the presentation of pups behind a barrier (phase I: Pup-seeking) resulted in a robust increase in accumbens DA release, which was further significantly augmented during active maternal interaction with pups (phase II: Active Caregiving). The adoption of a quiescent nursing posture over the pups by the mother (phase III: Passive Nursing) was associated with a small increase in the extracellular concentration of DA from baseline that did not reach statistical significance. DA concentrations returned to baseline levels during transitions between behavioral phases. In late postpartum, basal levels and the release dynamics of DA within accumbens followed a similar pattern. However, the magnitude of the maternal responding-associated increase in DA release was significantly attenuated relative to early postpartum. Taken together, these data suggest that changes in accumbens DA activity associated with mother-pup interactions may serve as a neural substrate for the dynamic motivational aspects of maternal behavior across postpartum. Supported by NICHD HD073710 awarded to MP

## P81 PRE-MATING ANXIETY, POSTPARTUM ANXIETY AND OFFSPRING CONTACT PREDICT BRAIN AMINE EXPRESSION IN FEMALE RATS

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Most women show increased positive mood during pregnancy and the postpartum period, but approximately 15-20% of postpartum women experience elevated anxiety which can greatly interfere with mother-infant bonding and infant neurobehavioral development. One of the strongest predictors of elevated postpartum anxiety is a history of high anxiety. Furthermore, in humans and rodents, physical contact with neonates can produce a temporary anxiolytic effect. Here, we determined if anxiety in female rats is consistent across reproductive stages, and if females' "trait" anxiety renders them differentially sensitive to the anxiety-modulating effects of offspring touch. We observed anxiety behaviours in a large pool of diestrus virgins in a light-dark box and then mated the 20 most- and least-anxious females. Postpartum they were tested in an elevated plus maze (EPM) with or without the presence of offspring before testing. Undisturbed maternal behaviour was also observed. We found that virgin anxiety was positively correlated with postpartum anxiety, particularly if dams had been separated from pups before EPM testing. After sacrifice, we measured protein expression of tryptophan hydroxylase 2 (TPH2, enzyme responsible for brain serotonin synthesis) in the dorsal raphe of the brain, and dopamine beta hydroxylase (DBH, enzyme responsible for brain noradrenaline synthesis) in the brainstem. In dams that were previously low-anxious virgins, high-licking dams expressed more TPH2 in the dorsal raphe than low-licking dams. Lastly, in the non-separated group, high-anxious females expressed less DBH in the brainstem than low-anxious females. Our results suggest that anxiety is stable across these two reproductive stages, and that some behavioural differences among dams are related to brainstem serotonin and noradrenaline expression. **Acknowledgements**: We would like to acknowledge Eman Ahmed, Sarah Armstrong, Kaitlyn Harding, and Katrina Linning for assistance with this project. This research was supported by NIH Grant #R01HD057962 to JSL.

## P82 "POSTNATAL" DEPRESSION IN MOTHERS AND FATHERS: DIFFERENTIAL EFFECTS ON PARENT-CHILD INTERACTION AND CHILD OUTCOME

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Maternal depression in the postnatal period is often associated with an overall decrease in responsiveness in interactions with infants, and with an increased risk of behavioural and emotional difficulties in children. The extent to which these associations are causal, and the

exact mechanisms by which risk transmission may occur is still uncertain in humans, though animal studies provide useful insights. The study of depression in fathers, early in childrens lives, gives an additional potential window into understanding the effects and impact of depression on children. Data from two longitundinal studies (the Oxford Fathers Study and the Avon Longitudinal Study of Parents and Children - ALSPAC) demonstrate differences in two areas. First, whereas depression in mothers in the postnatal period is associated with decreased responsiveness towards the infant, depression in fathers does not appear to affect this aspect of interaction; instead being associated with decreased engagement and less physicality in interactions. Second, maternal depression is associated with an increase in both emotional and behavioural problems in boys and girls, whereas depression in fathers appears to have a greater impact on boys than girls. The findings provide intriguing insights regarding putative mechanisms of risk, and also about potential targets for clinical intervention. Acknowledgments: Funding for both these studies was provided by the Wellcome Trust. The ALSPAC study additionally received funding from the Medical Research Council, UK, and the University of Bristol.

**P83 LONG LASTING EFFECTS OF EARLY INTERVENTIONS ON MATERNAL EMOTIONAL RESPONSE – PRELIMINARY DATA FROM A TRANSLATIONAL STUDY**

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Early environmental interventions have been extensively studied in pups using animal models. However, long term effects on the mother are poorly studied. This study aimed to verify if neonatal adversity induces lasting effects on maternal emotional response increasing their risk for depression; to verify this hypothesis, we used an animal model and also preliminary data from a human birth cohort study. Neonatal handling was used as a rat model of environmental adversity. We evaluated maternal behavior, response to stress (restraint 1hour/day for 7 days), depressive-like behaviors with forced swimming test (FST), baseline serum corticosterone and the adrenal weight after FST. We used the following instruments from preliminary results of IVAPSA birth cohort study (Bernardi, et al., 2012): What Being the Parent of a New Baby is Like; Karitane Parenting Confidence Scale; Perceived Maternal Parenting Self-Efficacy and the level of the Mother's Perceived Stress; depression was evaluated with Edinburgh Postnatal Depression Scale (EPDS). Dams of handled group show an altered maternal behavior and stress response, increased adrenal weight (only after stress) and also depressive-like behavior during FST training, independently of exposure to stress after weaning. Results in humans (n~130) apparently agree with these findings since EPDS scores were more associated with the parental skills than to perceived stress in the first month of the infant's life. Mothers reporting difficulty and less ability to deal with their newborns also have higher EPDS scores. Early environmental adversity can affect maternal behavior, emotional responses and predispose the mother to depression. Using this translational approach, we saw similar associations both in the animal model as well as in the human cohort. Our study is limited by the small n and lack of a prenatal depression assessment. **Acknowledges:** We would like to thank all members of IVAPSA study for their help and support. **Support:** CAPES, PRONEX-FAPERGS-CNPq

**P84 SEX HORMONES MEDIATE THE EFFECT OF EARLY LIFE STRESS ON HEDONIC SENSITIVENESS TO NATURAL REWARD**

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Aversive events during early life induce persistent epigenetic modifications that lead to neurobehavioral impairments in the individual. We have shown that prenatal restraint stressed (PRS) rats (45 min/day, the last 10 days of gestation) exhibit depressive-like disorders and increased vulnerability to drugs of abuse, with high propensity to self-administration and enhanced sensitivity to locomotor-activating effect of psychostimulant drugs. Interestingly, PRS acts in a sex-dependent manner with males and females displaying two distinct anxiety-like and neurochemical profiles. To further understanding mechanism underlying these sex effects we investigated possible sex differences in PRS and control rats in preference for natural high palatable (HP) food reinforcing stimulus (chocolate) in a conditioned place preference paradigm. We found that PRS induced a clear cut dimorphic profile with enhanced preference for natural reinforcement in males while PRS reduced it in females. Then, we addressed the issue of gonadal modulation in PRS-induced effect by comparing the behavior of adult intact, castrated, dihydrotestosterone (DHT, a testosterone metabolite *via* the 5-α reductase)- or testosterone-replaced PRS and control males. We report that in PRS males, DHT and not testosterone was involved in HP-food preference. Indeed, testosterone supplementation in adulthood exacerbated PRS rat sensibility to HP food-rewarding stimulus, while supplementation with finasteride, which blocks 5-α reductase, and thus conversion of testosterone into DHT, inhibited their preference. In addition, in controls, orchidectomy and testosterone replacement had no effect, whereas DHT replacement induced high preference. We also compared ovariectomized controls and estrogen ($E_2$)-replaced PRS females. $E_2$ supplementation induced preference in PRS rats, while ovariectomy decreased sensitiveness in controls. In conclusion, our results indicate that PRS exerts a strong impact in rat preference to natural reward and eliminates the natural sex differences in food preference. DHT, in males, and $E_2$, in females, play a key role in modulating sex dimorphic effects on this preference.

**P85 NEURAL PLASTICITY IN HUMAN FATHERS'BRAINS DURING THE EARLY POSTPARTUM PERIOD**

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The purpose of this study was to investigate the fathers' brain plasticity responsible for parental behaviors during the early postpartum period. In a previous longitudinal study we found in new mothers a grey matter (GM) volume increase in prefrontal cortex, hypothalamus, amygdala, and substantia nigra, which have an important role in maternal motivation and attuned behaviors, and in association to the thalamocingulate circuits were found involved in human maternal BOLD response associated to own infant cry and picture [Kim et al., 2010; Barrett&Fleming, 2010; Swain, et al., 2007; Swain, 2011]. However, anatomical changes and their relationships with parenting behaviors have never been examined in human father despite the importance of paternal care for child development. In this longitudinal study we investigated in a sample of 16 new fathers the GM volumes change amongst 2-4 weeks(T1) and 3-4 months(T2) postpartum. All analysis included covariates − fathers' age, first-time father, and scan interval between the two time-points considered. The voxel Based Morphometric (VBM) longitudinal analysis revealed an increase in GM Volumes ($p<.001$,FDR-corrected) from T1 to T2 in a great cluster referred to the left subgenual cingulate and striatum regions, important regions for parental motivation. This GM increase was correlated negatively with paternal preoccupation regarding infant's needs and well-being ($p<.032$), and the degree of the depression levels ($p<.033$) at T2. VBM longitudinal analysis revealed also a decrease in GM Volumes ($p<.01$,FDR-corrected) from T1 to T2 in a cluster centered on the right Orbitofrontal Cortex (OFC) . Decrease in OFC, a region involved in mood regulation, is correlated positively with the development of a positive father-child relationship ($p<.013$), and negatively with the level of paternal intrusiveness during dyadic interactions ($p<.044$). Results evidenced a relation between the emergent paternal role and attachment, and cerebral plasticity in regions previously similarly associated with maternal sensitive parenting behaviors.

**P86 A STUDY OF FUNCTIONAL CONNECTIVITY ANALYSIS IN NEW MOTHERS DURING THE EARLY POSTPARTUM PERIOD**

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Sensitive parental responses to infant signals play an important role in a child's emotional, social, and cognitive development. Neuroimaging studies using infant stimuli (i.e. cry or pictures) revealed the neurobiological substrates that are important for maternal motivation and sensitive behaviors, including the hypothalamus and amygdala [Swain, et al.,2007;Swain, 2011]. The studies also suggest the role of the anterior cingulate cortex and prefrontal cortex in processing and intergrating the infant-related somatosensory information and emotion regulation [Barrett&Fleming,2010]. However, how activity of these different neural regions while processing infant related stimuli are functionally connected to support sensitive parenting has never been examined. In a sample of ten new mothers, the current study investigated the functional connectivity (FC) amongst regions involved in response to mothers' own baby cry and control baby cries, at 2-4 weeks post-partum. For the seed location we focus on the right subgenual anterior cingulate cortex (sgACC, BA24,25,32). The FC analysis in response to own baby cry revealed significant positive functional connections of the sgACC activitiy with the left dorsal posterior cingulate cortex, left ventral ACC, and right orbitofrontal cortex activity (*ps*<.05,FDR-corrected). On the other hand, in response to control baby cry, significant positive functional connections were found among the sgACC activity and bilateral insular cortex and left dorsal ACC (*ps*<.05, FDR-corrected). Results evidenced in new mother the sgACC are functionally connected with several other cingulate regions in response to both own and control baby cry; however with the orbitofrontal cortex, a region that are important for maternal motivation amd mood regulation, only in response to own baby cry. We will update and present the results of the FC analysis and the relations between the FC and observed maternal behaviors during interactions with fiants from 28 mothers at the conference.

**P87 SOCIAL STRESS DURING LACTANCY AS AN ANIMAL MODEL FOR STUDYING DEVELOPMENTAL EFFECTS OF EARLY VIOLENT ENVIRONMENT**

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Early violent environment has been a consistent component of human society. Although different kinds of violence can be described, all have significant impact on children development. The outcomes and mechanism through which early violence impact physical and psychological development are still barely known, and ethological animal models for the

study of early violent environment effects are scarce. Wistar rats (8 weeks old) were supplied by the Animal Breading center of the Federal University of Rio Grande do Sul. At the age of 11 weeks, female estrous cycle evaluation began. On the evening of pro-estrous, each female were caged with one male for breeding. Pregnant females were kept 3 per cage until gestational day 19 and then isolated on new home-cages for labor. The day of birth was consider post-natal day 0 (PND-0). On PND1 all litters were set to 8±1 pup. On PND-3, 5, 7 and 9 a male intruder, 320–420 grams, was inserted in the home cage of the treated group, between 3 and 4 hours after lights on, for 5 minutes. Controls were left undisturbed. Treated male pups display significant less body weight on almost all days analyzed (PND-24 to 120). Treated group average body weight stays at 90% of the control group. Male and female pups diplayed increased anxiety-like behavior on elevated plus maze (PND-29) in comparison to controls of the same gender. Males also display significant cognitive loss on elevated T-maze and object recognition (PND-120). The animal model we propose is build upon ethological bases, having strong construct validity. Anxiety, body mass changes and cognitive loss are expected outcomes in humans exposed to early violent environment, confirming the face validity of the model. This preliminary data supports the use of social stress during lactancy as a possible animal model for studying early violent enviroment effects.

**P88 THE MATERNAL HORMONE IN THE MALE BRAIN: CENTRAL RESPONSIVENESS TO PROLACTIN IN MALE VS FEMALE MICE.**

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As the coordinator of lactation and maternal behaviour, prolactin deserves the title of "maternal hormone". However, the role of prolactin in the male brain has received little attention. Is prolactin promoting paternal behaviour? Is aggression, which in females is a strictly maternal behaviour, also modulated by prolactin in males? We have tackled these questions by evaluating brain responsiveness to exogenous prolactin on male and female mice, using immunohistochemical detection of PRL-induced phosphorylation of STAT5 (pSTAT5). As far as we know, this work constitutes the first attempt at evaluating the functional responsiveness to PRL in the male mouse brain. Under similar levels of prolactin, some nuclei showed pSTAT5-ir cells in both males and females, although females displayed generally more labelled cells. These include: a) the septofimbrial nucleus; b) the anteroventral and periventricular preoptic nuclei; c) the arcuate and ventromedial (VMHVL and VMHC) nuclei in the tuberal hypothalamus, as well as an area lateral to the latter; and d) the medial (MePD), central amygdala (CeM) and the intervening intraamygdaloid BST (bed nucleus of the stria terminalis). Several centres showed pSTAT5-ir only on females, including: a) the lateral septum; b) the whole BST and preoptic area (MPO, MPA, LPO); c) most of the anterior and tuberal hypothalamus (Pa, DMH, LH, MTu), subthalamus and zona incerta; d) the ventral medial (MePV) and basomedial amygdala (BM); and several regions of the periaqueductal grey and dorsal tegmentum. Our findings reflect a strong sexual dimorphism in the response to prolactin in most of the socio-sexual brain, including the key centres of maternal behaviour (BST-medial preoptic area). Interestingly, the hypothalamic area for aggression shows sensitivity to prolactin both in males and females, thus suggesting a role

for PRL in maternal aggression and, maybe, a modulatory action on intermale aggression. Funded by the MICINN-FEDER (BFU2010-16656).

**P89 EMERGENCE OF KISSPEPTIN EXCITATION OF OXYTOCIN NEURONS IN PREGNANCY**

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Oxytocin is synthesised by hypothalamic supraoptic nucleus (SON) and paraventricular neurons and is released from the posterior pituitary gland into the circulation to contract the uterus for delivery of the baby, and to contract the milk ducts for delivery of milk to the baby during suckling. We have shown that intracerebroventricular (ICV) kisspeptin does not affect the activity of SON oxytocin neurons in urethane-anaesthetized virgin rats (1). By contrast, we have now found that ICV kisspeptin causes an immediate, robust increase in oxytocin neuron firing rate in all SON oxytocin neurons recorded from rats on days 18 – 21 of pregnancy. The firing rate of some neurons returned to baseline within 10 min, but the higher firing rate persisted for tens of min in the remaining neurons. We are currently investigating the functional impact of the emergence of this central kisspeptin excitation of oxytocin neurons on pregnancy outcomes. Supported the Health Research Council of New Zealand

**P90 PATERNAL CARE IS CRITICALLY INVOLVED IN THE DEVELOPMENT OF CORTICOTROPIN RELEASING FACTOR (CRF)-EXPRESSING NEURONS IN THE RODENT ORBITOFRONTAL CORTEX, AMYGDALA AND HIPPOCAMPUS**

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In a variety of species including humans, both, the mother and father engage in the upbringing of the offspring. So far, the majority of experimental studies have focussed on the contribution of maternal care on the development of the brain and behavior of their offspring. In the biparental rodent Octodon degus we are testing the hypothesis that paternal care exerts a critical impact on brain development of his offspring. Here we show that three week old degus which were raised with their father display reduced densities of CRF-containing neurons in the orbitofrontal cortex (OFC) (lateral OFC: -69%, ventromedial OFC: -69%) and in the basolateral amygdaloid complex (- 44%). In contrast, in the dentate gyrus (+115%), and the innate dentate granule cell layer (+52%) three week old animals reared with their father showed increased densities of CRF-containing cells. These neurodevelopmental effects of paternal care are no longer detectable in adulthood. Taken together, this is the first evidence that paternal care affects the developmental time course

of stress-related CRF neurons in central prefrontal and limbic neuronal circuits. *Supported by grants from the BMBF (UBICA, TRANSGEN), the German-Israeli Foundation (GIF 101/2011), the Center of Brain and Behavioral Sciences (CBBS) and the European Regional Development Fund (ERDF).*

## P91 A COMPARATIVE STUDY OF PARENTING IN MOTHERS WITH SCHIZOPHRENIA

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**Background**: Schizophrenia poses formidable challenges to being a parent,due to the illness itself and from associated socioeconomic problems. Schizophrenia often reduces the ability to discern nonverbal cues, recognize affects from facial expressions, and negotiate social situations. Parenting adequacy, rather than optimal parenting, seems to provide the safest criterion for both children and mothers. **Aims**: to assess the parenting in mothers with schizophrenia and to examine if the facial emotion recognition deficits have an association with parenting. **Methodology**: The study included consenting subjects attending outpatient psychiatric services NIMHANS who have received a primary diagnosis of schizophrenia as confirmed by DSM-IV and were compared to controls(those without any psychiatric diagnosis).Tools include Positive and Negative Syndrome Scale, Parenting scale(Arnold et al),Parent Interview Schedule. TRENDS (Tool for Recognition of Emotions in Neuro-psychiatric Disorders)was used after modifications(children's photos were used instead of adults) for assessing emotion recognition in mothers with schizophrenia. **Results:** A total of 20 subjects were compared to 20 controls. The Positive symptom score and negative score in the subjects with Schizophrenia were 0-20 and 0-10 respectively. Emotions recognition in the mothers with schizophrenia was impaired compared to controls especially disgust,fear and surprise. Controls rated better on parenting aspects compared to mothers with schizophrenia. **Conlusions:** The above findings highlight the possibility of facial emotion recognition deficits in mothers with schizophrenia and its effect on parenting.

## P92 MATERNAL BEHAVIOR IN HETEROZYGOUS SF-1 KNOCKOUT MICE

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Parental behavior and care for offspring play an important role in offspring's survival. Maternal behavior in mice involves nest building, retrieving pups to the nest, nesting, licking and nursing the pups. In the mouse brain, the preoptic area and bed nucleus of the stria terminalis are thought to be involved in the regulation of maternal behaviors. Previous studies have shown that maternal behavior in mice of both sexes starts spontaneously within a few minutes after exposure to pups Mice with one disrupted allele of *sf-1* (SF-1+/-)

and wild type (WT) mice were tested for maternal behavior. Results revealed statistically significant difference in maternal behavior, especially in the retrieval of individual pups to the nest between WT and SF-1 +/- female mice with SF1+/- females needed more time for individual retrieves and spending less time nursing the pups. As reduced maternal behavior could be caused by an increase in anxiety- or depressive-like behaviors, mice were tested in elevated plus maze (EPM) and forced swim test (FST). There were no differences between groups in these behaviors, suggesting a specific effect of haploinsuficiency for the *sf-1* gene on maternal behavior. As reduced maternal behavior could be caused by poor maternal care by SF-1 +/- mothers of tested mice, pups from SF1+/- and WT mothers were cross-fostered on postnatal day 3. Pups from WT dams were given to SF1+/- dams and vice versa. In adulthood, females from these cross-fostered litters were tested for maternal behavior, depressive-like and anxiety-like behaviors. Results revealed that both WT and SF-1 +/- cross-fostered females had severely reduced maternal behavior in comparison to non-cross-fostered females while they performed similarly in the EPM and FST tests. These results suggest that cross-fostering has deleterious effects on maternal behavior in mice independent of any effects on anxiety and depressive-like behaviors.

## P93 THE MECHANISMS OF INDUCTION OF AMYLIN IN THE PREOPTIC AREA OF LACTATING DAMS

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Amylin, a peptide previously known as a pancreatic hormone, was found to be expressed in the preoptic area of mother rats in our recent microarray study. The increase in mRNA expression was validated by RT-PCR and the appearance of the peptide was detected by immunohistochemistry. Examining the time course of amylin induction, we found that amylin is not expressed in the brain before and during pregnancy but its significant increase was observed in rats and mice immediately after parturition in the preoptic area, a region whose lesion abolishes maternal behaviors. Ovariectomy had no effect on the activation of amylin neurons suggesting sexual steroid independent mechanisms. Within the preoptic area, the distribution of amylin neurons was the same as the neurons showing Fos activation by pup exposure: medial preoptic nucleus, parts of the medial preoptic area, and the ventral part of the bed nucleus of the stria terminalis. Amylin expression was also induced in virgin but maternally behaving (sensitized) virgin females with the same expression pattern as in dams. Almost all amylin neurons expressed Fos in response to pup exposure suggesting their activation in dams. Since our previous studies suggested that maternal motivation may be modulated by posterior thalamic neurons expressing tuberoinfundibular peptide of 39 residues (TIP39), we examined the relationship of amylin and TIP39. Fiber terminals containing TIP39 and the parathyroid hormone 2 receptor (the receptor of TIP39) have the same distribution as amylin neurons in the preoptic area. Furthermore, amylin neurons were closely apposed by TIP39 terminals suggesting their innervation by TIP39 neurons. These results imply that amylin is a novel neuropeptide with maternal functions, and that its maternal induction could be driven by posterior thalamic TIP39-containing neurons that

demonstrate a similar time course of maternal activation. **Acknowledgements:** Bolyai János Fellowship of the HAS, OTKA K100319 research grants.

## P94 STEROIDS HORMONES AND MORPHINE TREATMENT ALTERS BEHAVIOR PATTERN AND OPIOID GENE EXPRESSION IN FEMALE RATS

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The regulation of the secretion of pituitary gonadotropins results from a complex interplay between gonadal steroids and the influence of brain neurotransmitters in the hypothalamic-pituitary-adrenal axis. Studies show that this phenomenon involves brain opioid peptides that exert an inhibitory influence on gonadotropin secretion. Different types of brain opioids, such as beta-enkephalin, enkephalin, and dynorphin, exert their action by binding to specific opioid receptors (i.e., mu, delta, and kappa, respectively). Thus, the aim of the present study was to determine the effects of chronic treatment with morphine, estrogen, and progesterone on *Oprm1*, *Oprd1*, and *Oprk1* gene expression, mu opioid receptor (MOR), delta opioid receptor (DOR), and kappa opioid receptor (KOR) protein expression in the hypothalamus, striatum, and periaqueductal gray, and physiological and behavioral processes in adult virgin female ovariectomized rats. The results showed that chronic morphine treatment increased total locomotion and grooming behavior, decreased immobility time, and increased the latency to the first mount. The molecular biology results showed that morphine treatment increased *Oprm1* gene and MOR protein expression in the striatum. Additionally, a decrease in KOR protein expression was observed in the hypothalamus in animals that were assessed for general activity. The animals that were evaluated for sexual behavior exhibited an increase in *Oprm1* expression in the periaqueductal gray and an increase in KOR expression in the striatum. Altogether, these results suggest that both opioid system activation and sex hormones alter behavioral and molecular patterns in ovariectomized rats within a relatively short period of time. Support: FAPESP (2010/19970-1).

## P95 NEUROBIOLOGY OF MOTHER-INFANT BONDING PROCESS IN WOMEN WITH SEVERE POSTPARTUM PSYCHIATRIC DISORDERS - STUDY PROTOCOL AND PRELIMINARY DATA

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It is increasingly recognized that mother-infant bonding and affiliative behaviors are primarily mediated through the neurohormone oxytocin and there is an association with oxytocin receptor gene (OXTR) polymorphisms [1,2]. This vital evolutionary process is disrupted in women with postpartum psychosis. We present the initial findings of an ongoing research at NIMHANS, to understand the neurobiology of the mother-infant bonding in postpartum psychosis. Consecutive women with postpartum psychosis (severe mental illness during first 6 months of postpartum period) are recruited after an informed consent. Clinical and demographic details are recorded along with structured assessments using Brief Psychiatric Rating Scale (BPRS), Postpartum Bonding Questionnaire (PBQ), Edinburgh Postnatal Depression Scale (EPDS). Patients are then sampled for studying the OXTR gene polymorphisms. Thirty eight women with severe postpartum psychosis have been enrolled for the study over past 6 months. The mean age is 24.66 years (4.72) and mean baby age is 79.32 days (46.36). 17 (44.7%) patients have a diagnosis of acute psychosis, 14 (36.8%) patients of a mood disorder and 7 (18.42%) patients of a psychotic disorder. The mean BPRS score is 54.16 (18.84), mean EPDS score is 10.74 (6.03) and mean PBQ score is 26.74 (23.30). On F1-F4 subscale analysis of PBQ, mean F1=12.79 (10.86); mean F2 =8.58 (8.22); mean F3=4.03 (4.12); and mean F4=1.34 (2.41). There is a significant and strong correlation between total BPRS scores and total PBQ scores (r=0.50, p=0.001) and between total EPDS scores and total PBQ scores (r=0.60, p=0.000). As indicated by the preliminary findings, mother-infant bonding is related to the illness severity. The current study aims to unravel the neurobiology of this process by having a matched healthy control group for comparison of OXTR gene polymorphisms and behavioral phenotypic characteristics of the study populations. It is necessary to focus on subgroup of patients exhibiting infant harm.

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## P96 FAMILY MATTERS: BEING REARED IN OVERLAPPING LITTERS MODIFIES THE MATERNAL BEHAVIOUR OF ADULT FEMALE RATS

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Newborn pups reared in overlapped litters (OL: two different aged litters sharing the maternal nest) receive a different pattern of maternal stimulation compared with those

reared in control litters (CL: one litter with same aged pups). Thus, mothers reduce some maternal behaviour (MB) components (i.e. licking) towards them and, interestingly, juvenile pups from the first litter develop MB complementing the behaviour exherted by the mother. As early-life experience modulates rodents' brain function and MB is transmitted through generations, we hypothesized that the altered pattern of maternal stimulation received by pups reared in OL will modify their behaviour at adulthood. To probe this hypothesis we compared the maternal and affective behaviours of lactating rats that were reared under OL and CL conditions. The MB of the dams was recorded from day 1 to 7 postpartum and the maternal aggression and the anxiety behaviour in the plus-maze test were assessed on day 8 of lactation. As previously found in mothers with OL, female offspring from OL showed a decrease in licking behaviour and an increase in the time spent off the nest, as well as changes in nursing postures. However, the accompanying affective behaviours characteristic of lactation, increased aggression toward intruders and decreased anxiety, did not differ between OL and CL dams. Present results show that the modified early rearing environment product of the overlapping of litters shapes the behaviour of the females conditioning their own MB at adulthood. This effect probably is due to the different pattern in the behavior of mothers with OL, despite the MB exhibit by juveniles siblings. Acknowledgments: SNI-ANII and PEDECIBA for financial support.

**P97 PARENTAL OXYTOCIN DURING PARENT-INFANT INTERACTION IN SKIN-TO-SKIN CONTACT AFTER CESAREAN SECTION**

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Skin-to-skin contact (SSC) with the newborn infant during the first two hours after a vaginal birth stimulates a pre-programmed breastfeeding behavior in the infant, facilitates interaction between mother and infant and increases maternal oxytocin levels. Little is known about the effect of parent-infant skin-to-skin contact on parental oxytocin (OT) release immediately after a Caesarean section. In this report we compare the levels of OT during the first two hours after a planned caesarean section in mothers with or without skin-to-skin contact the first 30 minutes after birth and in fathers with or without skin-to-skin contact the first 30 minutes after birth. Healthy newborns were included and randomized to ultra early skin-to-skin contact following birth either with the mother or the father after five minutes skin-to-skin contact with the mothers. Blood-samples were collected in mothers and fathers up to two hours. OT levels were analyzed by RIA. The parent-infant interaction was videotaped and a protocol was developed. In this talk I will present some preliminay results and the findnings higlights the importance of immediate infant-parent skin-to skin contact after birth with Cesarean Section. The parents interacted differently with their infant. Mothers touched boys more than girls and fathers directed more speech towards boys than to girls. During the first hour after birth the OT levels in both mothers and fathers showed a rise irrespective of being in skin to skin contact with the infants or not. These results may

reflect a sensitive period after birth, when both mothers and fathers have increased oxytocin levels, which might facilitate bonding to the newborn infant.

## P98 CORTICOSTERONE SYNTHESIS INHIBITOR METYRAPONE PRESERVES CHANGES IN MATERNAL BEHAVIOR AND NEUROENDOCRINE RESPONSES DURING IMMUNOLOGICAL CHALLENGE IN LACTATING RATS

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It has been shown that lipopolysaccharide (LPS) can modulate prolactin (PRL) and oxytocin (OT) secretion. Therefore, we investigated effects of LPS on behavioral and hormonal responses of lactating female rats. Using metyrapone (glucocorticoids synthesis inhibitor), we also investigated whether these responses are mediated by glucocorticoids release, since it also modulates PRL and OT secretion. Lactating female rats (seventh lactation day) were divided into three groups (n=7): saline/saline, saline/LPS and metyrapone/LPS. Rats were treated with saline (1 mL/kg, i.p.) or metyrapone (50 mg/kg, i.p.) 10 and 2 hours before administration of LPS (500 µg/kg, i.p.) or saline (1 mL/kg, i.p.). The litter was removed from home cage and 2 hours after saline or LPS administration, pups were replaced in home cage and filmed during 30 minutes. In order to evaluate hormonal changes, blood samples were collected 15 minutes after the beginning of breastfeeding. Experiments were conducted with approval of Ethics Committee (255/2009). LPS treatment decreased licking pups (390.40±33.19 to 168±25.61s; $p < 0.001$), arched-nursing position (41.08±2.74 to 20.35±2.69 %; $p < 0.001$) and total maternal behavior (28.02±4.60 to 8.44±2.57 %; $p < 0.01$) when compared to control treatment. Pretreatment with metyrapone increased licking pups (168±25.61 to 275.00±51.25s; $p < 0.05$), arched-nursing position (20.35±2.69 to 59.44±4.09 %; $p < 0.001$) and total maternal behavior (8.44±2.57 to 43.71±6.73%; $p < 0.001$) when compared to LPS treatment. LPS treatment reduced OT (from 55.6±16 pg/mL to 11.9±3.8 pg/mL; $p < 0.05$) and PRL secretion (545±119 ng/mL to 167±31 ng/mL; $p < 0.05$) when compared to control. Metyrapone treatment increased OT (from 26.1±4.5 pg/mL to 49.7±8.2 pg/mL; $p < 0.05$) and PRL secretion (75.3±29 ng/mL to 334±37 ng/mL; $p < 0.05$) when compared to LPS treatment. LPS treatment attenuates maternal behavior in lactating female rats, followed by reduction in PRL and OT secretion. These changes may be due to glucocorticoids release because metyrapone reversed the behavioral and neuroendocrine responses produced by LPS.

**P99 MODULATION OF STRESS RESPONSIVENESS BY CALORIC DRAIN IN LATE LACTATING FEMALES**

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Lactating female rats exhibit a blunted responsiveness to several types of stressors. Although early lactating rats (PPD3-5) retain normal HPA responsiveness when the stressor represents a direct threat to the pups, late lactating (LL) females (PPD 14-16) display blunted responses regardless of stressor salience. Thus different mechanisms might contribute to stress hyporesponsiveness at different stages of lactation.We tested the hypothesis that the greater caloric drain in LL dams contributed to this difference in responsiveness by either eliminating milk output through cutting the galactophores (GC) prior to mating or providing a highly palatable diet supplement (DS). The effect of sweet taste alone was investigated by providing females with saccharin solution. Stress responses (CRF mRNA, plasma ACTH and CORT) to a tail clip stress (30min) were compared between virgin and LL females. Removal of the metabolic drain of lactation without eliminating the suckling stimulus partially restored the ACTH response to stress. LL mothers given access to the DS ate more calories, which were almost exclusively redirected toward their pups. In contrast, virgin females given access to the DS had higher body and fat pad weights than virgins on chow only. Access to DS did not affect expression of CRF in the PVN 90 min after tail clip in either virgins or dams, but it modestly reduced integrated ACTH responses to stress in both virgins and LL mothers and peak CORT secretion in mothers. Saccharin intake did not modify neuroendocrine responses in either reproductive state, suggesting that sweet taste alone is insufficient to alter stress responsiveness. Our results suggest that the increased caloric demand of lactation might partially contribute to the reduced HPA responsiveness of LL females but that suckling stimulation from the pups can also, directly or indirectly, suppress HPA responsivity. Supported by CIHR grant to BW and CDW.

**P100 THE CENTRAL VASOPRESSIN SYSTEM FACILITATES MATERNAL AGGRESSION IN LACTATING AND PUP SENSITIZED NULLIPAROUS RATS**

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Maternal aggression is an important component of maternal behaviour and the presence of offspring is required for its maintenance. Maternal aggression is modulated by offspring cues, with the intensity of aggression diminished when offspring are removed from the dam. Previously we have shown that the central vasopressin and oxytocin systems play a key role in regulating maternal behaviour, including maternal aggression. Dynamic transformations in specific brain oxytocin and vasopressin systems parallel the intensity of maternal aggression expressed across the peripartum period (e.g. Caughey et al. 2012).Here we investigated the role of central vasopression V1a receptors on maternal aggression and

immediate early gene (c-*fos*) expression in specific hypothalamic and limbic brain regions in lactating primiparous rats. We combined behavioural testing and Fos immunocytochemistry following intra cerebroventricular injection of a V1a-antagonist (V1a-A) or vehicle. V1a-A significantly attenuated all aspects of maternal aggression and Fos expression was significantly reduced in specific brain regions including the bed nucleus of the stria terminalis (BnST) and the paraventricular nucleus (PVN). Furthermore, we found significant correlations between Fos expression in the BnST and attack latency, and between Fos expression in the supraoptic nucleus (SON) and aggressive behaviour. In our second study we sought to determine the role of central V1b receptors (V1b) on maternal aggression in pup sensitized nulliparous rats. Fierce displays of pup protection are observed in nulliparous female rats that have been exposed to pups. Following subcutaneous V1b-antagonist (V1b-A) treatment all measured maternal aggressive parameters were significantly reduced compared to vehicle controls.Collectively, these studies provide further evidence to support the hypothesis that central vasopressin facilitates maternal aggression in rats displaying maternal care. Caughey et al (2011) J. Neuroendocrinol. 23:1113-1124. **Acknowledgements:** Research supported by the BBSRC (SLM).

## P101 MOTHERS WITH POSTPARTUM DEPRESSION SHOW REDUCED BRAIN RESPONSE TO OWN BABY IN THE MESOCORTICOLIMBIC DOPAMINE PATHWAY

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Neuronal activity within the nucleus accumbens (NAC) is modulated by dopaminergic input from the ventral tegmental area (VTA). Rewarding stimuli have been associated with activity in these regions. For example, the NAC and VTA are activated when mothers are viewing pictures of their own compared to an unfamiliar infant (Strathearn et al., 2008). This highlights the potential role of these regions in human goal-directed maternal behaviour and memory for infant-like features and is consistent with an extensive animal literature relating NAC dopamine to reward and mothering (Afonso et al., 2011; 2012; Numan et al., 2006). Mothers with postpartum depression (PPD) demonstrate altered processing of hedonic stimuli and show an altered ventral striatal reward response (Moses-Kolko et al., 2011), yet much remains to be understood about the neural bases of the altered hedonic processing in PPD. In humans, the ventral striatal reward response is thought to be directly modulated by the dorsolateral prefrontal cortex (DLPFC). As a result, using fMRI and block design, we investigated the brain response to smiling own (OWN) and smiling unfamiliar infant faces (UNF), in mothers with PPD (n=32) and without PPD (n=25), as determined by structured clinical interview based on DSM-IV-TR criteria. We adopted a region-of-interest approach to examine activation in the DLPFC, NAC and VTA, using simple mixed effects-group analyses. Preliminary results show that BOLD-response in the left NAC and bilateral DLPFC and VTA is greater in mothers without PPD compared to mothers with PPD. In mothers without PPD, BOLD responses are greater to own as opposed to an unfamiliar baby, differences which are not present in mothers with PPD. The blunted DLPFC response that we observe in mothers

with PPD may have an influence on the VTA and NAC reward response, which may ultimately impact their maternal behavior.

**P102 FLUOXETINE REVERSES DISRUPTED MATERNAL CARE BUT NOT DEPRESSIVE-LIKE BEHAVIOR IN A MODEL OF POSTPARTUM DEPRESSION**

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Women are twice as likely as men to suffer from depression and the postpartum period confers considerable risk for developing depression. Stress and glucocorticoids have been consistently associated with depressive disorders and individuals with depression generally have higher cortisol concentrations and impaired HPA axis negative feedback. In many rodent studies, chronic variable stressors or exogenous corticosterone (CORT; the primary glucocorticoid in most rodents) induce a depressive-like phenotype. However, most models of depression have primarily used males. Our prior research indicates that high CORT given to postpartum females reduces maternal care, increases depression-like behaviour, and alters hippocampal plasticity, which collectively represents a depressive-like phenotype. The goals of the present study were to understand how CORT alters behavior and the brain in females at different reproductive time points and to determine if a CORT-induced behavioral phenotype can be reversed using a common antidepressant, fluoxetine (FLX). Female Sprague Dawley rats were either mated or remained reproductively inexperienced (nulliparous) and then received either CORT or oil and FLX or saline (yielding 8 groups) every day for 22 days (for postpartum rats, this coincided with postpartum days 2-24). Maternal care was observed postpartum days 2-8 and depressive-like behaviors were assessed in the forced swim test (FST) on days 23-24. As previously established, postpartum CORT disrupted maternal care and increased immobility in the FST. Notably, FLX reversed CORT-induced changes in maternal care. However, FLX did not significantly decrease immobility in the FST in either nulliparous or postpartum females. However, nulliparous females spent more time immobile compared with postpartum females in response to CORT. We are currently investigating how CORT and FLX regulate hippocampal plasticity in this study. These data contribute to our understanding of how reproductive states may alter the susceptibility to depression and antidepressant efficacy in females.

## P103 READY FOR ACTION: A ROLE FOR THE HUMAN MIDBRAIN IN RESPONDING TO INFANT VOCALISATIONS

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Infant vocalisations are among the most biologically salient sounds in our environment. They attract attention and promote responses from parents and non-parents alike in both times of distress and joy. A region of the midbrain, the periaqueductal gray (PAG), has long been implicated in the control of urgent, survival-related behaviours. We tested whether the PAG is involved in the neural processing underlying responses to infant vocalisations. Local field potentials (LFPs) were recorded from macroelectrodes implanted in this region in four adults who had undergone Deep Brain Stimulation. We found a significant difference in activity in the PAG occurring as early as 49ms after listening to infant vocalisations compared to constructed control sounds. We also found significant differences at around 80ms between responses to infant vocalisations and adult and animal affective vocalisations. These differences were not present in recordings from thalamic electrodes implanted in three of the patients. Time frequency analyses revealed distinct patterns of activity in the PAG for the three sound categories. These results suggest that human infant vocalisations can be rapidly discriminated from other emotional or acoustically similar sounds subcortically, at an earlier stage of the auditory pathway than previously examined. We propose that this specific, rapid activity in response to infant vocalisations may reflect the initiation of a state of heightened alertness necessary to instigate protective parenting. **Acknowledgements:** This work was supported by the TrygFonden Charitable Foundation and the Medical Research Council, UK.

## P104 EVALUATION OF THE POLYMORPHISMS IN THE SEROTONIN TRANSPORTER GENE IN WOMEN WITH POSTPARTUM DEPRESSION

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**Introduction:** Postpartum depression (PPD) is a mood disorder. **Aim:** The purpose of the present study was to evaluate the association between the 5-*HTTLPR* and 5-*HTTVNTR* polymorphisms in the serotonin transporter gene (*SLC6A4*) in Brazilian women with diagnosed PPD and the presence of depressive symptoms. **Methods:** The cohort consisted of 128 white women from Pelotas, RS, who were characterized based on skin color and morphological characteristics**.** The Beck Depression Inventory (BDI) was used to diagnose PPD and to score the depressive symptoms. The promoter region of the gene containing the *5-HTTLPR* polymorphism and the region containing the second intron polymorphism *5-HTTVNTR* were analyzed by PCR-based methods. **Results**: The comparison of allele and genotype frequencies of polymorphisms among women who developed or not PPD were made by chi-square test with Yates correction ($p<0.05$). All subjects signed an informed consent form. The analysis of the distribution of genotype frequencies of polymorphisms showed that the population is under Hardy-Weinberg Equilibrium. No association was observed between the PPD diagnosis and either the 5-*HTTLPR* ($p=0.48$) or the 5-*HTTVNTR* ($p=0.77$) polymorphism. When the polymorphisms were analyzed together with haplotype data, the analyses demonstrated that women carriers of the L-12/L-12 diplotype have lower BDI scores (median:0.5; inter-quartile range:0.00-4.00; $p=0.04$) than women carrying other diplotypes (median:4.0; inter-quartile range:1.00-10.00). Our findings are important because few studies have investigated the association of haplotypes determined by the *5-HTTLPR* and *5-HTTVNTR* polymorphisms with PPD. In summary, we present evidence that postpartum women carrying the L-12/L-12 diplotype show less depression symptoms than those carrying other diplotypes. Moreover, this result implicates genetic variations in the serotonin transporter on the etiology of PPD. **Conclusion:** Present analyses may be considered an exploratory study for understanding PPD susceptibility in a specific life period, in which stress responses are considerably altered by several factors. Acknowledgements: Financial support CNPq.

**P105 CAN THE MOTHER AFFECT HOW PUPS REACT TO STIMULI? PUP'S FEAR EXPRESSION TOWARD UNFAMILIAR FEMALE ADULT RAT**

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Pups do not exhibit fear responses toward unfamiliar proestrus females (UPF) during the stress hyporesponsive period (SHRP) or afterwards. However, in the context of the home-cage, UPF represent an aversive stimulus for the mother and promote the display of maternal aggression and affect pups' care-taken activities. Since alterations of maternal behavior by the repeated exposure to an intruder promote pups' fear responses, we hypothesized that UPF can be conditioned as an aversive stimulus and exert fear responses in 8-day-old pups. To this aim, firstly we exposed mother-litters dyads in their home-cage to an UPF inside a cage (n=8) or an empty cage (n=8) from postnatal days 1-4. On postnatal day 8, one male and one female pups were exposed separately for 10 min to an anesthetized UPF and the number of ultrasonic vocalizations and immobility time were registered. Only female pups expressed fear responses toward the anesthetized female on postnatal day 8 (diminished ultrasonic vocalizations and increased immobility time). Secondly, to assess if the fear response toward the UPF was the result of a retrieval memory, UPF pre-exposed female pups (n= 6) were confronted to an anesthetized UPF on postnatal day 8 and then they were injected with cycloheximide (0.0, 0.2 mg/kg, sc.), a protein synthesis inhibitor that blocked the retrieval of consolidated memory. 24hs later they were re-exposed to an UPF and the fear responses were registered. Cycloheximide suppressed the expression of fear on postnatal day 9. These results suggest that pups can learn and avoid an aversive stimulus during the SHRP, probably as a consequence of changes in maternal behavior, and that these processes differ between sexes. Acknowledgements: CSIC and PEDECIBA for financial support

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## Programme Overview 5th Parental Brain, Regensburg, 11th - 14th July 2013

| Thu 11th | | Fri 12th | | Sat 13th | | Sun 14th | |
|---|---|---|---|---|---|---|---|
| | | **S 1 Maternal brain physiology** | | **Plenary PL-2** | | **S 6 Paternal behaviour** | |
| | | 8.30 - 8.55 | Dobolyi | 8.30 - 9.15 | Baram | 8.30 - 9.00 | Ziegler |
| | | 8.55 - 9.20 | Stolzenberg | | | 9.00 - 9.30 | Saltzman |
| | | 9.20 - 9.45 | Moses-Kolko | **S 5 Early life / adult soc behav** | | 9.30 - 10.00 | Champagne |
| | | 9.45 - 10.05 | Swain | 9.15 - 9.45 | Haller | **S 7 Hot Topics II** | |
| | | 10.05 - 10.30 | **Coffee break** | 9.45 - 10.15 | Sandi | 10.00 - 10.15 | Keebaugh |
| | | **S 2 Early-life adversity** | | 10.15 - 10.45 | Harold | 10.15 - 10.30 | Jonas |
| | | 10.30 - 11.00 | Maccari | 10.45 - 13.00 | **POSTERS 2 even numbers incl. lunch** | 10.30 - 10.45 | Moser |
| | | 11.00 - 11.30 | Krugers | | | 10.45 - 11.15 | **Coffee break** |
| | | 11.30 - 12.00 | Szyf | | | **S 8 Maternal brain plasticity** | |
| | | 12.00 - 13.30 | **Lunch** | | | 11.15 - 11.45 | Tsukamura |
| | | **S 3 Hot Topics I** | | FREE AFTERNOON<br><br>SOCIAL PROGRAMME | | 11.45 - 12.15 | Galea |
| | | 13.30 - 13.45 | Walker | | | 12.15 - 12.45 | Leuner |
| | | 13.45 - 14.00 | Perani | | | 12.45 | **CLOSING REMARKS** |
| | | 14.00 - 14.15 | Ragan | | | | |
| | | 14.15 - 14.30 | Zuluaga | | | | |
| | | 14.30 - 14.45 | Kuroda | | | | |
| | | 14.45 - 15.00 | Korosi | | | | |
| | | 15.00 - 15.30 | **Coffee break** | | | | |
| | | **S 4 Maternal mood & depression** | | | | | |
| | | 15.30 - 16.00 | Lonstein | | | | |
| 16.00 - 19.00 | **REGISTRATION** | 16.00 - 16.30 | Maguire | | | | |
| | | 16.30 - 17.00 | Meinlschmidt | | | | |
| | | 17.00 - 19.00 | **POSTERS 1 odd numbers incl. beer & brezel** | | | | |
| 19.00 - 19.15 | **WELCOME ADDRESS** | | | | | | |
| | **Plenary PL-1** | | | | | | |
| 19.15 - 20.00 | **Fleming** | **EXPLORE REGENSBURG BY NIGHT** | | 19.30 - 00.00 | **CONGRESS DINNER @ Historischer Salzstadl** | | |
| 20.00 - 22.00 | **OPENING RECEPTION** | | | | | | |