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## MATERNAL BEHAVIOUR IS MODULATED BY PRENATAL STRESS IN YOUNG BIRD

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Maternal behavior has a significant individual variability, as mothers take care differently to their young based on their own breeding experience or age. In this parent-youth system, we investigated whether the young played a role as modulator of maternal behavior. For this, we evaluated how adoptive quail (unstressed) raised chicks coming from stressed female (PS) or not (NPS) thank a social stress procedure during laying, known to modify the behavior of chicks. During breeding period, mothers showed no difference in the time spent warming. However, mothers of PS remained closer to their chicks than NPS mothers. These latter were more aggressive towards chicks throughout mothering. On the other hand, PS chicks had a different behavior during breeding period with more requests from their mother at the end. Finally, after mothering, PS and NPS chicks showed different profiles of emotivity and sociality. Results show that mothers respond to behavioral changes in chicks caused by prenatal stress, adapting their own maternal behavior. Behavioral development of these chicks is in turn influenced by maternal behavior. The mother-young relationship is a dynamic interactive system where the young plays a significant role.

## NEUROPSYCHOLOGICAL DEVELOPMENT AT 4 YEARS OLD: ASSOCIATION WITH SALIVARY CORTISOL, ALPHA-AMYLASE AND PSYCHOSOCIAL VARIABLES AT 14 MONTHS OF AGE

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Background and aims: Early life stress can have long-lasting effects on neurodevelopment. The aim of this study was to assess the association between stress system activity at 14 months of age and long-term

neuropsychological development at 4 years old, adjusting for the socio-demographic and the psychosocial variables that best predicted neuro-psychological development.

Method: The sample was part of a population-based birth cohort derived from the INMA (Infancia y Medio Ambiente [Environment and Childhood]) project in Gipuzkoa, Spain. The main analysis were based on 186 parent-child pairs with complete information on evening salivary cortisol and alpha-amylase levels at 14 months of age and child neuropsychological development at 4 years old. Multivariate regression analyses were used for the associations between both salivary cortisol and alpha-amylase and neuropsychological development.

Results: Both stress markers at 14 months of age showed an association with neuropsychological development at 4 years old. Salivary cortisol, showed a sex-specific pattern of association. In girls, cortisol levels at 14 months were negatively associated with long-term cognitive development (Long-Term Memory:  $\beta = -3.86$  [-6.7-(-1)];  $p = .010$ ; Executive function:  $\beta = -7.64$  [-15.3 to .03];  $p = .05$ ), whereas in boys cortisol levels were negatively associated with socio-emotional development (CAST scale: IRR = 1.35 [1.02-1.78];  $p = .03$ ). Salivary alpha-amylase was positively associated with socio-emotional development both in boys (CPSCS:  $\beta = 1.25$  [.12-2.5];  $p = .04$ ; Hyperactivity score: IRR = .83 [.70-.99];  $p = .045$ ) and girls (Hyperactivity: IRR = .80 [.67-.97];  $p = .02$ ).

Conclusion: Stress system's postnatal activity is associated with long-term neuropsychological development showing a sex-specific effect.

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## AMNIOTIC ODOR AS A CANALIZING EXPERIENCE

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Amniotic fluid contains chemical cues that serve as olfactory stimuli to activate the nipple attachment behavior of newborn rats. We added a novel olfactant to the amniotic fluid of rat fetuses and then paired the fluid with specific elements of labor and parturition (*viz.*, artificial labor contraction and birth canal compression, simulated maternal licking of the newborn, and postnatal thermal flux). Caesarian-delivered pups that experienced such pairings attached to the nipples sedated dams bearing the amniotic scent. Catecholamine titers also changed dramatically with these procedures. Thus, specific components of vaginal birth provide sufficient conditions for odor learning that canalizes the newborn's suckling behavior. In contrast, the absence of in utero compressions was associated with poor sucking onset. We will discuss how birth stimuli contribute to the first nipple attachment via release of catecholamines that co-act to constitute a context for learning to suckle. We will propose this learning

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as an *exaptation* based on processes that are primary adaptations to the critical transformation from uterine environment to postnatal life. Our perspective helps illuminate the challenges of suckling by babies born prematurely and thus do not experience the typical contingencies mediating onset of oral ingestion.

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#### INFANTS' PREFERENCE TO LOOK AT A SPEAKER'S MOUTH MODULATES ACTIVATION OF FRONTAL BRAIN AREAS DURING SPEECH PERCEPTION

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Infants' preference to look at a speaker's mouth has been related to their sensitivity for (mis) matches between auditory and visual speech cues. We extend these findings by investigating whether infants' recruitment of visual speech information modulates the neural processing of audiovisual speech. We presented 6-month-olds with matching and mismatching audiovisual speech and assessed (a) their preference to look at a speaker's mouth compared to her eyes, and (b) the activation of frontal brain areas. Results show stronger activation for matching than mismatching speech. Furthermore, activation in left frontal areas is modulated by infants' preference to look at the speaker's mouth.

#### THE ROLE OF ACETALDEHYDE IN THE PRENATAL ETHANOL EXPOSURE EFFECT ON THE NEONATE RAT

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It has been demonstrated that ethanol exposure on the last gestational days increases ethanol acceptance in neonate, infant and in adolescent rats. In previous experiments we have found that after prenatal exposure to ethanol, 1-day-old neonates recognize and crawl longer distances towards ethanol odor than neonates from water treated dams. We also found that manipulating the opioid receptor system decreases the prenatal ethanol exposure effect, reducing the attractiveness of ethanol odor. In addition to the relevance of the opioid system, acetaldehyde, the first metabolite of ethanol, has been recently implicated in the reinforcing properties of ethanol. The aim of this study was to determine the participation of acetaldehyde in the enhanced attractiveness of ethanol, induced by prenatal ethanol exposure, by evaluating newborn rats on postnatal day 1. Therefore, pregnant rats were administered with water, ethanol or ethanol + D-Penicillamine (DP) during gestational days 17, 18, 19 and 20. Twenty-four hours after birth the offspring of these dams was evaluated using the odor crawling locomotion technique, in which the distance travelled towards the odors of ethanol, water and vanilla was registered and used as an index of odor attractiveness.

#### INDIVIDUAL DIFFERENCES IN SPONTANEOUS EYE BLINKING ARE LINKED TO FRONTAL ASYMMETRY IN HUMAN INFANTS

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The rate of spontaneous eye blinking (SEB), a putative index of dopamine function (DA), is altered by some kinds of cognitive activities and under some pathological conditions. The present work is a continuation of a study investigating relationships between SEB and cognitive function in human infants. A unique contribution is our examination of the relationship between SEB and frontal asymmetry (FA). Relationships between DA-related genes and FA in infants and other studies of adults suggests that DA system function relates to some aspects of FA. Whereas our

previous analyses revealed task-related temporal variation in FA, the present work explores potential contributions of attention and emotion to this effect. Forty, healthy, term, 10-mo-olds completed a looking version of the A-not-B task. SEB was coded blind to task phase (Show, Hide, Reveal toy). EEG data were collected from three frontal regions (frontal pole Fp1, Fp2; medial frontal F3, F4; lateral frontal, F7, F8) at 512Hz. Previous analyses demonstrated that infants of high SEB exhibited greater left-FA activation during one phase of the task. In the present analysis, decreased HR (resulting from increased attention) was expected to correspond to the SEB rate changes. Although HR did change across the task, it did not correspond to the fluctuations observed in SEB. Analyses of the potential contribution of the experimenter's emotional tone are underway. Results of these analyses have implications for identifying neurophysiological mechanisms involved in cognitive processing during neuros' first year and provide new information on the temporal features of FA during infancy.

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#### AT THE INTERSECTION OF ANIMAL WELFARE, REPRODUCIBILITY, AND POLICY

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Every year, 50-100 million vertebrates are used in experimental procedures, of which greater than 80% are mice and rats. Increasingly researchers are pressured to justify such use also in the face of poor reproducibility of experimental results and evidence of abnormal behaviour and other signs of distress in rodents housed under standard laboratory housing conditions. Here, we will explore 1) whether impaired welfare induced by inadequate housing conditions may contribute to poor reproducibility of experimental results and 2) how environmental enrichment to improve animal welfare affects outcome variability and reproducibility.

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#### ADOLESCENT NICOTINE EXPOSURE FACILITATES RETRIEVAL OF TRAUMATIC FEAR MEMORY IN ABA RENEWAL

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Adolescent nicotine decreases the number of cells in the midbrain, hippocampus, and cortex (Trauth et al., 2000) and hippocampus-dependent context conditioning in rats is impaired following adolescent nicotine exposure (Spaeth et al., 2010). Here we examined whether adolescent nicotine would impair a more complex form of context learning known as "renewal". In renewal, an animal learns a task in one context (A) then receives extinction treatment in a different context (B). If returned to the original training context (A) the previously extinguished behavior recovers, or "renews". Renewal implies that one form of context learning involves the ability of contextual cues to modulate memory retrieval (Bouton, 2002). If adolescent nicotine impairs complex aspects of context learning (renewal) in the same way as simpler forms of context learning (context conditioning) - presumably by disrupting hippocampus function - then adolescent nicotine should impair renewal. Adolescent rats received 2x/day intraperitoneal injections of nicotine (saline, 0.15 mg/kg, 0.40 mg/kg) from PD28-PD54 followed by a 20-day abstinence interval. Beginning on PD75 all animals were exposed to pairings of a light with footshock (Light-shock) then subsequent light extinction, presentation of the Light with no shock (L-). Extinction occurred either in the same or different context as original Light-shock training. Animals were tested for fear of the light in the original training context using fear-potentiated startle (FPS). Adolescent nicotine did not impair but actually facilitated context-dependent memory retrieval (renewal). Findings suggest adolescent nicotine may facilitate encoding or retrieval of traumatic fear memory long after the nicotine exposure period.

### IMITATION PRACTICE MAKES IMITATION PERFECT: IMITATION ENHANCES MOTOR-SPATIAL LEARNING BY PRESCHOOLERS IN A BRIEF TRAINING STUDY

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The ability to vicariously learn information from others' in order to replicate their responses (i.e. imitation), is essential to cognitive development and predicts later academic success in children (e.g., Riggins, Cheatham, Stark, & Bauer, 2013). Here we explored whether training individual learning in general improved imitation performance specifically. To that end, we tested whether task-general learning and memory training or task-specific imitation training improved motor-spatial imitation performance on a touchscreen task with 3- and 4-year-olds. When compared to the No Practice and Trial and Error groups, only domain- (motor-spatial) and task- (imitation) specific practice significantly improved motor-spatial imitation performance from pre- to post-testing. [NSF BCS-0748717 to F. Subiaul and NSF BCS-1023772 to R. Barr and P. Gerhardstein].

### SEX, STRESS, AND DOPAMINE: POTENTIAL MECHANISMS UNDERLYING SEX DIFFERENCES IN EARLY-LIFE STRESS ASSOCIATED PATHOLOGY

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Early life stress (ELS) has profound effects on neural and behavioral development, and is associated with a significant increase in the risk of developing affective pathology. Affective disorders peak during the adolescent period, with females being nearly twice as likely as males to develop stress-associated pathology. However, the mechanisms underlying sex differences in risk for pathology are not well understood. Recently, multiple groups have proposed that negative symptoms associated with depression are consequence of disturbance in reward processing. Here, we used a mouse model of ELS, maternal bedding restriction, to test for ELS associated changes in affective behavior as well as expression of dopamine receptor and dopamine-related genes in neural structures associated with reward processing. We found that ELS led to significant sex differences in the development of negative symptoms of depressive-like behaviors, including lethargy, anhedonia, enhanced risk assessment, and sleep disturbance in females but not males. We collected tissue and measured gene expression in striatum, frontal cortex, ventral tegmental area, and substantia nigra of male and female mice and used realtime qPCR to measure changes in gene expression. We observed significant and selective effects of ELS on DRD4 expression (elevated in female frontal cortex), with no effects on gene expression in male mice. Studies are currently underway to test a potential direct relationship between these observed effects.

### BEHAVIORAL LATERALIZATION SCALE: A NEW METHOD FOR CHARACTERIZING MULTIPLE LATERALIZED PREFERENCES IN BOBWHITE QUAIL CHICKS (*Colinus virginianus*)

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Hemispheric lateralization is observed across a wide range of vertebrates. This specialized brain organization enables separate and parallel processing, thus maximizing efficiency and improving fitness. In precocial birds, prenatal light experience affects the expression of several lateralized behavioral responses including hatch degree, turn preferences, and footed-

ness. A lack of lateralized behaviors may indicate a reduction in sensory integration. The aim of this study was to assess the magnitude of the relationship between several behavioral lateralization preferences and various prenatal light conditions, and to create an overall behavioral lateralization index of these preferences. We experimentally modified the amount of prenatal light experience available during late embryogenesis. The experimental light conditions included no light exposure, 2 hr of light exposure, 6 hr of light exposure, and normal low-light incubation. Post-hatch egg shells were examined for hatch degree and all birds were tested for laterality preferences during a T-maze task and during stair-climbing at three developmental age points, 12, 24, and 48 hr following hatch. Individual lateralized behaviors were scored on a scale ranging from 0-2 with 0 representing no behavioral lateralization and 2 representing normal species typical lateralization at each age point. Scores for each lateralized behavior were summed, creating a Behavioral Lateralization Scale (BLS) for each subject. Pending results indicate a gradual decline in the BLS in relationship to the amount of in prenatal light experience. This scale should be helpful in characterizing the magnitude of hemispheric specialization and its plasticity for future experimentation.

### BROADER IMPACTS: GLOBAL INTERSECTIONS AND INTEGRATIVE ETHICAL CONSIDERATION OF ANIMAL RESEARCH AND POLICY.

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Significant escalating challenges to animal research highlight an urgent need for partnership between the scientific community and broader public to better inform policy and practices that affect research. Science plays a core role to provide knowledge, but also to inform decisions that affect individual, species, societal, and environmental health. Decisions made in absence of full consideration of the science can jeopardize both public interests and animal welfare. Thus, scientists' active engagement is essential to develop integrated approaches and a more expansive framework for ethical consideration that is needed in order to responsibly address the future of research with nonhuman animals.

### MATERNAL DIET INFLUENCES OFFSPRING FEEDING BEHAVIOR AND FEARFULNESS IN BIRDS

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Bird embryos are known to perceive and memorize chemosensory signals of the surrounding environment; however, the potential impact of the maternal diet has not previously been investigated. We hypothesized that bird embryos memorize the chemical signals of the maternal diet and that this perceptual learning may orient subsequent feeding behavior of the hatchlings. We fed laying hens standard food enriched with 2% menhaden oil (MH group) or 2% soybean oil (controls). The scent of menhaden was significantly more detected in MH egg yolks than in control yolks by a human panel. We analyzed the development and behavior of offspring towards different types of food, bearing or not bearing the menhaden scent. In a 3-min choice test with unfamiliar food (mashed cereals) MH chicks showed a clear positive orientation toward the unfamiliar food bearing the menhaden scent. By contrast, control chicks showed a preference for the non-odorized unfamiliar food. MH chicks expressed higher emotional reactivity level than control chicks as expressed by food neophobia and longer immobility in a restraint test. Chicks exposed in ovo to menhaden oil via the maternal diet preferentially oriented their feeding behavior towards food containing menhaden oil, but only when the food was unfamiliar. We propose that oil in the maternal diet engenders maternal effects and contributes to the development of behavioral phenotype in the offspring. In ovo chemosensory learning may have evolved to prepare precocial offspring for their environment. This

suggests a common principle of embryonic chemosensory learning across vertebrate taxa.

[FeedPhobic ANR-12-JSV7-0011-01]

#### EMBRYONIC EXPOSURE TO COOL TEMPERATURE ENHANCES THE EXPRESSION OF FEAR-RELATED BEHAVIORS IN BIRDS

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In oviparous animals an embryo is likely to encounter periods when incubation temperatures are unfavourable. In birds, optimal development of avian embryos takes place within a narrow range of incubation temperatures. As parents occasionally leave the nest, embryos could be exposed chronically to cool sub-optimal temperatures. We tested whether unpredictable exposure to cool temperature influences the development of socio-emotional behaviors and cognitive capacity in a precocial species. A group of chicken (*Gallus g. domesticus*) embryos was incubated in a constant optimal temperature of 37.8°C (control group). Another group of embryos (c-chicks) was exposed unpredictably to a temperature of 27.2°C two times a day for 1 hr between embryonic days 12 and 20 (the day before hatching). Exposure to cool temperature did not affect significantly hatching success. A reduced growth was observed in chicks exposed to cool temperature. A significantly longer latency to touch a novel food was observed in c-chicks compared to controls. C-chicks also showed significantly longer duration of tonic-immobility and longer time immobile in a novel environment. The prenatal treatment did not affect the motivation to join congeners. C-chicks exhibited impaired performances in a detour task compared to controls. Our data showed that unpredictable exposure to cool temperature enhances the expression of fear-related behaviors in young birds. In addition to maternal effects engendered by the quality of eggs, incubation temperature also plays part in the construction of behavioral phenotypes.

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#### EFFECTS OF UNPREDICTABLE VARIABLE PRENATAL STRESS (UVPS) ON BDNF DNA METHYLATION AND TELOMERE LENGTH IN THE ADULT RAT BRAIN

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In utero exposure to stress can shape neurobiological and behavioral outcomes in offspring, producing vulnerability to psychopathology later in life. Animal models of prenatal stress likewise have demonstrated long-term alterations in brain function and behavioral deficits in offspring. For example, using a rodent model of unpredictable variable prenatal stress (UVPS), in which dams are exposed to unpredictable, variable stress across pregnancy, we have found alterations in body weight and anxiety-like behavior in adult male offspring. DNA methylation (addition of methyl groups to cytosines which normally represses gene transcription) and changes in telomere length (TTAGGG repeats on the ends of

chromosomes) are two molecular modifications that result from stress and could be responsible for the long-term effects of UVPS. Here, we measured methylation of brain-derived neurotrophic factor (*bdnf*), a gene important in development and plasticity, and telomere length in the brains of adult offspring from the UVPS model. Results indicate that prenatally stressed adult males have greater methylation in the medial prefrontal cortex (mPFC) compared to non-stressed controls, while females have greater methylation in the ventral hippocampus compared to controls. Further, prenatally stressed males had shorter telomeres than controls in the mPFC. These findings demonstrate the ability of UVPS to produce epigenetic alterations and changes in telomere length across behaviorally-relevant brain regions, which may have implications for the phenotypic outcomes.

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#### NEUROBEHAVIORAL TOXICITY OF ADOLESCENT METHYLMERCURY EXPOSURE IN MICE

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The developing fetus is particularly vulnerable to the neurobiology- and behavior-altering effects of exposure to methylmercury (MeHg), an environmental neurotoxicant that bioaccumulates in fish. It is well established though that the brain continues to develop after birth and throughout early life, as major neurobiological and behavioral changes unfold during the adolescent period. However, the neurobehavioral effects of adolescent MeHg exposure remain virtually unknown. The current experiments were designed to assess the effects of adolescent MeHg exposure on delay discounting (i.e., the preference for small, immediate reinforcers over large, delayed ones) and sensitivity to amphetamine (a dopamine agonist) using a mouse model. Thirty-six male C57Bl/6n mice were exposed to 0, 0.3, and 3.0 ppm MeHg via drinking water from postnatal day 21 to 59, the murine adolescent period. As adults, mice were allowed to respond for a droplet of milk delivered immediately and four droplets delivered after a series of delays for 35 sessions, which were followed by a dose-response determination of d-amphetamine (i.p.: 0.1 - 1.7 mg/kg). Adolescent MeHg exposure significantly impaired the acquisition of impulsive choice relative to controls. MeHg-exposed mice were also more sensitive to amphetamine-induced reductions in sensitivity to reinforcer amount and delay compared to controls. The current study is the first to demonstrate that adolescence is a period in which MeHg exposure may have long-lasting neurobehavioral effects. These findings carry significant implications for public health and policy.

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#### ONTOGENY OF ULTRASONIC VOCALIZATION AND RESPIRATORY RESPONSES TO AN AVERSIVE EVENT IN RATS

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When confronted with highly emotional events, either positive or negative, rats have been shown to emit vocalizations in the ultrasonic range (USVs). Although vocalizations are emitted at all developmental ages, they evolve throughout the rat's life, both in terms of quantity and quality. However, until now, very few studies have been exploring USVs with similar paradigms throughout the ontogenesis. Therefore, in this study, we investigated the simultaneous evolution of the behavior, USV and associated respiratory rate emitted in response to a mild foot-shock at three developmental ages: infant (PN 12-14), juvenile (PN 22-24) and adult (PN 80-90). The foot-shock induced sustained emission of USVs at all ages, with significant differences in USVs frequencies and durations throughout development. We also characterized the reciprocal influences

of the respiratory rate and freezing on USVs emission. Results suggest that USVs extend the expiration duration in adult, and to a lesser extent in juvenile rats, while they do not influence the respiratory rate in infants. Moreover, while USVs are mainly emitted during freezing behavior in adults, this seems less clear in juveniles and is not supported in infants. Finally we investigated whether the emission of USVs was modulated as a function of the predictability of the foot-shock arrival. We showed that when the shock was unpredicted, the level of USVs was significantly greater than when the shock was predicted. Interestingly, this difference was only observed in infant rats, with adult and juvenile animals showing similar levels of USVs emission in predictable and unpredictable conditions.

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#### EPIGENETIC MECHANISMS MEDIATING PERINATAL STRESS-INDUCED TRANSGENERATIONAL NEURONAL AND SYNAPTIC CHANGES IN PREFRONTAL-LIMBIC-HYPOTHALAMIC (PLH) CIRCUITS

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Perinatal stress has been shown to program the developing organism to adapt brain and behavioral functions to cope with daily life challenges. We present evidence that the specific and individual effects of early life stress (ELS) on the functional development of brain and behavior emerge as a function of the type, intensity, timing and the duration of the adverse environment. Our research indicates that on one hand ELS may leave functional “scars” in prefrontal and limbic circuits and thereby impair stress coping, but on the other hand also supports the concept of “stress inoculation”, resulting in resilience against stress and other adversities later in life. We also show that epigenetic and behavioral consequences of ELS can be transmitted to 2nd and 3rd generations.

#### ASSOCIATIONS BETWEEN SOCIOECONOMIC STATUS, EEG POWER AT BIRTH, AND COGNITIVE SKILLS DURING INFANCY

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Childhood socioeconomic status (SES), typically characterized by parental education, family income, and parental occupation (McLoyd, 1998), is strongly associated with children’s cognitive development (Brooks-Gunn & Duncan, 1997). We previously observed socioeconomic disparities emerging between 15 and 21 months of age for both language and declarative memory skills during the first years of life (Noble et al., in press). The present study examined associations between SES, resting EEG power at birth, and cognitive skills at 15-months in a sample of 66 full-term infants (gestational age = 37–42 weeks). These infants were originally recruited from a cohort of participants in a longitudinal study investigating the relation between prenatal exposures and birth outcomes (<http://safepassagestudy.org/>). Results indicated no associations between SES and EEG power at birth. EEG power at birth, however, was related to both language and memory outcomes at 15-months, controlling for both sex and gestational age. Left-frontal gamma power was related to later VPC memory scores ( $\beta = 0.36$ ,  $p = 0.02$ ,  $R^2 = .16$ ) and left-parietal low-gamma power was related to later PLS-Auditory language scores ( $\beta = 0.27$ ,  $p = 0.04$ ,  $R^2 = .11$ ). Results suggest SES disparities in brain activity are not apparent at birth, but differences in EEG power at birth may influence trajectories for early cognitive skills.

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#### ASSOCIATIONS BETWEEN MU RHYTHM REACTIVITY AND IMITATION IN INFANCY: A PILOT STUDY

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The EEG mu rhythm (infant: 6- to 9-Hz), which is recorded from central sites overlying the sensorimotor cortex, reacts (i.e., decreases in power relative to baseline) to the observation and execution of actions, and is thus theorized to be an analog of activity within a human neural mirroring system. Similarities in mu reactivity to both action observation and execution have led to the hypothesis that perception of another’s actions is mapped onto an internal motor representation of the observer (Cannon et al., 2014). Therefore, mu rhythm has been postulated to be associated with imitation (Oberman et al., 2008), though associations between mu rhythm and imitation in infancy remain relatively uninvestigated. The current study used the puppet imitation task (Barr et al., 1996) to examine associations between mu rhythm and imitation in infancy. EEG was recorded while infants observed a baseline stimulus (non-biological motion) and an adult demonstrate a sequence of actions on a puppet, and while infants imitated these actions. At 6 months of age ( $n = 6$ ), there was a negative trend between imitation scores and mu rhythm reactivity during the observation of the target actions,  $r(4) = -.54$ . In contrast, during later infancy (age range: 12-24 months,  $n = 11$ ), there was a positive association between left hemisphere mu reactivity during demonstration and imitation scores,  $r(9) = .66$ ,  $p = .03$ . These initial findings suggest that mu rhythm reactivity is associated with imitation during infancy, but there are potential age-related shifts in the nature of this association.

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#### THE DEVELOPMENTAL CASCADE OF A HAND PREFERENCE FOR ACQUIRING OBJECTS INTO A HAND PREFERENCE FOR THEIR UNIMANUAL MANIPULATION

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Michel’s Cascade Theory (1983) proposes that hand preference develops as the result of a sequence of previous experiences provided by lateralized asymmetric behaviors. To investigate whether one asymmetric behavior has an influence on the development of a subsequent asymmetric behavior, hand preferences for two manual actions were recorded. Object acquisition and unimanual manipulation were observed, using separate assessment procedures, monthly from 6 to 14 months of age. During different play scenarios, objects either were presented to the infant on the table (acquisition) or two identical objects were pressed into the infant’s hands simultaneously (unimanual manipulation). The relative frequency of use of the right and left hand were then recorded for analysis. A latent class analysis identified three developmental trajectories in the acquisition data; one exhibiting development of a right hand preference, one exhibiting a development of a left hand preference and one with no clear preference. The relative frequency of left- and right-hand unimanual manipulation actions across all months also were subjected to hierarchical linear modeling to investigate the relation between the acquisition hand preference (as identified by latent class) and unimanual manipulations. The results show that, although hand preference for acquisition is distinguishable from 6 months of age, a hand preference for unimanual manipulation does not begin to appear until 11 months of age. These results support the Cascade Theory’s proposal that one established laterally asymmetric behavior (acquisition hand preference) will influence the subsequent development of a lateral asymmetry for another behavior (i.e., unimanual hand preference).

### HUMAN NEONATAL CONSUMPTION OF THE COLOSTRUM, A BIOCULTURAL EXPERIENCE

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The first results of an ongoing research program on human colostrum highlight that the mother's gift of the colostrum to the newborn follows extremely variable biocultural rules. The colostrum transfer to the newborn is indeed under the control of complex social and cultural processes. From ethnographical data collected in Bolivia, Brazil, Burkina Faso, Cambodia, France, Germany, and Morocco, we will show that multiple cultural processes (public health policies, food habits, body techniques, impurity representations, folk biology and physiology, medicinal practices, native health conceptions) can improve or disrupt the neonate infants' exposure to continuity between amniotic and lacteal experiences.

[This research is funded by ANR.]

### CORTICOSTEROID RECEPTOR EXPRESSION IS LINEARLY RELATED TO INDIVIDUAL DIFFERENCES IN NOVELTY EXPLORATION

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Human behavioral inhibition (BI) is characterized by low novelty exploration (neophobia) and susceptibility to internalizing disorders. Animal models have demonstrated that, similar to humans, neophobic rodents have elevated basal and novelty-induced hypothalamic-pituitary-adrenal (HPA) axis activity. HPA and emotion regulation are associated with mineralocorticoid, glucocorticoid, and corticotropin releasing hormone receptor (MR, GR, CRHR1) activity in the hippocampus, hypothalamus, and prefrontal cortex (PFC), and altered receptor signaling in these regions is associated with anxiety and depression. We tested whether young adult exploratory behavior predicts later adulthood MR, GR, and CRHR1 mRNA expression and anxiety- and depression-like behavior. In male Sprague-Dawley rats, exploratory behavior was measured at two months of age in two novel arenas (one social, one non-social), and then anxiety- and depression-like behavior were measured with the elevated plus maze and sucrose preference test at the same age and 2 months later (2 and 4 months of age). Exploratory behavior at 2 months was not strongly related to anxiety- or depression-like behavior at the same age, but did predict anxiety-like behavior 2 months later (at 4 months of age). Young adult exploratory behavior also linearly predicted hippocampal and hypothalamic GR, and PFC CRHR1 expression, with longer latencies (i.e., neophobia) predicting reduced mRNA expression. Exploratory behavior did not predict MR expression in any area. We are analyzing GR and MR protein levels in the hippocampus and hypothalamus to assess subregion-specific changes in receptor expression. Results suggest that BI-related susceptibility to mood disorders may be related to altered corticosteroid receptor signaling in multiple areas.

### PERSISTENCE OF ETHANOL-INDUCED SENSITIZATION DURING THE PREWEANLING PERIOD OF THE RAT

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Drugs of abuse as amphetamine or cocaine induce sensitization to the locomotor stimulating effect in adult and in preweanling rats. However, during infancy this learning effect is observed only after a short interval

of time, between training and testing. During infancy, particularly during the 2nd postnatal week of life, rats are highly sensitive to ethanol. In a previous study we have shown short-term ethanol-induced sensitization when subjects were trained during the 2nd postnatal week. This effect was context-dependent, in that it was only observed when pups were trained and tested in different contexts. The present series of experiments was designed to explore the persistence of the sensitization effect across the preweanling period. Pups were trained with ethanol during the second or the third postnatal week of life, and were tested 2 or 7 days later. Our results showed that, contrarily to what has been observed with other drugs during infancy, sensitization to ethanol persisted at least 7 days in rats trained during the 2nd postnatal week of life. In older pups, the same procedure induced tolerance instead sensitization. This pattern of results suggests that infancy is a valuable period for the study of the neurobiological determinants underlying ethanol-induced sensitization and the relationship of this effect with ethanol intake.

[PICT 0999 FONCYT to JCM]

### NEONATAL AND INFANTILE ATTRACTION TO ODORS FROM MATERNAL DIET DURING GESTATION: THE PARTICULAR CASE OF ALCOHOL

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Fetal exposure in the amniotic fluid to chemosensory stimuli coming from maternal diet may define neonatal and infantile attraction to those stimuli, determining later acceptance of substances as part of the diet. When the pregnant rat consumes alcohol, the distinctive flavor of this drug becomes more attractive for the offspring, resulting in increased consumption and liking of alcohol in neonates, infants, and even adolescents. Considering that maternal alcohol ingestion exposes fetuses to the chemosensory and the pharmacological aspects of alcohol, I will discuss the possible interactions between these facets of the drug to explain the results of our last studies.

### THE BEHAVIORAL EFFECT OF POSTNATAL CORTICOSTERONE ADMINISTRATION IN DEVELOPING RATS DEPENDS ON ITS DURATION AND PATTERN OF ELEVATION

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Recent emphasis has been given to the effects of early-life stress in developmentally immature and vulnerable organisms that persist into adulthood. Activation of the hypothalamic-pituitary-adrenal axis in response to stress includes a release of glucocorticoids which can result in positive or negative effects on cognitive performance across the lifespan. It is generally accepted that very low and very high levels of circulating glucocorticoids are detrimental to learning and memory while moderate levels can be facilitatory. Because tasks engaging the hippocampus are particularly sensitive to glucocorticoid actions, and the hippocampus has a critical role in learning and memory, this interplay between glucocorticoids and the development of learning can be examined using trace eyeblink classical conditioning. Here we present a series of studies in which we administered the glucocorticoid corticosterone (CORT) to Long Evans rat pups on postnatal Day 15 and assessed learning on Day 24 using trace eyeblink classical conditioning. Release of corticosterone into the bloodstream at both a high pharmacological dose (subcutaneous pellets) over 5 days and at a modest elevation (subcutaneous osmotic minipumps) over 2 days impaired acquisition of trace eyeblink conditioning. In contrast, CORT injections (twice daily, subcutaneous) which delivered a very high dose for less than 4 hr at a time, facilitated learning. Across all studies, males appeared to be more sensitive to the effects of corticosterone. Together, these data suggest that the overall level, duration and pattern of elevation of corticosterone play a role in the lasting behavioral effects observed.

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## SEX DIFFERENCES IN EEG ACTIVITY DURING EXECUTIVE PROCESSING: A COMPARISON OF INFANTS AND YOUNG CHILDREN

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Executive functions (EFs) are linked with optimal cognitive and social-emotional development. Despite behavioral evidence of sex differences in early childhood EF, little is known about potential sex differences in corresponding brain-behavior associations. The present study examined changes in 4-year-olds' ( $n = 144$ ) 6–9 Hz EEG power and coherence in response to increased executive processing demands (“Stroop-like” vs. “non-Stroop” day-night tasks). Although there were no sex differences in task performance, an examination of multiple scalp electrode sites revealed that boys exhibited more widespread changes in EEG power as compared to girls. Further, multiple regression analyses controlling for maternal education and non-EF performance indicated that individual differences in boys' and girls' EF performance were associated with different frontal neural correlates (i.e., different frontal scalp sites and different measures of EEG power). However, 6–9 Hz frontal functional connectivity (EEG coherence) did not differ as a function of increased inhibitory demands. For comparison purposes, we reanalyzed our data with 10-month-olds ( $n = 173$ ) to determine whether sex differences in EF-related EEG were present during infancy. Although infants exhibited increases in 6–9 Hz frontal functional connectivity (EEG coherence) in response to added inhibitory demands (i.e., reversal versus non-reversal trials on the A-not-B task) there were no changes in 6–9 Hz EEG power (Cuevas, Swingler, Bell, Marcovitch, & Calkins, 2012). However, there were no significant Condition  $\times$  Sex interactions for either EEG measure. The data reveal valuable information concerning the emergence of sex differences in the neural systems underlying executive processing during infancy and early childhood. [NIH grant R01HD049878 to MAB.]

## CORTISOL IN MOTHER'S MILK IN THE NEONATAL PERIOD INFLUENCES LATER INFANT SOCIAL BEHAVIOR AND COGNITION IN RHESUS MONKEYS

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Mother's milk contains hormones, such as cortisol, that are increasingly thought to influence neonatal and subsequent infant development. Recent studies have linked cortisol in mother's milk with infant temperament in both human and nonhuman primates, but no studies have examined how cortisol in milk affects infant behavior in a social setting or cognitive functioning. We studied rhesus macaque mother infant dyads (*Macaca mulatta*,  $N = 24$ ) from birth through 8 months. Milk samples were collected twice in the first 30 days of life and assayed for cortisol concentrations. From months 4–8, we observed each infant twice weekly in 10-min sessions to study their social behavior in a group setting (e.g., initiate and receive play, grooming, and mounting). For a subset of infants ( $n = 8$ ), we collected cognitive data in their group living environment at the same time to assess performance on a response inhibition task. We found that higher cortisol concentrations in mother's milk in the first 30 days of life were negatively correlated with initiation of social behaviors later in development ( $r = -0.445$ ,  $p = 0.029$ ), and positively correlated with percentage of trials correct on the cognitive task to assess inhibitory control ( $r = 0.733$ ,  $p = 0.039$ ). Collectively, these findings lend support to the “lactational programming” hypothesis, whereby glucocorticoids ingested through milk contribute to the development of infant behavioral phenotype.

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## INFLUENCE OF OLFACTORY FEAR CONDITIONING ON OLFACTORY NEUROANATOMY AND SENSITIVITY IN SUBSEQUENTLY CONCEIVED GENERATIONS

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Historical events have generated data indicating that stressors experienced by a generation also affect descendant generations not directly exposed to those stressors. Using an animal model of olfactory fear conditioning, my research (and talk) aims to shed light on the nature and mechanisms by which such inter- and trans-generational transmission and inheritance occur.

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## THE EXPERIENCE OF CANCER AFFECTS THE RELATIONSHIP BETWEEN PARENT AND CHILD HYPOTHALAMIC PITUITARY ADRENAL (HPA) FUNCTION

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Rodent studies show that offspring experience of moderate stress can modify the association between the infant's and the mother's HPA function. Therefore, having a mother with poor HPA function does not mean that her offspring will necessarily have similarly poor function. Here we examine whether this modifiability of the relation between parental and child HPA function generalizes to humans. HPA function was examined in parents and their children from healthy control (HC) and pediatric cancer survivor (CS) families. Multilevel modeling was applied to data from a nested-design study (85 children, 5–18 years old, from 64 families, HC:  $n = 32$ ; CS:  $n = 32$ ) to characterize the relation between parent (baseline and post-stress salivary) and child (hair) cortisol measures within HC and CS groups, controlling for child age, sex and parent ethnicity. A second analysis was performed; examining whether corticosteroid exposure as part of cancer treatment affects the association between parent and child cortisol. The interaction effect between cancer experience and parental cortisol on child HPA function was significant (Baseline:  $F(1,46.23) = 4.53$ ,  $p = .039$ ; Post-Stress:  $F(1,47.21) = 8.99$ ,  $p = .004$ ) with a more positive association between parent and child cortisol in HC compared to CS families. The interaction effect between child corticosteroid exposure and parent cortisol was significant (Baseline:  $F(1,61.02) = 4.76$ ,  $p = .033$ ; Post-stress:  $F(1,61.42) = 6.04$ ,  $p = .017$ ) with a more positive association between parent and child cortisol in the non-exposed ( $N = 67$ ), compared to the exposed group ( $N = 11$ ). Parallel to findings from the rodent model, these results reveal a modifiability of the relation between parent and child HPA function by child corticosteroid exposure and indicate plasticity of HPA function beyond infancy.

## CHILD EXECUTIVE FUNCTIONING IS PREDICTED BY PARENT HYPOTHALAMIC PITUITARY ADRENAL (HPA) FUNCTION IN BOTH CANCER SURVIVORS AND HEALTHY CONTROL CHILDREN

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Exposure of infant rats to mild stress associated with a relatively novel non-home environment can modify the influence of maternal HPA function on offspring cognitive function. To determine whether the impact of these converging early life influences generalize to humans, we investigated whether experience of cancer, a major chronic stressor, can change the influence of parent HPA function on child executive function (EF). Eighty-one children, ages 5–18, from 63 families (Healthy Controls = 32, Cancer Survivors = 31) were included in a nested-design study. To identify major dimensions underlying EF, principle component analysis was performed on 9 measures of EF (NIH Examiner). The first three components accounted for 78.47% variance with the first interpreted as attention control, the second as responsivity to stimuli, and the third as response inhibition. Parent HPA function was indexed by normalized evoked salivary cortisol response ( $CORT_{ne} = \text{PreStress} - \text{PostStress} / \text{PreStress}$ ) to the Trier Social Stressor Task (TSST). Multilevel modeling was applied to each of these three components with cancer experience and parental cortisol as predictor variables controlling for child age, showing a significant main effect of parent  $CORT_{ne}$  on the component of child attention control ( $F(1,51.35) = 4.08, p = .049$ ) parents with higher rise in cortisol response to the TSST had children with higher levels of attention control. This result suggests that parent ability to increase cortisol output in response to a stressful event can predict child attention control across different stress conditions. Therefore improving parent self-stress regulation may positively contribute to cognitive development in children experiencing different levels of stress.

#### ADOLESCENT FEAR MEMORIES AND DNA METHYLATION FOLLOWING EXPOSURE TO CAREGIVER MALTREATMENT

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Rats exposed to adversity early in life display altered developmental trajectories of fear behavior. The mechanisms underlying these behavioral shifts remain to be elucidated, though epigenetic alterations such as DNA methylation are an excellent candidate. Specifically, methylation of plasticity-related genes, including *bdnf*, may contribute to altered fear behavior following disruption of the caregiving environment. Previously we assessed alterations in DNA methylation in adolescent rats that had been exposed to our caregiver maltreatment paradigm and discovered that females exhibited gene-specific (*bdnf*) changes in response to maltreatment whereas maltreated-males exhibited changes on a global level, including global alterations in DNA hydroxymethylation, a recently identified cytosine modification that plays a role in learning and memory. The aim of the current study was to assess fear behavior outcomes in adolescent rats exposed to our caregiver maltreatment paradigm and to assess whether there is a relationship between these outcomes and our measures of global and gene-specific epigenetic alterations in the adolescent brain. Infant male and female Long Evans rats were subjected to either nurturing care (from their biological mother or foster dam) or maltreatment from a foster dam for 30 min daily from postnatal day (PN) 1 to PN7. Between PN30 and PN35 we investigated cued fear conditioning, extinction, and recall. Results will be discussed in the framework of consequences and mechanisms of early-life stress.

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#### PERCEIVED MALTREATMENT AND DEVELOPMENT OF RISKY PERSONALITY FACTORS AND FUTURE ORIENTATION: RISK FOR ALCOHOL USE DURING ADOLESCENCE

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Research has indicated a strong relationship between maltreatment and earlier initiation of drinking, higher rates of alcohol abuse and later dependence in adolescents. However, the underlying pathways of these relationships are not clear. We examined the effects of perceived maltreatment (i.e., perceived neglect and violence) on risky personality factors (including anxiety sensitivity, hopelessness, impulsivity, and sensation seeking) and future orientation (i.e., the ability of time perspective, planning ahead, and anticipation of future consequences) and tested if these factors mediate the relationship between perceived maltreatment and alcohol use in adolescents. Adolescents ( $n = 142$ , 51% females) aged 13–17 years old ( $M = 14.48$ ,  $SD = 1.09$ ) were assessed. Results indicated that higher perceived violence was associated with higher levels of hopelessness, impulsivity, and sensation seeking, whereas, higher perceived neglect only increased hopelessness. In addition, both perceived neglect and violence were associated with lower levels of future orientation. Sensation seeking emerged significant over and above other mediators (i.e., impulsivity and future orientation) in the relationship between violence and recency of alcohol use ( $F(4, 124) = 13.32, p < .001$ ). Findings suggest that adolescents who experienced violence may use alcohol to enhance positive affect and experience intense stimulation. Intervention programs for alcohol use in adolescents should consider the effects of maltreatment, particularly violence. Maltreated adolescents with higher risk of alcohol use would benefit from interventions that target their feelings, decision making, motivations, and behavioural control.

#### INDIVIDUAL DIFFERENCES IN STRESS REACTIVITY IN A HIGH RISK SAMPLE

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This study examined the association between prenatal tobacco exposure (PTE) and the rate of change in cortisol in response to frustration at 16 months of child age. Data were collected from 212 mother-infant dyads (66 non-smokers and 146 smokers) using a prospective design with sample recruited in pregnancy. PTE was assessed using maternal salivary cotinine and self-reports in pregnancy and infant meconium after delivery. Toddler reactivity was assessed during an arm restraint paradigm designed to elicit frustration. Saliva for cortisol was collected at pre-task, post-task 1 (20 min after frustration), and post-task 2 (40 min after frustration). Latent growth modeling was used to examine study hypotheses. Results indicated significant variability in intercept ( $t = 5.52, p < .001$ ) and slope ( $t = 3.75, p < .001$ ), and a significant association between the intercept and the slope ( $r = -.24$ ). Higher pre-task cortisol was associated with less change from pre to post-task. The conditional growth model with PTE status regressed on intercept and slope fit the data well ( $\chi^2 = 7.40, p = .12, CFI = .99, RMSEA = .06$ ). PTE was significantly associated with both intercept ( $\beta = -.24, t = -2.95, p = .003$ ) and slope ( $\beta = .21, t = 2.19, p = .03$ ). Children in the PTE group had lower pre-task cortisol and a greater increase in cortisol from pre to post-task compared to the control group. Results indicate that PTE is associated with changes in the stress-response system perhaps as a result of toxic stress.

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#### INVESTIGATING THE FACTORS AFFECTING YOUNG CHILDREN'S SOCIAL AND ASOCIAL LEARNING PREFERENCES

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The current study examined the trajectory of children's decisions about learning socially or individually. Ninety-six children (48 girls) aged 3- and 5-year-olds were shown two novel puzzle boxes (one hard, one easy). They were asked if they would like to attempt to try to open it on their own (individual) or after watching an adult model (social); these preference were either met or violated. 79% of children chose to learn by watching a model. Children who had their learning preference met in both conditions were also significantly quicker at beginning the task ( $t(71) = 2.00, p = .050$ ), and retrieving the reward ( $t(73) = 2.78, p = .007$ ). [ESRC Grant ES/J021385/1 to EGF and L-AG]

#### ASSESSING NEWBORN CRAWLING IN RESPONSE TO TERRESTRIAL OPTIC FLOW

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We have recently reported a very precocious coupling between vision and crawling in humans, evidenced by 3 day-old newborns increasing their leg stepping in response to terrestrial optic flows simulating their motion forward or backward. However, as few full arm steps were observed in the aforementioned study it was difficult to determine if optic flows modified arm stepping. Here we investigated whether coding leg and arm movements based on the number of individual flexion and extension movements, rather than on the number of flexion-extension cycles, would yield additional results. Twenty-six 3 day-old infants were video recorded in a prone position on a transparent water-mattress, through which a checkerboard pattern was projected. Three conditions were presented randomly for 1 min to each infant: (1) Static—the checkerboard was static, (2) Toward—the checkerboard moved toward the infant simulating forward self-motion, and (3) Away—the checkerboard moved away from the infant simulating backward propulsion. A significant effect of Condition for the number of leg flexions and extensions,  $F(2, 50) = 3.2, p < .05$ , revealed that Toward and Away elicited significantly more leg movements than Static. Though no effect of Condition on arm movements was observed, more movements were made on the right side,  $F(1, 25) = 6.8, p < .05$  and a significant interaction between movement type (flexion/extension) and Side,  $F(1, 25) = 5.1, p = .03$  revealed no differences on the left side but more flexion than extension movements on the right side. The new method provides further insight into the character of newborn crawling.

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#### THE EFFECT OF D-PENICILLAMINE ADMINISTRATION DURING PRENATAL ETHANOL EXPOSURE IN 5 AND 14 DAY-OLD RATS

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Ethanol exposure during the last days of gestation increases ethanol acceptance in neonate, in infant and in adolescent rats. Recent studies with neonate rats evidenced the crucial implication of acetaldehyde, the first metabolite of ethanol, in ethanol reinforcement at this early age. Previous studies in our and other laboratories have shown that after ethanol exposure during the last gestational days, the intake and palatability of ethanol increases when measured on postnatal day (PD) 1, 5 and 14. Therefore, in this study we investigated the role of acetaldehyde on the prenatal ethanol exposure effect. We administered dams during gestational days 17-20 with water, ethanol or ethanol + D-Penicillamine (DP) and the offspring was tested with three different procedures. On Postnatal day 5 (Experiment 1) pups were assessed with an operant conditioning procedure using ethanol 6% as the reinforcer. On PD 14 (Experiment 2) pups' ethanol (6%) consumption was evaluated as well as

their taste reactivity to this same ethanol solution. The results of both experiments confirmed that eliminating acetaldehyde produced after prenatal ethanol exposure reduces the postnatal positive response to ethanol, highlighting the important role of acetaldehyde on ethanol reinforcing properties during early development.

#### PRENATAL EXPERIENCE SHAPES PERCEPTION OF PROSODY AT BIRTH

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In four NIRS studies, we explored how prenatal experience with language shapes speech perception abilities at birth. As speech heard in utero is filtered by maternal tissues, it is mainly prosodic information that is transmitted to the fetus. We therefore investigated whether the perception of prosody at birth shows the influence of the prosodic patterns of the language(s) heard prenatally. We found that monolingual French newborns grouped tone sequences that contrasted in duration in a French, adult-like manner, i.e. iambically, as short-long, as is found in the prosody of French, but showed no grouping for pitch, a cue less used in French prosody, whereas the bilinguals whose other language relies on pitch contrasts showed an adult-like, trochaic (high-low) grouping for pitch, suggesting an important prenatal influence.

#### THE PERCEPTION OF TIME-COMPRESSED SPEECH AT BIRTH

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Adults rapidly adapt to time-compressed speech up to 40% compression with respect to the original duration in their native language, as well as in unfamiliar languages, if those are rhythmically similar to their native language, suggesting that adaptation is based on auditory, rather than syntactic or semantic cues. However, it remains unclear whether this adaptation ability is the result of extensive experience with language or whether it is automatically achieved by the auditory system. In three NIRS and EEG studies with newborns, we have explored whether newborns are able to adapt to time-compressed speech. We have found that French-exposed newborns readily adapt to accelerated French and Spanish, a rhythmically similar language, at 60% compression, but not at 30% compression, showing a similar adaptation pattern as adults. This suggests that prenatal experience with the prosody of the native language already shapes the speech perception system early in development.

#### COMPARING THE EFFICACY OF MATERNAL FLUOXETINE AND EXERCISE IN A RODENT MODEL OF POSTPARTUM DEPRESSION: OUTCOME OF BOTH MOTHER AND MALE AND FEMALE OFFSPRING

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Postpartum depression (PPD) affects approximately 15% of mothers and can have negative effects on the mother-infant dyad. Pharmacological antidepressants such as fluoxetine (Prozac) are commonly used to treat PPD. However, fluoxetine can remain active in breast milk and potentially impact offspring development. For this reason, non-pharmacological therapies, such as exercise, may be more agreeable. Unfortunately, it is unclear whether exercise is efficacious for treating PPD while preserving normal offspring development. To investigate this, we treated dams daily with high levels of corticosterone (40 mg/kg), to induce a depressive-like

phenotype, or oil during the postpartum. Within the oil and corticosterone conditions, four additional antidepressant groups were created: 1. Fluoxetine (Prozac; 10 mg/kg) + exercise (voluntary access to running wheel); 2. Fluoxetine + no exercise; 3. Saline (vehicle for fluoxetine) + exercise; 4. Saline + no exercise. Male and female offspring were weaned and then tested in adulthood for anxiety-like behaviour using the novelty suppressed feeding task and for stress reactivity using the dexamethasone suppression test. Preliminary findings indicate that maternal postpartum fluoxetine reversed corticosterone-induced disruptions in maternal care, regardless of exercise condition. Additionally, preliminary findings indicate that exercise had a greater antidepressant-like effect than fluoxetine for the dams. For this reason, we predict that exercise will result in a protective effect particularly in the adult male offspring. Our findings will shed light on how the postpartum antidepressant treatments (Prozac, exercise) differentially affect the well-being of the mother as well as the male and female offspring.  
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#### A POSITIVE TACER-3 ALCOHOL SCREEN IN PREGNANCY PREDICTS LATER ALCOHOL USE PROBLEMS IN CHILDREN

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Identifying prenatal alcohol consumption is essential to prevention of fetal alcohol spectrum disorders (FASD). Our prior research showed that the TACER-3 alcohol screen is effective at selectively identifying both women drinking at fetal risk levels and neurobehavioral effects associated with prenatal alcohol exposure in 4-year old children. The current research was designed to further validate the TACER-3. We hypothesized that more alcohol-related problems would be seen in teens born to mothers who had a positive prenatal TACER-3 screen than in teens born to TACER-3-negative mothers in a prospective high-risk urban cohort. At 14 years old, TACER-3-positive teens were more likely than TACER-3-negative teens to meet criteria for alcohol abuse (10.5% vs. 1.4%,  $\chi^2 = 5.5$ ,  $p = 0.019$ ) and to report problems due to current drinking (42.9% vs. 17.2%,  $\chi^2 = 7.6$ ,  $p = 0.006$ ). Similarly, at 19 years old, 36.4% of TACER-3-positive teens met criteria for alcohol abuse or dependence via parent or teen report compared to only 12.7% of TACER-3-negative teens ( $\chi^2 = 8.1$ ,  $p < 0.004$ ). Similar results were found after controlling for many important maternal and family characteristics in logistic regression analyses. The results suggest that the relatively simple TACER-3 alcohol screen administered during pregnancy effectively predicts later alcohol use problems in teen offspring. The risk drinking in pregnancy that is detected by the TACER-3 has cross-generational impact on sensitivity to early alcohol use problems. The results also imply that alcohol use/abuse problems may be associated with FASD.

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#### MODERATELY-PREATURE AND FULL-TERM INFANTS PERFORM DIFFERENTLY ON A COGNITIVE/EYE-HAND "TOUCHPAD TASK" AT 4-MONTHS (SAME GA)

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Introduction: Eighty-four percent of the 15 million premature births in the world each year occur between 32–37 weeks Gestational Age (GA). Most infants survive without intensive care; gross development is unremarkable and they are not closely monitored. However, in the early school years about 30% of them have compromised neuropsychological profiles, relative to their full-term peers. This research aimed to detect performance differences in a cognitive/eye-hand task between 4-month old full-term infants ( $n = 30$ ) and their corrected age preterm peers ( $n = 14$ ).

Procedure: The task used here is one of several tasks programmed into a touchpad ("Baby Learn©", 2014). Here, each touch on a small Smiley-Face target caused it to jump 2cm to a new location while saying, "Bravo Bébé!". Otherwise, the target did not move or speak. The precise location (in mm-coordinates) and temporal characteristics (in ms) of each touch were recorded.

Results: Almost all infants were self-motivated to interact with the Smiley Face. Statistically, premature infants made fewer on-target-touches/min, had longer latencies between touches and made more discrepant off-target-touches than their full-term peers.

Conclusion: Differences can be detected in how moderate pre-term and full-term infants perform on a task requiring contingency learning, sustained attention, fine motor control and eye-hand coordination. The infants' performances on other tasks in "Baby Learn©" are used to isolate the source of the differences seen here, e.g., insensitivity to response contingencies and/or less fine-motor control. We are also assessing the long-term predictive validity of the "Baby Learn©" test battery.

#### CHILDREN IMITATE ACTIONS WITH OBJECTS AFTER A DELAY WITHOUT OBVIOUS USE OF RATIONAL INFERENTIAL PROCESSES

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It has been proposed that infants imitate actions with objects based on rational inferential processes. As example, Gergely, Bekkering & Király, (2002) reported imitation of a novel action only if the hands of the experimenter were visible, not when they were covered. In order to replicate these findings, sixty-one children with a mean age of 14.8 months (95% CI [14.3, 15.3]) were tested (36 girls) with the hands of the experimenter visible ( $n = 26$ ) or occupied ( $n = 35$ ). The children were observed in the laboratory, at home or at daycare. The head touch procedure (Meltzoff, 1988) was used. The object consisted of a round plastic lamp mounted on a black wooden block, an object the infants had never seen before. The novel action demonstrated in the deferred imitation condition was for the experimenter to lean forward and press down the panel with the top of her forehead so that the lamp was turned on. We found an imitation rate of 27% when hands were visible and 37% when hands were occupied. Differences between conditions are not significant (Fisher's exact test,  $p = .58$ ). The higher frequency was observed in the hands occupied condition, counter to Gergely et al's results. One explanation for our lower imitation rate is that about half the sample was tested at home. Using only the results from the lab imitation rates of 40% (visible hands) and 53% (occupied hands) were observed ( $p = .70$ ). Thus, no support for rational imitation was observed.

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#### MK-801 IMPAIRS THE ACQUISITION OF CONTEXTUAL FEAR IN THE CONTEXT PRE-EXPOSURE FACILITATION EFFECT (CPFE) PARADIGM IN ADOLESCENT RATS

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The context pre-exposure facilitation effect (CPFE) is a contextual fear conditioning paradigm in which there are three phases: learning about the context, acquiring the context-shock association, and retrieving/expressing the context-shock association. In adult rats, NMDA receptor antagonism during standard contextual fear conditioning impairs retention but not

postshock freezing (Sanders and Fanselow, 2003). In contrast, antagonizing NMDA receptor functioning in the basolateral amygdala (BLA) on the training day of the CPFE impairs freezing during retention (Matus-Amat et al., 2007). The role of NMDA receptors during the training day of the CPFE in developing rats is currently unknown. Therefore, the current study assessed the effects of training day injections of MK-801 on post-shock freezing and retention in postnatal day (PD) 31 rats. In Experiment 1, i.p. injections of .1 mg/kg MK-801 given before training impaired retention test freezing relative to saline controls. In Experiment 2, the same dose of MK-801 given before training disrupted post-shock freezing. Experiment 3 replicated the findings of our previous experiments by assessing both post-shock and retention test freezing following systemic injections of 0, .025, .05, or .1 mg/kg MK-801 before CPFE training. Only the highest dose impaired postshock and retention freezing. In summary, acquisition of the context-shock association during the training day of the CPFE is NMDA receptor dependent in developing rats. The CPFE paradigm may make post-shock freezing NMDA-receptor dependent in a manner that contrasts with standard contextual fear. Future experiments examining postshock freezing at earlier stages of ontogeny may help elucidate the mechanisms of the CPFE.  
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#### PRENATAL MATERNAL EFFECTS ARE MODULATED BY A PRE-SOCIAL BIRD'S POSTNATAL MATERNAL CARE

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As for mammalian species, maternal influences play a fundamental role in the behavioural development birds' offspring, and thereby in the emergence of phenotypic variability. Prenatal maternal effects are mediated notably by maternal steroids in egg vitellus whose levels are influenced by females' characteristics/environment and modulate chicks' development. During the postnatal period, females' presence or maternal care affects offspring's emotive and social behaviours. Surprisingly, interactions between these two maternal effects have been poorly analysed although they play a crucial role during behavioural development making understanding them essential. In this context, we investigated the potential modulation of postnatal maternal care on the consequences of a prenatal stress in Japanese quail chicks. Previous reports showed that social instability in laying quails increased their offspring's emotional reactivity in relation to the increase of yolk testosterone levels in their eggs. We raised offspring of stressed females either with an adoptive mother (mothered set,  $N=29$ ) or in group of young (non-mothered set,  $N=27$ ). Our results showed that mothered chicks were lighter during their first three weeks and their emotional reactivity levels were lower than non-mothered chicks. Thus, our results highlight that, as mothered chicks became less emotive than non-mothered chicks, birds' maternal care can reverse the phenotypic consequences of a prenatal stress. Mechanisms of such interactions need to be explored, particularly by analysing mother-offspring interactions during the mothering period.  
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#### INTERVENING EARLY TO AFFECT TELOMERE LENGTH

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In a randomized clinical trial, we assessed whether a brief parenting intervention reduced telomere attrition among children adopted internationally. Children adopted internationally often exhibit physical, cognitive, and social delays as a result of their early experiences of care (Gunnar et al. 2000). Telomere length, which indicates cellular aging, is associated with early stress, and may be a mechanism through which stress causes disease and aging (Price et al. 2012). Early adverse experiences, such as orphanage care and neglect, are associated with shorter telomere length (Asok et al., 2013; Drury et al., 2011). Forty-nine children (around 2 years old) adopted into families in the United States were randomly assigned to one of two intervention conditions. The parents of children assigned to the experimental intervention received Attachment and Biobehavioral Catch-up, a 10-session intervention targeting parental nurturance and sensitivity; parents of children in the control intervention condition received an intervention of the same duration, length, and frequency that targeted cognitive and physical development. A third non-randomized group ( $n=15$ ) was included with no intervention component. Children's telomeres were assessed when children were about 5 years old ( $M=66.30$  months,  $SD=7.82$ ). Children whose parents received the experimental intervention had longer telomeres (T/S ratio) than children in the other two groups  $F(2, 50)=4.57, p=.015$ . These results highlight the power of a brief intervention in remediating biological effects of early deprivation and indicate that experimental manipulation of telomere length is possible.

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#### NEONATAL MERCURY EXPOSURE ALTERS HIPPOCAMPUS-DEPENDENT MEMORY AND ANXIETY IN RATS

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Mercury is a teratogen and prenatal exposure to this heavy metal can produced significant negative effects in the offspring. Work with humans has revealed that cognitive deficits are long-lasting and may be more severe when exposure occurred during the third trimester of pregnancy. Here we use a model of neonatal mercury exposure wherein rats were injected with mercury (0, 1, or 2 mg/kg) once daily on postnatal days 4–9. Animals were tested in early adolescence. Major findings were that hippocampus-dependent tasks (trace and contextual fear conditioning) were more sensitive to mercury effects than was delay conditioning; mercury-exposed animals expressed less conditioned fear than controls. Further, the highest dose (2 mg/kg) resulted in abnormal responses on measures of anxiety (elevated plus maze and open field tests), the pattern of which suggests reduced anxiety in mercury-exposed animals. Collectively the results indicate that “third-trimester equivalent” exposure to mercury can produce deficits in some types of memory, and exposure to higher levels produces more general effects through reduced fear/anxiety. These results confirm that mercury is a teratogenic agent that has long-lasting consequences for cognitive and emotional behaviors.

#### EARLY FACE-TO-FACE INTERACTIONS IMPROVE SOCIAL DEVELOPMENT IN NURSERY-REARED INFANT RHESUS MACAQUES (MACACA MULATTA)

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Children who face social neglect in early childhood exhibit problems in regulating their social behavior later in life, such as difficulty to form social bonds, lack of understanding social cues, and failure to seek comfort from a caregiver. While a broad range of studies has shown how early social experience can affect development, evidence that the effects of neglect can be buffered or even reversed is still scant. To investigate

this question, we used rhesus macaques as a model species since, similarly to humans, mother and infant macaques form strong social bonds and frequently engage in face-to-face interactions during the first month of life. Infant macaques were separated from their mothers on the day of birth and reared by human caretakers in a primate nursery. Infants were randomly assigned to receive either 1. Face-to-face interactions and handling by human caregivers, 2. Handling only, or 3. Standard care for the first 28 days of life. At 40 days old, our data show that infants under the face-to-face intervention both spent more time looking at social interactions as measured by eyetracking technology and displayed higher rates of social contact when interacting with peers compared to both controls, but that by 6 month old, all groups displayed comparable social preferences. Our study offers the first evidence that the provision of face-to-face social interactions early in life can enhance social development. [NIH grant: PO1HD064653 to PFF]

#### NEW LEARNING VS UNLEARNING: EXAMINATION OF THE INFRA-LIMBIC CORTEX-AMYGDALA-HIPPOCAMPUS CIRCUITRY IN EXTINCTION OF CONDITIONED FEAR

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Extinction of conditioned fear refers to the decrease in conditioned responding to a fear-eliciting stimulus due to the repeated presentation of that stimulus without any outcome. Extinction involves the formation of a new memory of "safety" that competes with the original fear memory ("danger") in adult rats. This is evidenced by rats exhibiting the return of fear when tested in a context different to extinction (i.e., renewal). The prevailing theory proposes that extinction memory consolidation involves the amygdala communicating to the ventral hippocampus (vHPC) and infralimbic cortex (IL). Therefore, we temporarily disconnected this circuitry at the time of extinction by simultaneously inactivating the IL and vHPC by infusing muscimol, a GABA<sub>A</sub> agonist, prior to extinction. The cannulas were implanted in the IL and the vHPC in one of three ways: ipsilateral, contralateral and bilateral. We observed that rats treated with saline displayed robust renewal of extinguished fear, as did rats infused with muscimol in the ipsilateral condition. Rats that received contralateral or bilateral infusions of muscimol prior to extinction failed to display renewal of fear when tested the day after extinction. These results suggest that extinction may "unlearn" the original fear memory when the IL-amygdala-vHPC circuitry is disrupted. This finding is consistent with the idea that extinction reverses the original fear memory in juvenile rats, in which the connections between those brain regions are immature. We are now using retrograde tracers to map projections from the amygdala to vHPC and IL, and co-labelling it with c-Fos.

#### EFFECTS OF PERINATAL STRESS AND FLUOXETINE ON CIRCADIAN BEHAVIOUR OF ADULT MICE

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Women of child-bearing age are the population group at highest risk for depression. Fluoxetine (Flx) is the antidepressant most commonly used by pregnant women. Flx and maternal stress can both affect fetal development. We previously demonstrated that perinatal exposure to Flx alters circadian rhythms of mouse offspring. The present study is the first to investigate the combined effects of maternal stress and perinatal exposure to the SSRI Flx on the circadian behaviour of mice as adults. **METHODS:** Mouse dams were exposed to chronic unpredictable stress (embryonic (E) day 7 to E18), Flx (E15- postnatal day 12), and combination of stress and Flx. A separate control group consisted of animals that were not exposed to stress or Flx. At two months of age, male offspring were placed in

recording chambers and circadian organization of wheel running rhythms and phase shifts to photic and non-photoc stimuli were assessed. **RESULTS:** We found that prenatal stress lead to smaller phase-delays to light during the early subjective night. Furthermore, mice exposed to perinatal stress and Flx took longer to re-entrain to 8-hr light phase advance in the animal model of jetlag. Mice exposed to perinatal Flx and mice exposed to perinatal stress showed increased phase-advances to light during the late subjective night. Interestingly, combination of stress and Flx normalized behavioural phase shifts to late-night light exposure. **CONCLUSION:** Our results suggest that perinatal exposure to Flx, maternal stress, and their combination, lead to discernible, persistent changes in circadian system function of adult mouse offspring. [Support Contributed By: NSERC PGS-D and AIHS doctoral scholarships to VK, NSERC Discovery grants to RHD and MCA, and CIHR operating grant to RHD.]

#### SOME LIKE IT HOT: TEMPERATURE PREFERENCE AND REPRODUCTION IN HARTLEY AND HAIRLESS GUINEA PIGS

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Hairless guinea pigs are the result of a spontaneous recessive mutation first identified in 1978. Recommendations for the care of this strain often include housing at warmer temperatures (24°C), even though it is unknown if these conditions are beneficial to the animal. The aim of this study was two-fold: (a) determine the impact of temperature on reproduction in female Hairless guinea pigs, and (b) compare temperature preference of the Hairless and Hartley strains. Weight, estrus cycle, and pregnancy outcomes were recorded for females maintained at both 22 and 24°C. Temperature preference was determined by observing each strain in a ring-shaped apparatus containing a non-linear gradient, maintained by separately controlled heating mats (24–38°C). Guinea pigs were placed either singly or in pairs at randomized starting points within the apparatus, and observed for 30 min. When placed alone in the apparatus, all 3 groups spent more time in the 30°C zones. However, when tested as pairs, Hartley females preferred the cooler zones (24–30°C), while Hairless guinea pigs preferred a warmer range (30–38°C). Hairless females maintained in warmer housing conditions (24°C) became obese over time. However, when transferred to a 22°C environment, weight and reproductive measures returned to baseline. These results confirm a thermoneutral temperature preference (30 ± 2°C) for both strains, and suggest that housing temperature may have significant impact on reproductive factors. Additionally, these studies reveal the important role of social context in thermoregulatory behavior for both Hartley and Hairless guinea pigs.

#### SLEEP AFTER LEARNING ENHANCES FLEXIBILITY OF MEMORY RETRIEVAL IN 12-MONTH-OLD INFANTS

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In the present study, we examined the effect of sleep on the flexibility of declarative memory retrieval using a deferred imitation paradigm (Barr et al., 1996; Hayne et al., 1997). Forty-one 12-month-old infants were randomly assigned to a nap condition, a no-nap condition, or a baseline-control condition. In a demonstration session, infants in the nap and no-nap condition watched an experimenter perform three target actions on a hand puppet. To enhance encoding opportunities, infants were allowed to practice the target actions three times immediately afterwards (Hayne et al., 2003). Flexibility of memory retrieval was assessed in a test session 4-hr later with a puppet that was identical in shape but different in color from the one used during the demonstrations. Infants in the nap condition were scheduled to sleep (>30 min) during the 4-hr interval while infants in the no-nap condition were naturally scheduled to stay awake. Sleeping behavior was monitored using actigraphy. Infants in the baseline-control condition only saw the stimuli during the test session to assess spontaneous production of the target actions. The results indicate that

only infants in the nap condition performed a significantly higher number of target actions at test than infants in the baseline-control condition,  $t(20.99) = -2.202, p = .039$ .

Our results point towards a facilitative effect of sleep on the flexibility of memory retrieval in 12-month-old infants. This indicates that sleep-dependent memory consolidation can change the quality of memory traces already in infants.

[This research was supported by Deutsche Forschungsgemeinschaft Grant SE 2154/2-1.]

#### NEUROMOTOR (POSTURAL) DEVELOPMENT AS A PREDICTOR OF DEVELOPMENTAL CHANGE IN INFANT HANDEDNESS

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A dynamic systems perspective suggests that the posture of an infant may illicit changes in an infant's handedness (Corbetta & Thelen, 1996). Previous research found that posture influenced the amount of symmetrical (bimanual) reaching during infancy, but not hand preference (Babik, Michel, Sheu, & Campbell, 2014). Although distinguishing the developmental features between posture and hand use was useful, less useful was having age as a predictor to identify the change in hand preference. Because age is an arbitrary predictor of development, it is not useful for predicting other developmental trajectories. The objective of the current study was to explore whether an infant's postural abilities could predict changes in an infant's hand preference, irrespective of age. Three hundred and three infants were observed using Touwen's indices of neuromotor development to specify the infant's development of motor and postural control monthly from ages 6-14 months. Hand preference for acquisition was also observed during these same months. Separate group based trajectory analyses were conducted to identify latent groups of infants who were developing along different neuromotor trajectories (especially in control of their posture) and hand preference trajectories. The infants were compared for their latent group assignments for both their neuromotor and hand preference development so as to identify the relation between these two developing abilities. The results show that there is a relation between neuromotor (postural) development and the development of a hand preference. Neuromotor development, rather than age, may be a better predictor of developmental process of hand preference.

#### HOW ESTABLISHED HAND PREFERENCE FOR ACQUISITION INFLUENCES THE CONSISTENCY OF HAND PREFERENCE FOR MANIPULATION

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Recent work established that the development of hand preference for object acquisition during infancy predicts hand preference for unimanual manipulation (Campbell, Marcinowski, Babik, & Michel, 2015). This discovery supports the cascade theory (Michel, 1983), which states that the development and stabilization of one lateralized behavior will influence the development of later lateralized behaviors. Further examination of this data is intended to clarify whether monthly fluctuations in unimanual hand preference differ for infants with either a right, left, or no preference for acquisition. Handedness for acquiring objects was determined based on a valid assessment of handedness (Michel, Ovrut, & Harkins, 1986). Infants were then selected according to their acquisition hand preference (30 right, 30 left, and 30 no preference). Unimanual manipulation was assessed by placing two identical toys in each of the infant's hands for 17 trials. The frequency of the actions performed were analyzed from video recordings. Acquisition hand preference groups were compared according to four criteria: 1) the number of times that an infant switched between a positive and a negative manipulation hand index (HI) score 2) number of positive HI scores that an infant exhibited across all observations 3) the number of significant HI scores and 4) the number of switches between significant HI scores. Results show that infants without

a hand preference for acquisition switch between positive and negative HI scores more often than infants with a right or left preference, and also switch more frequently between significant right and left HI scores. This indicates that infants with a left or right hand preference for acquiring objects are consistent in using their left or right hand (respectively) for manipulating them.

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#### CREATING A PARADIGM FOR STUDYING CROSS-MODAL ASSOCIATIVE EPISODIC MEMORY IN PRESCHOOLERS

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Memory is not made of single items but rather the associations among those items. Despite this, most memory research has focused on associations within a single modality, often limited to the visual realm. The present work represents a methodology to study how memory for associations of features occurs in the auditory-visual domain for realistic items. In the present study, eighteen children (ages 4-5) studied animal/sound pairings and then were tested on intact and rearranged pairs of items that were composed of an animal picture and a species typical sound. Crucially, there were multiple instances of each type of animal so the memory test required episodic memory to distinguish intact and rearranged animal/sound pairs. That is, it was not enough to remember one saw a cat because two cats were presented, each with a distinct meow. When piloting the present work, a primary problem was in getting the children to understand the task. That is, it was difficult for children to understand that two different cats made two different meows and that this was important information to which to attend. The participants were resistant to learn this distinction and instead focused on the fact that the cats were making the "correct" sound. During these initial pilot tests, children responded "yes" to every item. After extensive training, participants were successful at discriminating intact and rearranged items, although the false alarm rate remained high. The poster will describe both the effective methodology as well as the attempts that were less successful.

#### SENSITIVE PERIODS IN AFFECTIVE DEVELOPMENT: NONLINEAR MATURATION OF FEAR LEARNING

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Fear learning emerges early in life, but the capacity to express and extinguish fear memories undergoes dynamic changes across development. In particular, during adolescence, extinction learning for cued fear memory is diminished. During this same time frame period, rodent studies have uncovered a coinciding sensitive period of suppressed expression of contextual fear. We draw upon the model of critical period regulation within the visual system and present burgeoning evidence suggesting that parallel mechanisms may regulate the qualitative changes in fear learning across development.

#### ANIMAL RESEARCH: TIME TO TALK!

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Despite its clearly recognized achievements, promise for future discoveries, and ongoing public outreach efforts, nonhuman animal research is often not well understood and is commonly misrepresented. The scientific community can and must play an essential role in efforts to advance public education, promote public dialogue, and shape policy and practice. This talk will describe a range of efforts and venues by which scientists can actively contribute to public education and dialogue in order to

improve broad understanding of the role nonhuman animal research plays in promoting the welfare of both people and other animals.

#### LOOKING FOR POTENTIATION OF LATENT INHIBITION IN PREWEALING RATS

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Non-reinforced preexposure to a cue usually weakens subsequent conditioning in which that cue is used as the conditioned stimulus (CS). Studies with adult rats have shown that the presence of an added cue during preexposure to the target can modulate the magnitude of this latent inhibition effect. When the target and the added cues are from the same sensorial modality (e.g., two flavors) the magnitude of the latent inhibition to the target is reduced (e.g., Honey & Hall, 1988; 1989). However, when the target is an odor (e.g., almond) and the added cue is a taste (e.g., salt), the latent inhibition suffered by the target is enhanced (e.g., Rodríguez & Hall, 2008). In the present study, we tested whether using this latter set of stimuli in a procedure with prewealing rats as subjects may produce a potentiation of latent inhibition as observed with adult rats. In total three phases were carried out: preexposure (postnatal days 14, 15, and 16), conditioning, (postnatal days 17 and 18) and test (postnatal day 19) Results are discussed in terms of the generality of currently proposed mechanisms of latent inhibition (e.g., Hall & Rodríguez, 2010) to be applied to early stages of ontogeny.

#### METHAMPHETAMINE ABUSE IN ADOLESCENCE: EXAMINATION OF DRUG INTAKE, EXTINCTION AND REINSTATEMENT USING THE INTRAVENOUS SELF-ADMINISTRATION PARADIGM

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Methamphetamine abuse is a growing problem in Australia, particularly among adolescents. Here we used the intravenous self-administration paradigm to compare methamphetamine abuse-related behaviour in adolescent (postnatal day 35) and adult (postnatal day 70) rats. Rats were trained to lever press to obtain methamphetamine at a dose of 0.03 mg/kg/infusion. Methamphetamine delivery was paired with a cue light which served as the conditioned stimulus. Following acquisition, responding to a high (0.1 mg/kg/infusion) and low (0.01 mg/kg/infusion) dose was tested. Rats' lever pressing was subsequently extinguished by removal of drug and cue. To model cue exposure therapy, we also gave 0, 1, or 2 sessions of 120 presentations of the cue light in the absence of the lever (i.e., cue extinction). All rats were then subjected to a cue-induced reinstatement test. Both adolescent and adult rats acquired methamphetamine self-administration in a similar manner, but once acquired, adolescent rats administered more methamphetamine per kg ( $p < 0.05$ ), an effect recapitulated at the high dose ( $p < 0.05$ ). Rats of both ages exhibited robust cue-induced drug-seeking following extinction, but reinstatement was reduced in rats that received cue extinction ( $p < 0.05$ ). Overall, our results suggest that adolescents may be less susceptible to the aversive effects of methamphetamine compared to adults, which may contribute to their increased abuse liability. We have also identified CS extinction training as a behavioural intervention that may effectively reduce cue-induced craving and relapse in both adolescents and adults.

#### EXTINCTION OF CONDITIONED CUES REDUCES INCUBATION OF COCAINE CRAVING IN ADOLESCENT AND ADULT RATS

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Relapse to drug use can occur in addicted individuals even despite long periods of abstinence, and this is often precipitated by exposure to drug associated cues the evoke craving. In both animals and humans it has been observed that cue-induced drug craving actually increases over the first few weeks of abstinence, a phenomenon termed 'incubation of craving'. As adolescence represents a unique period of vulnerability to developing drug addiction, the first aim of this study was to compare incubation of cocaine craving in adolescent and adult rats. P35 (adolescent) and P70 (adult) rats were trained to lever press to obtain intravenous cocaine at a dose of 0.3 mg/kg/infusion, and drug delivery was paired with illumination of a stimulus light (conditioned stimulus, CS). Following acquisition of stable responding, rats were tested for cue-induced cocaine-seeking after either 1 or 30 days of abstinence. A third group rats was also tested after 30 days of abstinence, however these rats received 4 CS extinction sessions during the abstinence period (120 non-contingent CS presentations without drug). Adolescent and adult rats acquired and maintained a similar level of cocaine self-administration, and rats of both ages exhibited a higher level of cue-induced cocaine-seeking if they were tested after 30 days of abstinence compared to 1 day. Incubation of cocaine craving was significantly reduced in rats that received CS extinction training. These results indicate that CS extinction during abstinence may effectively reduce cue-induced relapse at a time when cue-induced drug craving is usually high.

#### THE EFFECT OF EARLY LIFE ADVERSITY ON EMOTIONAL MEMORIES DURING DEVELOPMENT

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Acute traumatic events and prolonged stress incurred early in life increase the risk of developing anxiety and depressive-like behaviors in both humans and animal models. It is hypothesized that these early life experiences alter the development and functioning of circuits that are critical for processing and learning about emotional stimuli. Here, we sought to test the effects of a form of early life stress (ELS) on the development of learning and memory of cues that predict adverse outcomes. ELS consisted of reducing maternal access to bedding and nesting materials from postnatal days 4 to 11. Subsequently, on postnatal day 21, 28, or 50, control reared or ELS mice underwent fear conditioning, where a tone was co-terminated with a foot-shock. Consistent with previous work, we observed no effect of age on fear memories in control mice. However, in ELS reared mice, both male and female mice were found to have significantly lower levels of freezing following conditioning at postnatal day 21, compared with all other groups. In addition, we observed significant sex differences in the rates of within session learning beginning at postnatal day 28. Based upon these results, we hypothesize that ELS can alter the development and expression of even the most basic forms of fear learning and expression, which may manifest differently in males and females. This work holds relevance for understanding how ELS impacts basic processing and learning about emotional cues in the environment. However, more work will be required to understand the mechanisms underlying these behavioral observations.

#### DOES INFANT HANDEDNESS TRAJECTORY AFFECT STACKING ABILITY?

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The Modified Progressive Lateralization Theory of Handedness suggests that a hand preference results from a history of cascading manual asymmetries for a variety of actions throughout infancy (Michel, 1983). An infant who consistently uses their preferred hand for a variety of actions would gain proficiency using that preferred hand and consequently, perform more proficiently on other challenging manual sensorimotor tasks, such as stacking. The ability to stack has been linked with a number of cognitive abilities, including spatial abilities and language; so linking infant handed-

ness with stacking could provide one behavioral mechanism by which handedness might affect cognitive development. This project tested the relation between infant handedness and stacking ability. One hundred and eighteen infants (65 males) were assessed for hand preference (6–14 months) and stacking ability (11–14 months) at monthly visits. A multilevel Poisson longitudinal model revealed that stacking increased quadratically across the 11–14 month ages and stable right-handers changed differently from infants with no hand preference. In addition, a greater proportion of stable and shifting right-handed infants used their right hands to stack; yet there were no significant differences in hand use for infants with a left or no preference. These results provide the first evidence that an infant hand preference enables infants to perform burgeoning manual skills (stacking), and future studies should examine whether these differences extend to the development of other, more sophisticated cognitive abilities.

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#### OXYTOCIN, MATERNAL BEHAVIOR, AND EXCITATORY-INHIBITORY BALANCE

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Oxytocin is important for social interactions and maternal behavior. However, little is known about when, where, and how oxytocin modulates neural circuits to improve social cognition. Here I will discuss new data from our lab on how oxytocin enables maternal behavior in new mother mice. Specifically I will focus on experience-dependent plasticity in the auditory cortex related to recognizing the significance of pup distress calls, which are important for mother mice retrieving lost pups back to the nest. Expression of retrieval behavior required left but not right auditory cortex, was accelerated by oxytocin in left auditory cortex, and oxytocin receptors were preferentially expressed in left auditory cortex. Neural responses to pup calls were also lateralized, with co-tuned and temporally-precise call-evoked excitatory and inhibitory responses in left cortex of maternal but not pup-naïve adults. Pairing calls with oxytocin enhanced call-evoked responses by balancing the magnitude and timing of inhibition with excitation in virgins. Our results describe fundamental synaptic mechanisms by which oxytocin increases the salience of acoustic social stimuli. Furthermore, oxytocin-induced plasticity provides a biological basis for lateralization of auditory cortical processing.

#### BILINGUAL EXPOSURE SHAPES RESTING STATE BRAIN NETWORKS BY 4 MONTHS OF AGE

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To test whether bilingual exposure (as a long-term environmental factor) affects the developing language neural circuitry, we measured the resting state brain networks in 4-month-old infants from monolingual and bilingual environments using a near-infrared spectroscopy system. Functional connectivity was evaluated by computing the correlation between the time courses of the oxy-, deoxy- and total hemoglobin signals. Network metrics of intra-hemispheric and inter-hemispheric connectivity revealed that a bilingual environment affects the configuration and the development of resting state functional brain networks, as it requires the engagement of additional bilateral frontal and temporal brain regions.

#### DOES UNPREDICTABLE VARIABLE PRENATAL STRESS (UVPS) ALTER MATERNAL CARE AND MODULATE TELOMERE LENGTH IN ADULT RAT BRAIN?

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Exposure to stress in the womb can influence neurobiological and behavioral outcomes in offspring, leading to increased vulnerability to psychopathology in later life. Using a rat model, we previously reported increased body weight and anxiety-like behavior in stress-exposed adult male, but not female, offspring. Our companion poster (Blaze et al., ISDP, 2015) reports significant alterations in telomere length (TTAGGG repeats on the ends of chromosomes) in adult male rat brain following UVPS. Sprague-Dawley female rats were time mated, then confirmed sperm positive (Gestational day [GJ]0). Beginning on G1 dams were randomly assigned to either: Unpredictable, Variable Prenatal Stress (UVPS) or Non-Stressed (NS) Control conditions throughout gestation. UVPS dams were exposed daily to three different stressors: (1) White Noise, (2) Strobe Light, and (3) Tube Restraint. Stressors were presented individually once per day on an unpredictable schedule (morning [0600–1200 hr]; afternoon [1200–1800 hr]; evening [1800–2400 hr]) for one of three durations (15, 30, or 60 min). Parturition was videographed in UVPS and control dams. We analyzed pup delivery times, as well as characteristic forms of maternal care, including nursing and pup licking. Our preliminary findings suggest that shortened telomere length in the medial prefrontal cortex (mPFC) of adult males (reported by Blaze et al., ISDP 2015) may be modulated by maternal care patterns. [NICHD (1R01HD50201) to AER and NIGMS (1P20GM103653).]

#### AN EARLY LIFE TREATMENT THAT INCREASES MATERNAL BEHAVIOR DECREASES INCENTIVE SALIENCE IN A SEX-DEPENDENT MANNER IN RATS

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Although exposure to early life stress (ELS) may induce at adulthood an increase in the vulnerability to Psychopathology, under some circumstances ELS may also increase resilience and coping to further stressors. We studied the long-term sex-dependent effects of an ELS model that consisted in the restriction of the nesting material during the first postnatal days, in Long Evans rats. The treatment increased maternal behavior (arched-back and licking-grooming) and decreased the time spent off the nest. In adulthood, half of the animals were exposed to an acute immobilization session (IMO), whereas the others remained undisturbed. Fourteen days after IMO animals were exposed to 5 days of autoshaping to study the incentive salience of cues paired with food, in food-deprived animals. ELS in IMO-exposed rats decreased in females the sign-tracking behavior towards the food paired cues. At the same time, in situ hybridization analysis indicated that tyrosine hydroxylase expression in the ventral tegmental area in females exposed to IMO decreased in ELS animals. Such as sign-tracking behavior has been related to the development of drug addiction, these results suggest that the superimposition of early and adult stress may exert “protective effects”. [Plan Nacional sobre Drogas 2011/021 to RN, Red de Trastornos Adictivos RD12\_0028\_0014 to AA]

#### THE INFLUENCE OF MATERNAL ANTENATAL STRESS AND CORTISOL ON BIRTH OUTCOMES

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Recent studies have investigated the biological mechanisms underlying the association between maternal stress during pregnancy and negative birth and infant outcomes. There is some evidence that an anomalous functioning of the maternal Hypothalamic Pituitary Adrenal (HPA) axis during pregnancy can affect the length of gestation and several birth outcomes, such as weight, body length, and head circumference, although results are not unequivocal. The main objective of this ongoing study was to explore the effects of maternal antenatal stress (i.e. depressive and anxiety symptoms) and HPA functioning, as indexed by salivary cortisol, on birth outcomes. As part of a wider longitudinal study, 28 pregnant women completed the Edinburgh Postnatal Depression Scale (EPDS) and the State-Trait Anxiety Inventory (STAI) between 30 and 33 gestational weeks, and provided three saliva samples per day on two consecutive days between 34 and 36 gestational weeks (upon waking; 30 min post-waking and before going to bed). New-borns' (all >37 gestational weeks) birth weight, body length and head circumference were determined from medical records.

Hierarchical multiple regressions indicated that both maternal anxiety symptoms and cortisol levels, separately, predicted infant birth weight, after controlling for pre-pregnancy BMI, current BMI and infant's gender, while only maternal cortisol significantly predicted infant body length and head circumference. The implications of the current findings will be further discussed in light of the prenatal programming model.

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#### THE EFFECTS OF EARLY, PROFOUND DEPRIVATION ON BRAIN AND BEHAVIORAL DEVELOPMENT: TIMING IS EVERYTHING

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In this talk I will discuss the effects of profound early deprivation on brain and behavioral development within the context of the Bucharest Early Intervention Project (BEIP). Following a baseline assessment (average age = 22 months), institutionalized infants were either randomly assigned to high quality foster care or to remain in institutional care. Across many domains of development, children assigned to foster care had better outcomes than those assigned to care as usual; importantly, evidence of sensitive periods was observed in specific domains (EEG, IQ, Attachment, Language). Children placed before age 2 experienced better outcomes than those placed after this age. These findings will be discussed in the context of the larger literature on sensitive periods in human development.

#### DEFERRED IMITATION, ASSOCIATIVE MEMORY AND COMMUNICATION IN 14-MONTH-OLD CHILDREN

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The presentation will build on two recent studies that combine behavioral observations of memory (deferred imitation, DI), electrophysiological (Event-Related Potentials, ERP) measures of associative memory and parental reports of language in 14-months-old children. In both studies, an ERP (Nc) response indicating associative memory as well as a correlation between Nc and DI was observed. Further analysis revealed strong individual variability: The clearest relationship with ERP was noted for

the subgroup of children performing non-optimally on the DI tasks. In addition, we also found a statistically significant correlation between parental report of receptive language and our ERP measure of associative memory.

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#### HIGH FREQUENCY ELECTROCORTICAL COHERENCE: EFFECTS OF SEX AND SLEEP POSITION

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The prone sleep position is a risk factor for Sudden Infant Death Syndrome (SIDS); however, it is unclear why prone sleeping increases SIDS risk. Electroencephalogram (EEG) coherence (COH) is a measure of synchrony in activity at different sites. This study assessed EEG COH during sleep in prone and supine positions in newborn and 1 month old infants, an age of increased vulnerability to SIDS. This current study tested the hypothesis that EEG COH would be greater in the prone sleep position, a known risk factor for SIDS. High density (128 lead) EEG was recorded from sleeping infants (GA >36) during a 10 min baseline period. Inspection of results suggested effects of position on COH were more pronounced at higher frequencies and only in newborns. As one example, COH between the right frontal polar and right occipital brain regions, at 22–24 Hz, were: newborn prone =  $0.56 \pm 0.02$ , newborn supine =  $0.40 \pm 0.04$ ; 1 month prone =  $0.42 \pm 0.02$ , 1 month supine =  $0.39 \pm 0.04$ . Two-way ANOVA revealed a significant position by age interaction ( $p = 0.041$ ). Post-hoc analyses showed that COH declined with age, but only in the prone position (prone  $p < 0.005$ ; supine  $p = 0.49$ ), and that prone COH was higher than supine but only in newborns (newborns  $p < 0.0001$ ; 1 month  $p = 0.93$ ). Perhaps increased coherence at high frequencies in the prone position at newborn age reflects a CNS adaptive response to this positional vulnerability, a response that is no longer elicited at 1 month when the infants are at greater risk for SIDS.

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#### THE INCIDENCE OF DEPRESSION IN PREGNANT WOMEN IS HIGH IN A URUGUAYAN POPULATION AND PREDICTED BY EMOTIONAL AND PHYSICAL ABUSE IN MOTHERS' FAMILY OF ORIGIN: A PILOT STUDY

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Many studies show a high incidence (5–30%) of depression during pregnancy (prenatal depression) around the world. Prenatal depression is also predictor of postpartum depression. There has been no study in the Uruguayan population of the factors that trigger prenatal depression or predict it. In the current study we investigated whether a history of child trauma and parental bonding predicts prenatal depression. Fifty pregnant women from a heterogeneous Uruguayan population recruited in two health institutions were randomly invited to participate and complete demographic information, and the Spanish versions of the Child Trauma Questionnaire (CTQ), the parental bonding instrument (PBI), and the Edinburgh Postnatal Depression Scale (EPDS). Twenty percent of the recruited population showed symptoms of prenatal depression (Edinburgh score >10). EPDS scores were predicted by CTQ factors, Emotional abuse ( $R^2 = .52$ ) and Physical abuse ( $R^2 = .49$ ) and by PBI factor, Maternal Care ( $R^2 = -.26$ ). Stepwise or logistic regression showed that the emotional abuse dimension could alone predict as much as the other dimensions of the CTQ or variables of PBI. There was no relationship

between EPDS during pregnancy and age, educational level, or income. This study suggested that, like other forms of depression, prenatal depression is high in the Uruguayan population. Besides, emotional and physical abuse are important risk factors, and the screening of depression and child trauma during pregnancy using EPDS and CTQ scales could permit the early detection of unattended severe cases of depression in pregnant women.

#### SEX AND GESTATIONAL AGE DIFFERENCES IN AUTONOMIC CONTROL OF HEALTHY NEWBORNS DURING SLEEP

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Late preterm newborns (LPT, born at 35–36 weeks) show immature autonomic nervous system (ANS) control during sleep compared to full term newborn infants (FT, born at 39–40 weeks), Burtchen et al 2015. It is also recognized that males are at higher risk than females for neonatal morbidity and mortality and a range of neurodevelopmental disorders. Previous studies have shown that there are significant differences between male and female newborns in brain activity, as measured by electroencephalogram during sleep, Piraquive et al 2014. In this current study we asked if there were significant effects of sex and gestational age at birth with regard to ANS control of heart rate (HR). Three groups of infants were studied within 72 hr of delivery: late preterm (LPT, 35–36 wks GA; 29 male 40 female), early term (ET, 37–38 wks GA; 41 male, 38 female) and full term (FT, 39–40 wks GA; 63 male, 59 female). Markers of ANS functioning during active sleep were basal HR and average beat to beat change in RR-intervals (rMSSD). Across all infants, rMSSD increased as a function of gestational age ( $p < 0.05$ ). HR decreased from LPT to FT ( $p < 0.05$ ). Across all ages, male newborns had lower HR than females (122.9bpm vs. 126.5bpm,  $p < 0.05$ ) and higher rMSSD (0.015 ms vs. 0.012 ms,  $p < 0.05$ ). Sex differences were more pronounced in the FT group (HR  $p < 0.01$ , rMSSD  $p < 0.05$ ). Future studies will investigate whether sex differences in developmental trajectories of autonomic control are related to sex differences observed in neurodevelopmental disorders. [Supported by NIH Grant R37HD32774.]

#### SYNCHRONICITY IN MILK ODOR AND NEONATAL MILK ODOR ATTRACTION AND SUCKLING IN THE LABORATORY MOUSE

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Synchronicity of maternal-infantile actions conditions mammalian reproduction. It is thus essential to understand the sensory/neural/behavioral events that time mother-infant exchanges around milk. Using different behavioral assays (2-odor choice and suckling tests), we exposed mouse pups of different ages (birth to weaning) to the odors of milk collected at various postpartum times. Our data indicate that the younger the pups the more they preferred age-matched milk/nipples to non age-matched milk/nipples. This selective response disappeared in preweaning pups. These findings will be discussed in the light of perinatal learning processes and situated in the context of the murine communal nursing.

#### EARLY LIFE STRESS ALTERS GENE EXPRESSION AND ACTIVITY PATTERNS IN THE MESOLIMBIC DOPAMINE SYSTEM AND ENHANCES SUSCEPTIBILITY TO DEPRESSION

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Adverse experiences and stress during childhood enhance the risk of depression and other psychiatric disorders in adulthood. However, knowledge of the neurobiological and transcriptional mechanisms underlying these outcomes is still limited. We have developed a paradigm in mice whereby postnatal stress in a sensitive period alters susceptibility to depression-like behavioral abnormalities and are accompanied by broad changes within the brain's reward circuitry. Mice were standard reared or exposed to early life stress (ELS) at different time periods, reared normally during adolescence, and then half of each group underwent chronic social defeat stress in adulthood. Depression-like behaviors were tested, physiological recordings were captured in the ventral tegmental area (VTA), and RNA-sequencing was performed on nucleus accumbens (NAc) and VTA brain samples. Postnatal ELS in a sensitive period significantly enhanced susceptibility to social defeat stress in adulthood. Several measures of anhedonia and anxiety were heightened with ELS in combination with social defeat. RNA-sequencing revealed distinct patterns of gene expression in VTA and NAc subsequent to ELS, and may represent a pre-depressive pro-susceptible transcriptional state prior to behavioral onset of depression. ELS alone likewise altered the firing rate and other physiological responses in VTA dopamine neurons, suggesting that activity in this area may be an early marker of enhanced susceptibility to a depressive state. Novel, bioinformatically identified, upstream regulator gene targets were manipulated virally and were able to prevent depression-like behavior. These studies may inform new targets for therapeutic intervention in early life critical periods. [Supported by NIMH and HDRF awards to E.J.N.]

#### NEUROBEHAVIORAL CONSEQUENCES OF EARLY LIFE ABUSE: FEAR, AGGRESSION, AND MATERNAL PROTECTION OF PUPS

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Infant abuse produces increased sensitivity to threat and a heightened prevalence of aggressive and violent behaviors emerging by adolescence in humans. Here we use a rodent model of infant abuse to assess the expression of fear and aggression, and investigate the neurobiological underpinnings mediating the effects of abuse. Rat pups were reared with a normal or abusive mother (postnatal days 8–12), and tested in a Threat Response Selection Test (TRST) and Resident Intruder Test (RIT) as adults. In the TRST, individuals were placed in the center of a tri-sectioned arena and given the option to approach a predator odor, or hide in a hut. In the RIT, animals were single-housed for a week, before introducing a same-sex intruder into their home cage for 10 min. Previously abused rats displayed decreased hiding, increased approach and interaction with the predator odor, and decreased amygdala c-Fos activation. Furthermore, infant abused mothers showed poor protection of their pups in the TRST. Additionally, infant abused rats showed increased offensive behaviors in the RIT. The presentation of maternal odor during the RIT and TRST normalized the behavior of previously abused rats, through a circuit involving the prefrontal cortex. Infant abuse alters behavioral responses and amygdala activation to threat, making it more likely for one to place itself in harm's way. Understanding the neurobiology of threat responding and its modulation by infant experience will provide insight for treatment of fear and aggression-related disorders that occur after abuse. [NIH MH091451, NIH DC009910 to RMS; NIH T32MH096331 to REP]

#### EFFECTS OF MATERNAL CARE ETHANOL PREFERENCE AND SENSITIVITY TO ETHANOL INDUCED SEDATION HYPNOSIS

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We investigated the influence of natural variations in maternal care on ethanol consumption and sensitivity to ethanol-induced sedation. Long Evans litters were categorized into high or low licking and grooming (LG). Using a free two-bottle choice test, high and low offspring were tested for 5% v/v ethanol consumption and preference for four weeks (PND 32–57). Using the loss of righting reflex (LORR) paradigm, offspring were tested at PND 42 (mid-adolescence) for sensitivity to acute 20% v/v ethanol-induced sedation at 3.0 g/kg and 3.5 g/kg ethanol dose. Male offspring were also tested with LORR at 3.0 g/kg or 3.5 g/kg ethanol dose at PND 50 (late adolescence), and 3.0 g/kg at PND 92–95 (adulthood). Low-LG female, consumed less total fluid (ethanol + water) in general, and preferred 5% ethanol to water over the last three weeks of consumption compared to High-LG female. Maternal care had no effect on male ethanol consumption, preference, and total fluid consumption. While maternal care didn't alter sensitivity to acute ethanol-induced sedation during mid-adolescence, Low-LG male were more sensitive to ethanol-induced sedation than High-LG at all tested doses during late adolescence and adulthood. LG frequency also negatively correlated with sensitivity during late adolescence while the correlation approached ( $p = 0.057$ ) significance in adults. Therefore, maternal care sex-dependently influences alcohol consumption, and age-dependently mediates male sensitivity to alcohol-induced sedation. We are currently investigating this age dependent effect on sensitivity in female, and also the mechanisms underlying these behavioral effects.

#### TRAIT ANXIETY PREDICTS MEDIAL PREFRONTAL CORTEX GABA SYSTEM PROTEIN EXPRESSION IN POSTPARTUM RATS

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Typically, early postpartum females have lower anxiety compared to nulliparous females, but some postpartum women (and laboratory rats) experience elevated anxiety after giving birth that interferes with mother-infant interactions and socioemotional development of offspring. This peripartum anxiety is strongly predicted by previous high anxiety in humans and maternal rats. Although the neurobiological mechanisms associated with differences in anxiety among mothers is unclear, central GABA neurotransmission has been implicated in anxiety in nulliparous and randomly-selected postpartum females. In the current study, we selected 8 low-anxious and 8 high-anxious female rats based on the time spent in the open arms of an elevated plus maze on postpartum day 7. We then analyzed protein expression of GAD<sub>65</sub> (responsible for synthesis of GABA released from terminals), and the vesicular GABA transporter (vGAT; responsible for uptake and storage of GABA into vesicles) in the medial prefrontal cortex (mPFC), an area associated with emotion regulation. We found a negative correlation between vGAT expression in the mPFC and the number of open arm entries driven by the high-anxious females. We also found a trend suggesting a positive correlation between GAD<sub>65</sub> expression and open arm time in the low-anxious females. There was no relationship between vGAT expression and open arm entries, nor between GAD<sub>65</sub> expression and anxiety, in the high-anxious females. There was no association between vGAT expression and open arm time nor GAD<sub>65</sub> and anxiety in the low-anxious females. These data suggest that differential cortical GABA regulation may contribute to behavioral differences between high- vs. low-anxious mothers.

#### ELECTROPHYSIOLOGICAL RESPONSES DURING ERROR MONITORING AS A POTENTIAL BIOMARKER FOR ANXIETY

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Anxiety disorders are one of the most common psychological disorders observed within a pediatric population. Thus, understanding the neural mechanisms underlying the etiology of anxiety may be useful in identifying potential biomarkers which may be used to inform both

treatment and diagnosis. One potential biomarker for anxiety is the error-related negativity (ERN), an event-related potential (ERP) component associated with error detection (Moser et al. 2013). Specifically, individuals with anxiety have been shown to display greater ERN amplitude compared to healthy individuals (Ladouceur et al., 2006). However, few studies have examined these differences within a pediatric population. The current study examined the ERN in youth with an anxiety disorder ( $N = 10$ , 7 male, 11.60 years) and non-anxious youth ( $N = 11$ , 7 male, 12.98 years). Participants completed 384 trials (50% congruent) of the arrow version of the Eriksen flanker task while simultaneous EEG was collected. Data were filtered, segmented, and baseline corrected offline and the ERN was identified within a 0–75 ms time window post-error. Repeated measures ANOVA with site (Fz, Cz) as the within subjects factor and group (anxious, non-anxious) as the between subjects factor was conducted. A significant site  $\times$  group effect was found ( $F(1,19) = 14.432$ ,  $p < .01$ ). Follow-up  $t$ -tests determined that the ERN was marginally greater in youth with anxiety compared to healthy youth at Cz ( $t = -2.087$ ,  $p = .051$ ) but not Fz. These findings provide further evidence for increased neural activation during error monitoring in youth with anxiety suggesting that the ERN may be a potential biomarker of risk for the development of anxiety.

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#### EFFECT OF SPATIAL MANIPULATIONS AND NMDA-RECEPTOR ANTAGONISM ON THE ONTOGENY OF OBJECT-IN-CONTEXT RECOGNITION IN THE RAT

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The ontogeny of contextual learning and memory remains controversial for developmental behavioral neuroscientists (Revillo et al., *Physiol Behav.*, 2015, in press). A key difficulty surrounds the spatial versus nonspatial nature of the contextual cues processed by preweanling rats (e.g., Pugh & Rudy, *Dev Psychobiol.*, 1996, 29(2), 87–100). Using the object-in-context recognition (OiC) task, we previously demonstrated that postnatal day (PD) 17 rats can learn associations between contextual stimuli and objects and retain these memories over short retention intervals when contexts are defined by salient proximal and distal cues (Ramsaran, Westbrook, & Stanton, ISDP 2013, San Diego, CA). In the current study, we manipulated the contextual cues or object placements in our OiC preparation to examine whether the ontogenetic profile and/or role of NMDA receptors would be altered in task variants that were explicitly spatial in nature. We report that OiC memory emerges in the rat before PD17 when contexts were distinguished by different proximal and distal cues. In contrast, when contexts could be discriminated only by the distal spatial environment or when spatial information about the objects needed to be associated with contextual stimuli (object-place-context recognition; OPC task), task performance emerged between PD21 and 26 and PD26 and 31, respectively. In addition, systemic injections of .06 mg/kg MK-801 prior to training impaired performance in the latter spatial task variants, but not in our standard OiC task. Thus, the ontogeny and NMDA-receptor-dependence of contextual learning and memory are influenced by the degree of spatial processing necessary for task performance.

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#### ROLE OF CONTEXT IN THE EXTINCTION PARADIGM IN PREWEANLING RATS

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While Pavlovian extinction has been widely studied in adult organisms, only few studies have focused on this effect during infancy. Although it is currently accepted that the extinction effect reflects new –context-dependent– learning, this is not so clear during infancy, because some studies did not find recovery of the extinguished CR before postnatal day (PD) 21.

The authors concluded that extinction during infancy erases the CS-US association. However, we have recently reported evidences of renewal, more rapid reacquisition, reinstatement and spontaneous recovery of an extinguished CR in preweanling rats. The present study analyzed the possibility of recovering an extinguished CR with a reinstatement procedure in a fear conditioning paradigm, on PD17 (Experiment 1–4) and on PD23 (Experiment 5). At the same time, it was explored the role of context salience as a procedural variable that may affect extinction during the preweanling period. In accordance with previous studies from our laboratory, results shown that preweanling rats expressed a previously extinguished CR after a single experience with an unsignaled US (Experiments 2 and 4a). Furthermore, this result was only found when subjects were trained and tested in salient contexts, but not in standard ones (Experiments 3 and 4b). Finally, Experiment 5 demonstrated the reinstatement effect on PD23 in a standard context. These results are in agreement with previous findings showing that the extinction effect during infancy shares features with extinction learning in adult organisms. [BID-PICT 0892 to G. Paglini and C. Arias]

#### PATHWAY TO PATHOLOGY: EARLY LIFE TRAUMA AND AMYGDALA SEROTONIN

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Infant experiences program brain development and alter later life behaviors. Although infants are biologically predisposed to attach to their caregiver, adverse early life experiences involving the caregiver negatively program neural systems controlling mood, memory, and emotion, and confer susceptibility to later life psychopathology. Clues from clinical and basic research suggest this is due to compromised brain development and disturbed emotion regulation, although the underlying mechanisms remain poorly understood. For my dissertation, I employed complementary rodent models of infant trauma, which result in adverse and enduring effects that parallel the neurobiological sequelae of childhood abuse, to better understand the developmental mechanisms by which infant trauma programs a pathway to later life psychopathology. Both infant trauma paradigms converged in producing a later life depressive-like behavioral phenotype characterized by impaired social interactions, high immobility in the Forced Swim Test (FST), and amygdala dysfunction. Surprisingly, olfactory trauma-linked cues had an unexpected positive value in adulthood and actually repaired the adult neurobehavioral dysregulation induced by infant trauma. Blocking amygdala 5-HT eliminated the rescue effect; increasing amygdala 5-HT and blocking CORT mimicked it, highlighting a role for an amygdala 5-HT/CORT interaction as the underlying mechanism. These findings provide insights into the link between childhood abuse and later depression, but also suggest that trauma-linked cues share properties with antidepressants and safety signals, which alter amygdala activity to provide relief from stress and fearful states.

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#### REAL-TIME ANALYSIS OF COVERT ATTENTION USING STEADY-STATE VISUAL EVOKED POTENTIALS REVEALS ROBUST INHIBITION OF RETURN DURING FREE-LOOKING BY YOUNG INFANTS

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We probed the dynamics of visual foraging in 3-month-olds in real-time using steady-state visual evoked potentials (SSVEPs) to detect the spontaneous allocation of covert attention to non-fixated, peripheral objects. The objects were 3 toy ducks (separated horizontally by 11 deg) flickering at 8, 10 or 12 Hz. Amplitudes of SSVEPs driven by each object

were extracted using point-by-point Fourier analysis of the EEG signal from scalp electrodes over extra-striate cortex. When the infant was fixating the center object and SSVEP amplitudes indicated that covert attention to one peripheral object had been high and the other low for 250 ms (HiLo), an event (synchronous  $\pm 45$  deg rotation of both peripheral objects at 2 cycles/s for 2 s) was triggered 31 or 625 ms after HiLo ended. Reactive gaze shifts to peripheral objects were analyzed off-line from video-recorded corneal reflections of the objects. Gaze shifts to the peripheral object that had been the target of covert attention during HiLo were substantially slower than shifts to the opposite side ( $1219 \pm 115$  vs.  $887 \pm 81$  ms after event onset,  $p = .02$ ). The proportion of shifts to the opposite side did not differ from 0.5, and shifts during events triggered after short and long delays did not differ in direction or latency. The results demonstrate robust inhibition of return (IOR) following the spontaneous (un-cued), brief allocation of covert attention during free-look in 3-month-olds. IOR during infant free-look is likely to promote visual exploration by facilitating inspection of potentially more informative locations.

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#### INTRA-DORSAL HIPPOCAMPAL ANTAGONISM OF MUSCARINIC ACETYLCHOLINE RECEPTORS DISRUPTS THE CONTEXT PREEXPOSURE FACILITATION EFFECT

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Cholinergic dysfunction produced by neonatal alcohol exposure can be mitigated by developmental cholinergic enhancement (Monk, et al., 2012, *Hippocampus* 22:1750–1757). This dysfunction also contributes to learning impairments in juvenile rats tested in a variant of context fear conditioning known as the context preexposure facilitation effect (CPFE) (Dokovna et al., 2013, *Behavioral Brain Research*, 248:114–120). However the specific brain regions subserving cholinergic effects on the CPFE during development are not known. Scopolamine, a muscarinic acetylcholine receptor antagonist, disrupts the CPFE in juvenile rats, when administered systemically before preexposure, training and testing, or before any single phase alone (Dokovna, & Stanton, 2012, *ISDP Abstract*). The current experiment extended these findings by locally infusing scopolamine into the dorsal hippocampus on the preexposure day. On PD 31, juvenile rats received bilateral infusions of scopolamine (35ug) or PBS 10mins before preexposure to the training context (Pre group) or an alternate context (Alt-Pre group). Twenty-four hours later, all animals immediately received two 2s, 1.5mA shocks in the training context. Testing occurred in the training context 24 hr later. The Pre group exhibited significantly more fear to the training context than the Alt pre group. However, Pre group animals given scopolamine before preexposure were not significantly different from the Alt-Pre group. This finding illustrates a specific role of dorsal hippocampal cholinergic function in contextual fear conditioning in juveniles. Enhancing hippocampal cholinergic function may reverse deficits in the CPFE produced by neonatal alcohol exposure.

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#### ADOLESCENT ETHANOL CONSUMPTION ENHANCES ETHANOL REINFORCEMENT DURING ADULTHOOD IN ALCOHOL-PREFERRING (P) RATS

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Adolescent ethanol consumption (AEC) is associated with an increase rate of alcoholism during adulthood, which is enhanced in individuals with a family history of alcoholism. In a series of experiments, the effects of AEC on adult EtOH-related behaviors were determined in P rats. In the first experiment, P rats were allowed to self-administer EtOH or saccharin (Sac) during adolescence and the tested for EtOH self-administration during adulthood. The reinforcing properties of oral EtOH consumption

was quantitatively examined through use of a progressive ratio test. AEC, but not adolescent Sac consumption (ASC), increased the acquisition and decreased the rate of extinction of EtOH self-administration during adulthood. In addition AEC, but not ASC, increased the breakpoint value for EtOH during adulthood. The effects of AEC on the effects of EtOH within the posterior ventral tegmental area (pVTA) were also assessed. The results indicate that AEC reduced the EtOH concentration required to support self-administration directly into the pVTA. In addition, AEC reduced the EtOH concentration required to be microinjected into the pVTA to stimulate dopamine release in the nucleus accumbens shell (effect was also potentiated by AEC). The data indicate that AEC in a rodent model of alcoholism produced persistent alterations in the drug reward pathway that is indicative of increased sensitivity to EtOH and a potentiated/prolonged response to EtOH. The increase in reward sensitivity during adulthood following AEC may be a biological basis for the long-lasting deleterious priming effects that AEC has for adult alcoholism.

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#### UNPREDICTABLE VARIABLE PRENATAL STRESS PROGRAMS ENDURING EFFECTS ON THE STRESS AXIS IN MALE AND FEMALE RATS

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We previously reported programming effects of unpredictable, variable prenatal stress (UVPS) on adult body weight and anxiety responses in male, but not female offspring. The adrenal gland regulates a number of essential physiological functions in adult organisms through the production of steroids and catecholamines. Maintenance of adrenal structure and function is regulated through the integration of extra- and intracellular signals. We hypothesized concomitant changes in the expression of four key genes within the stress axis of three-month-old male, but not female, rats exposed to UVPS. We used reverse transcription and fluorescence based quantitative real-time polymerase chain reaction (RT-PCR) to analyze expression of: (1) Proopiomelanocortin (POMC) polypeptide, the precursor of the pituitary adrenocorticotrophic hormone (ACTH), (2) ACTH receptor/melanocortin 2 receptor (MC2R) the mechanism by which POMC regulates adrenal glucocorticoid (GC) biosynthesis and secretion, (3) Steroidogenic Acute Regulatory Protein (StAR), a mitochondrial protein stimulated by ACTH, and (4) Cytochrome P450, family 11, subfamily A, polypeptide 1 (P45011a1), [CYP], an enzyme that localizes to the mitochondrial inner membrane and catalyzes the conversion of cholesterol to pregnenolone, the first and rate-limiting step in the synthesis of the steroid hormones. Sprague-Dawley female rats were time mated, then confirmed sperm positive (Gestational day [G]0). On G1 dams were randomly assigned to either: Unpredictable, Variable Prenatal Stress (UVPS) or Non-Stressed (NS) Control conditions. UVPS dams were exposed daily to three different stressors: (1) White Noise, (2) Strobe Light, and (3) Tube Restraint. Stressors were presented individually once per day on an unpredictable schedule (morning [0600-1200hr]; afternoon [1200-1800 hr]; evening [1800-2400 hr]) for one of three durations (15, 30 or 60 min). To control for potential changes in postnatal maternal care, newborn pups were fostered to non-manipulated, newly parturient dams. A significant difference was observed in pituitary POMC across stress conditions ( $p < .01$ ), with a trend ( $p = .08$ ) observed for adrenal StAR. A

significant sex difference was observed for adrenal CYP ( $p < .01$ ), with a trend ( $p = .06$ ) observed for MC2R. Collectively, our findings provide evidence that unpredictable, variable stress experienced during fetal life shapes the adult stress axis in males and females.

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#### DOES BILINGUALISM DELAY LANGUAGE ACQUISITION OR SPEED IT UP? EVIDENCE FROM A SIMULTANEOUS EEG-FNIRS STUDY

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So far, it is not clear whether bilingualism beneficially or rather adversely affects language development. To address this question a language learning study was performed in 6-month-old bilingual and monolingual infants. Brain plasticity effects were monitored by the electroencephalography (EEG) and the functional near-infrared spectroscopy (fNIRS) while infants underwent a semantic word learning training. Results showed training-induced modulations and transfer effects to untrained items suggesting an increased flexibility in word learning reflected by more mature neuronal responses in bilingual compared to monolingual infants. We will discuss these results highlighting the importance of combining EEG and fNIRS in assessing language development.

#### EPIGENETIC CONSEQUENCES AND TRANSGENERATIONAL INHERITANCE OF STRESS

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Epigenetic alterations have emerged as biomarkers for measuring the impact of stress and as mechanisms by which adversity could interact with DNA to affect brain function and health, including the increased risk for a range of psychiatric disorders within and across generations. I will introduce the topics of epigenetics and transgenerational inheritance, and in doing so briefly highlight some of our own studies providing empirical support for the ability of maltreatment to produce epigenetic alterations within and across generations.

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#### NEUROBEHAVIORAL CONSEQUENCES OF DISRUPTED MOTHER-INFANT RELATIONSHIP: NONHUMAN PRIMATES

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Maternal care plays a critical role in the regulation and development of social, emotional and stress responses in primate infants. Taking advantage of a naturalistic animal model of adverse maternal caregiving we have observed long-term alterations in attachment, social behavior (increased aggression, decreased affiliation) and emotional and stress regulation of infants that experienced adverse caregiving. Brain regions controlling these functions, in particular, prefrontal-amygdala circuits and the brain serotonin system are also affected. The possibility that adverse caregiving accelerates the maturation of prefrontal-amygdala circuits critical for emotional regulation in primates will be discussed.

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#### STRESS IMPAIRS COGNITIVE FLEXIBILITY IN 15-MONTH-OLD INFANTS

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Stress affects cognitive functioning in human adults. Learning and memory under acute stress are characterized by an increased use of rigid habitual response strategies, at the cost of flexible cognitive strategies. Glucocorticoids play a crucial role in promoting this shift from hippocampus-dependent to dorsal striatum-dependent memory. However, the immediate effects of stress on infant cognitive functioning are not well understood. We examined the effect of acute stress on 15-month-old infants' cognitive flexibility. Twenty-six infants were randomly assigned to a stress or to a no-stress condition. After a stress manipulation phase, infants in both conditions participated in an instrumental learning task. In this task, infants first learned to push two different buttons, each one producing a distinct sound and light effect. Then, infants were allowed to push one of the buttons until this action became habitual. At test, infants had access to both buttons. Pushing them did not produce any effect. Infants who had undergone stress induction continued to perform the hitherto effective habitual action at test. Infants in the no-stress condition flexibly adjusted their behavior by disengaging from the habitual action in favor of exploring an alternative action (i.e., pushing the button they had not learned to push habitually). These findings show that stress impairs infants' ability to learn from the consequences of their actions and thus to adjust their behavior to changing demands of their environment. By disrupting the development of a flexible behavioral repertoire, frequent exposure to stress during the first years of life could restrict knowledge acquisition.

#### COMPARISON OF SENSORY, MOTOR AND COGNITIVE DEVELOPMENT IN 3XTG-AD AND 5XFAD MOUSE MODELS OF ALZHEIMER'S DISEASE

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The 5XFAD mouse model of Alzheimer's disease (AD) exhibits impaired motor performance in the Rotorod by 10 months of age, while the 3xTg-AD mouse model shows better performance as early as 6 months of age. Due to the difference in motor behaviour phenotype and earlier onset of AD pathology in 5xTg mice, this study compared the neurodevelopmental profile of 5XFAD and 3xTg-AD mouse models to their respective wildtype (WT) controls. A neurodevelopmental test battery assessing sensory, motor and cognitive memory development was performed on 5xTg-AD pups and their WT controls from 2 to 24 days of age. Both 3xTg-AD and 5XFAD mice developed auditory startle sooner than WT controls. In comparison to the WT controls, there was an earlier onset of forelimb grasp and hindlimb grasp reflexes in the 5XFAD and 3xTg-AD mice, respectively. 5XFAD mice showed no delay in motor development, while 3xTg-AD mice showed delayed development in the righting reflex, negative geotaxis, and forelimb grip strength. 3xTg-AD mice exhibited less activity in the open field while the female 5XFAD mice had increased rearing activity. The 3xTg-AD mice showed impaired memory unlike the 5xTg-AD mice, as 3xTg-AD mice did not habituate to the novel object. 5XFAD mice also demonstrated advanced cognitive abilities as they burrowed in the home bedding sooner than WT controls. Unlike the 3xTg-AD mice, the 5XFAD mice showed no neurodevelopmental deficits. This study highlights the importance of investigating the consequences of genetic manipulation on early development of transgenic mouse models of AD.

#### PREMATURITY AND UNDERWEIGHT: PREDICTORS FOR PSYCHOMOTOR DEVELOPMENT?

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The literature suggests that prematurity and low birth weight are related to worse neurological development and poorer school performance later in life. Thus, the aim of this study is to analyze the effects of prematurity and weight on psychomotor development in a group of premature newborns at the corrected age of 24 months. The study sample consisted of 135 children born in 2011, prior to 37 weeks. Psychomotor development was measured with the Bayley Scales of Infant and Toddler Development, Third Edition (BSID-III), which assesses 5 areas of development: cognitive, receptive and expressive language, and fine and gross motor skills. Linear regressions were conducted to evaluate whether gestational age and weight at birth predicted BSID-III scores in the overall sample, as well as separately in the, early prematures ( $n=42$ ; birth before 32 weeks) and late prematures ( $n=73$ ; birth between 34 and 36+6 weeks). Whereas gestational age did not predict psychomotor development, children's weight at birth ( $z$  score) did; infants with lower weight for their gestational age had worse fine motor performance. This effect was even greater in the late premature's group, where weight at birth also predicted cognitive performance. However, in the analysis of the early premature group the gestational age but not the weight at birth has an important effect over all developmental areas. This preliminary data suggest a differential effect of both predictors according to the prematurity level. Besides, results reinforce the interest of late premature's group in the study of significant predictor variables for neurodevelopment.

#### FLEXOR AND EXTENSOR MUSCLE RECRUITMENT DURING LEG MOVEMENTS IN CHICK EMBRYOS

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Prior to hatching, chick embryos produce repetitive limb movements (RLMs). RLMs exhibit features of stepping in hatchlings, including leg flexor and extensor alternation at step cycle frequencies. Typically, flexor activity is rhythmic for many cycles, whereas extensor activity often drops out. We hypothesize that the spinal pattern generator for stepping more readily recruits leg flexor muscles than extensors. The purpose of this study is to determine if flexor and extensor muscle recruitment differs during RLMs. Embryonic day 20, we recorded spontaneously generated RLMs from either hip and ankle muscles ipsilaterally, or ankle muscles bilaterally. To test for differences in flexor and extensor recruitment, RLM burst counts and burst amplitudes for antagonist muscles of the hip and/or ankle were compared within embryo ( $N=21$ , Wilcoxon signed rank test). Results indicated that flexor bursts outnumbered extensor bursts in 35 of 37 antagonist muscle pairs, and the difference was significant ( $p<0.001$ ). Flexor peak burst amplitude was lowest if the extensor was not recruited during the RLM, and greatest if the extensor participated in all cycles of the RLM ( $p<0.006$ ). Our results provide evidence that flexor muscle recruitment and extensor recruitment differ during RLMs. Results suggest that flexor muscles are recruited at lower levels of pattern generator drive, and extensors are recruited as drive increases, consistent with our

hypothesis. Our findings also suggest that the spinal pattern generator preferentially recruits flexor motor pools independent of extensors, and rarely recruits extensors independent of flexors.  
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#### DNA METHYLATION MEDIATING THE IMPACT OF MATERNAL SOCIAL STATE ON OFFSPRING PHENOTYPE

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Early life adversity is known to have long-lasting impact on the phenotype of the offspring, particularly important are the associations between early life adversity and development of psychiatric disorders later in life. What are the mechanisms that mediate between exposure to stress during gestation and long-term effects on mental health? We have been testing in the last decade the hypothesis that epigenetic processes such as DNA methylation mediate the impact of the environment on the phenotype later in life. DNA methylation is a mechanism that marks genes during development and provides identical DNA sequences with different identities. Experiments in rodents demonstrated that low maternal care resulted in changes in DNA methylation in the glucocorticoid receptor gene in the hippocampus, which remained throughout life and altered the life long behavior of the offspring increasing anxiety and responsivity to stress. Similarly in humans we noted differences in DNA methylation in the glucocorticoid gene in hippocampi of adults who were abused as children. Our recent studies show that these changes in DNA methylation in response to early adversity affect broad regions of the genome and that they are not limited to the brain and occur in the immune system as well. We propose that the changes in DNA methylation in response to early life adversity are “adaptive genomic” mechanisms that adapts life-long genome programming to the anticipated life-long environment based on stress signals received during gestation and early life. We will present data from nonhuman primates and humans indicating that overlapping genes are altered in response to both prenatal and postnatal stress in multiple tissues; placenta, the immune system and the prefrontal cortex. A fraction of these alterations in the methylome remain in a gender specific way into adulthood. We have evidence from a study of a natural disaster in humans that objective stress is associated with changes in DNA methylation that are detectable in T cells and remain into adolescence. 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.

#### MECHANISMS OF CRITICAL PERIOD BRAIN DEVELOPMENT

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Developing neural circuits are dramatically impacted by the environment, but such plasticity declines with age, restricting therapeutic approaches to improve adult brain function. A focus on the cellular and molecular mechanisms underlying these developmental trajectories across brain regions has identified specific events controlling the onset and closure of such critical periods. The onset of the critical period is triggered by the maturation of specific GABAergic inhibitory circuits. Targeting these circuits using pharmacological or genetic manipulations can either accelerate onset or induce a delay. Critical period closure occurs by the

emergence of molecular brake-like factors, which stabilize neural networks and pose limitations on circuit rewiring. Interestingly, many of these factors are found within the inhibitory circuitry and surrounding extracellular milieu. Lifting these brakes reinstates critical periods, opening windows of plasticity to restructure adult circuitry. Thus, identifying neural targets that switch on and off critical periods will have far-reaching impact, including therapeutic strategies for neurodevelopmental and psychiatric disorders, recovery from brain injury, and lifelong learning.

#### THE ROLE OF LANGUAGE CUES ON FLEXIBLE MEMORY RETRIEVAL AT 12-MONTHS OF AGE

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From 12-months of age, infants can flexibly retrieve their memories in the puppet imitation task across a change in the form or colour of the puppet after a 10 min delay but not across a change in the form and the colour of the puppet (Hayne et al., 1997; Jones & Herbert, 2008). Language cues can enhance flexible memory retrieval across a change in the form of the puppet at 12-months of age (Herbert, 2011). The present study investigated the role of language cues for facilitating flexible memory retrieval across a change in the colour and form of the puppet. Twelve-month old infants were shown three target actions with a puppet and were given the opportunity to reproduce those actions on a puppet that differed in form and colour 10min later. Half the infants heard verbal labels during the demonstration and test, and half the infants did not. Imitation performance by infants in the full language and empty language groups did not exceed baseline performance. Thus, language cues do not facilitate flexible memory retrieval on a task that is too difficult for 12-month old infants. CDI data revealed no correlations between infant's language comprehension and their imitation performance in either group. Given that there was no relationship between infants' language comprehension and imitation performance in the full language group, the present experiment suggests that language cues may direct attention to relevant parts of the demonstration rather than providing an additional cue for recall (see Balaban & Waxman, 1997).

#### MATERNAL BUFFERING OF ADOLESCENT RISK TAKING: INSIGHTS FROM NEUROSCIENCE

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Despite being one of the healthiest developmental periods, morbidity and mortality rates increase dramatically during adolescence, largely due to preventable, risky behaviors. Because neural regions involved in motivation and cognitive processes undergo significant reorganization during adolescence (Nelson et al., 2005), the adolescent brain is thought to be highly flexible and malleable (Crone and Dahl, 2012) and therefore particularly sensitive to social influences. While prior work has focused on the social contexts which may increase risk taking, for instance peer presence (Chein et al., 2011), social contexts can also decrease risk taking, such as parental presence. Indeed, parents represent one of the most direct and proximal sources of influence over teenagers. In the current study, we examined how maternal presence influences adolescents' safe and risky decisions. Twenty-four adolescents were scanned as they completed a simulated driving course in the presence of their mother and alone during fMRI. We find that adolescents make significantly fewer risky decisions in the presence of their mother compared to alone, which was associated with greater recruitment of the VLPFC when making safe decisions, decreased activation in the ventral striatum following risky decisions, and greater functional coupling between the ventral striatum and VLPFC when making safe decisions. Our findings suggest that mothers serve to buffer adolescents' engagement in risky behaviors by altering their neural processing. Importantly, we show that parents do not merely decrease adolescent risk-taking by serving as gatekeepers but that parents may actually change the ways in which adolescents think and reason about risks.

THE BENEFICIAL EFFECTS OF A POSITIVE ATTENTION BIAS AMONGST CHILDREN WITH A HISTORY OF PSYCHOSOCIAL DEPRIVATION: REDUCING ANXIETY AND STRESS REACTIVITY

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Children raised in institutions experience psychosocial deprivation that has been shown to negatively impact attention, emotion regulation, and increase prevalence of psychiatric disorders. The current study examined the relations between attention biases and anxiety in children in the Bucharest Early Intervention Project. 136 children abandoned into institutional care were randomized to receive a high-quality foster care intervention or care-as-usual. At age 12, 33 care-as-usual and 30 foster care children performed a behavioral dot-probe task with both threat and happy face stimuli, and indices of attention biases to threat and positive stimuli were calculated. As well, children were seen in a modified Trier stress paradigm and saliva was collected and measures of cortisol reactivity were computed. Results showed that children placed into the foster care intervention had a significant attention bias toward positive stimuli ( $t(29) = 3.631, p = .001$ ) but no bias towards threat, while children who received care-as-usual showed no bias to either threat or positive stimuli. The magnitude of the positive bias was predicted by the percentage of time a child had spent in high-quality foster care ( $\beta = .283, t(61) = 2.308, p = .024$ ) and was associated with less social withdrawal ( $r(43) = -.302, p = .044$ ), overanxious behavior ( $r(43) = -.300, p = .045$ ), and social anxiety ( $r(43) = -.298, p = .046$ ). Additionally, within the foster care group, happy biases were related to better (less blunted) cortisol reactivity during a social stress task ( $\beta = .322, t(28) = 2.118, p = .034$ ). Research assessing attention biases in children experiencing early environmental stress may refine our understanding of happy biases as a potential protective mechanism for stress reactivity and anxiety disorders.

MANIPULATION OF THE PRE- AND POST-WEANING SOCIAL ENVIRONMENT AND ITS EFFECTS OF PREPULSE INHIBITION OF THE ACOUSTIC STARTLE RESPONSE ON C57BL/6

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Pre-pulse inhibition (PPI) is a tool that may be used to identify how early life stress can result in a deficient adult nervous system. Since both animals and humans demonstrate a PPI, animal research on PPI can be used to model the relation of the early social environment to later susceptibility to maladaptive adult behavioural phenotypes. The current study examined the effect on adult PPI of early life stress in C57BL/6 offspring reared under four social conditions: Animal-Facility Reared (Control), Early Handling (EH, daily 15 min separation), Maternal Separation (MS, daily 4 hr. separation from dam) and Maternal Peer Separation (MPS, daily 4 hr. separation from dam and of littermates); and two post weaning housing conditions: Socially Housed (SH, 2-3 individuals/cage) and Social Isolation (IH, 1 individual/cage). Four different PPI types; 0, 76, 80, or 84 dB; each 20ms duration, and a startle stimulus of 120 dB, 40ms duration, were presented and the percentage reduction of the startle response that occurred with a prepulse in comparison to the startle response that occurred without a prepulse (i.e., 0 dB prepulse) was calculated. Preliminary analyses indicate that EH subjects displayed lower levels of PPI and ASR than AFR, MS & MPS offspring. The post weaning manipulation does not seem to affect display

of PPI or the ASR and consistent with the human and animal literature, male mice display a greater ASR and PPI of the ASR than females.

SLEEP-MEDIATED CONSOLIDATION OF EPISODIC MEMORY IN CHILDREN AND ADULTS

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A recent study in human adults indicated sleep's beneficial role for "what-where-when" episodic-like memory utilizing eye tracking. Using the same paradigm we investigate, if the advantage of deeper and longer sleep in school children (8–12 yrs.) further impacts episodic memory consolidation. Children experienced two short episodes 1 hr apart, each comprising four distinct female faces at different locations in a 3 × 3 grid on a PC screen. Episodic memory was tested implicitly by tracking eyes and explicitly by oral report, either 1 hr later after the encoding (Pre-sleep group), or after a ~10.5 hr retention interval that contained either an overnight sleep (Sleep group), or daytime wakefulness (Wake group). Preliminary results in children reflected performances of the same adult groups on the explicit "what-where-when" memory and was better in the Pre-sleep and Sleep group as compared to the Wake group children, while all groups had above chance performance. Unlike in adults, the implicit measures in the eye exploration pattern did not reflect children's explicit performance. We present ongoing work with a detailed comparison of adults and children's explicit vs. implicit measures and their relation to sleep-mediated consolidation.

STRESS BUFFERING OF CORTISOL RESPONSE IN GUINEA PIG PUPS: THE EFFECTS OF SOCIAL INTERACTIONS WITH UNFAMILIAR ADULT MALES

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In mammals, the presence of a social partner can reduce or "buffer" hypothalamic-pituitary-adrenal (HPA) stress responses in threatening conditions. These effects are generally observed in partners who are closely bonded (e.g., mother-infant; male-female monogamous mating partners). Previously, we compared the stress buffering effects on HPA activity of the mother, a familiar littermate, and an unfamiliar adult male in guinea pig pups exposed to a novel environment. As expected, the mother significantly reduced the cortisol stress response while the littermate did not. Surprisingly, the unfamiliar adult male reduced cortisol levels of the pups as effectively as did the mother. Further examination revealed that the adult male interacted with the pups more than did other social partners. It was hypothesized in the current study that social interactions between the pup and the adult male suppressed the cortisol response. Therefore, we examined effects of males that could interact with pups (conscious males) and males that could not (anesthetized males). Social interactions were frequently observed between the conscious adult male and the pups. Once again, the conscious male greatly suppressed plasma cortisol levels of pups. On the other hand, the cortisol levels of pups tested with the anesthetized male were as high as those of pups tested alone. The finding confirmed our hypothesis that social interactions were responsible for stress buffering effects of the males. This may be due to the pups perceiving the interactions as play. Ongoing studies are currently investigating possible brain mechanisms underlying this effect.

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TRANSGENERATIONAL EPIGENETIC PROGRAMMING OF HYPOTHALAMIC MECHANISMS THAT REGULATE FEEDING AND OBESITY BY HIGH FAT DIET

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Parental obesity can affect the children's likelihood to overeat and develop obesity. Changes in epigenetic programming have been implicated as one of the mechanisms underlying this phenomenon. Using a rat model, we designed a study in which we exposed only the first generation to chronic high fat diet (HFD) and followed the effect on two consecutive generations of standard fed offspring. We focused on the promoter of the hypothalamic neuropeptide *Pomc*, which is crucially involved in control of food intake. HFD consumption by non-mated female rats (FO) significantly increased body weight and plasma leptin levels and attenuated *Pomc* mRNA expression. This was associated with hypermethylation of the *Pomc* promoter. Although as expected the HFD resulted in up-regulation of the transcription factor Sp1, the binding of Sp1 to the hypermethylated *Pomc* promoter was significantly reduced. Furthermore, perinatal exposure to maternal HFD lead to long term acquired alteration in DNA methylation patterns and posttranslational modifications of histone H3 lysine 9 (H3K9) that affect *Pomc* transcription in the F1 and F2 offspring. In addition, as a potential mechanism underlying the regulation of *Pomc* expression we found an involvement of a repressor complex including the binding of methyl binding domain 1 (MBD1) to the *Pomc* promoter, interacting with SETDB1 methyltransferase to promote the formation of methylation of H3K9. These findings contribute to our understanding of the mechanisms through which environmental cues are translated into stable changes in the *Pomc* gene, leading to obesity.

#### FRONTAL HIGH FREQUENCY EEG SPECTRAL POWER IS INCREASED DURING ACTIVE SLEEP IN NEWBORNS WITH CONGENITAL HEART DISEASE COMPARED TO HEALTHY CONTROLS

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Congenital heart disease (CHD) is the leading cause of mortality and morbidity among infants with birth defects, and children born with severe forms of CHD are at high risk for a wide spectrum of neurocognitive difficulties. In this study, we investigated whether neurodevelopmental deficits associated with altered hemodynamics in fetuses with CHD were reflected postpartum in alterations to high frequency electroencephalogram (EEG) spectra, and whether EEG parameters could be used as early markers of neurodevelopmental deficits. We hypothesized high frequency EEG power would be lower in infants with CHD. Frontal EEG was specifically examined due to the region's importance for executive function and attention in infants and children. High-density EEG was recorded during sleep from infants (37–40 w gestational age) diagnosed with CHD ( $n = 39$ ) and healthy full-term controls ( $n = 233$ ) within 72 hr of birth. EEG power was divided into three contiguous bands - beta (12–23 Hz), low gamma (24–36 Hz), and high gamma (37–48 Hz). During active sleep, there was an unexpected significant increase in power in the CHD cohort compared to controls within beta (13–24 Hz,  $p < 0.01$ ) and low gamma (25–36 Hz,  $p < 0.05$ ), with a similar though non-significant trend in high gamma (37–48 Hz). Interestingly, no significant changes were observed in quiet sleep. We hypothesize that the increased high frequency EEG power during active sleep may signify a stress response or compensatory adaptation generated by changes in oxygen and nutrient delivery to the fetal brain due to structural heart defects and, for reasons unknown, these effects were sleep state dependent.

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#### EARLY DEPRIVATION ALTERS THE DEVELOPMENT OF AFFECTIVE AND SOCIAL BEHAVIOR IN RATS SELECTIVELY BRED FOR AN INFANTILE TRAIT

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Animal models of child neglect have been valuable in understanding the deleterious effects of an early negative environment on brain development. There is mounting evidence that a history of early childhood maltreatment greatly increases the risk of developing a psychiatric disorder when there is also a genetic vulnerability. Negative effects have been shown to alter behavioral phenotypes of rodents via epigenetic mechanisms. In this study, the effects of Early Deprivation (ED) were examined in rats selectively bred for an infantile affective trait: high and low rates of ultrasonic calls (USVs) after brief maternal separation. High and Low male and female rat pups were isolated individually for 3 hr a day for the first week of life. At one week of age, High line subjects vocalized more than Lows, as expected, and had greater USV reductions after ED. No sex differences were observed in neonates. Line and sex differences were detected in behaviors on the zero maze with interactions with a prior ED history in adults. Low subjects also showed increased social behaviors as juveniles compared to High subjects. Similar to our findings with a positive early experience, Communal Nesting, a possible epigenetic effect of altered early environment was seen in measures of anxiety behavior, but not in measures of social behavior, in this genetic rodent model. These results parallel, with some interesting species differences, the recent findings by Kundakovic, Lim, Gudsruk and Champagne (2013) using a mouse model of maternal separation.

#### LIMITS ON THE BILINGUAL ADVANTAGE IN INFANT MEMORY GENERALIZATION ON A TRANSFER TASK

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Bilingual infants from 6- to 24-months show an advantage in memory generalization, flexibly reproducing actions on novel objects significantly more than age-matched monolinguals. Prior research demonstrated that a novel label helped monolingual 24-month-olds but not 18-month-olds generalize between perceptually different stimuli (Herbert & Hayne, 2000) but that 24-month-old bilinguals were able to generalize without novel labels (Brito, Grenell, & Barr, 2014). In the present study, we examined whether a novel would enhance memory generalization in bilingual 18-month-olds. During the demonstration an experimenter provided a novel label ("meewa" or "thornby") for the rattle and animal stimuli during demonstration and prior to the test 24 hr later. Infants were tested with the same stimulus set (cued recall) and with a novel version of the other stimulus set (memory generalization). Infants assigned to the baseline condition did not receive a demonstration. Our preliminary findings replicated those of Herbert and Hayne demonstrating that cued recall performance significantly exceeded baseline ( $M_{\text{baseline}} = 0.54$ ,  $M_{\text{experimental}} = 1.46$ ) but memory generalization did not exceed baseline across the 24-hr delay, and there were no significant effects of language status. These findings are consistent studies that have shown that during the second year of life, toddlers were not able to utilize novel labels in difficult transfer of learning tasks (Herbert & Hayne, 2000; Zack et al., 2013). The present study extends these findings by demonstrating that the memory generalization advantage is not due to overgeneralization or lack of discrimination by bilinguals and that there are constraints on the bilingual generalization advantage.

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#### AGE-RELATED CHANGES AND SEX DIFFERENCES IN VISUOSPATIAL WORKING MEMORY IN 2- TO 4-YEAR-OLDS

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Visuospatial working memory (VSWM) is the ability to briefly retain and manipulate visual and spatial information. Age-related improvements in VSWM on the A B task have been documented during infancy (Diamond, 1990) and between 3 and 7 years using search tasks (Ewing-Cobbs, Prasad, Landry, Kramer, & Leon, 2004). However, less work has investigated age-related differences across the preschool years. We tested 528 2-, 3-, and 4-year-olds using a VSWM object occlusion task, Spin the Pots (STP; Hughes & Ensor, 2005). Six stickers were hidden under six of eight colored cups. A lid covered the cups, the apparatus was spun 180 degrees and on each trial the child was allowed to find one sticker. Trials continued until all 6 stickers were retrieved. To succeed, children must update their memory about the location of the remaining stickers after each trial.  $3(\text{Age}) \times 2(\text{sex})$  ANOVAs showed the success

rate (stickers/#trials) was similar in 2- and 3-year-olds ( $M_2 = .42$ ,  $SD_2 = 0.17$ ,  $M_3 = .45$ ,  $SD_3 = 0.18$ ) but significantly increased in 4-year-olds ( $M_4 = .54$ ,  $SD_4 = 0.20$ ),  $F(2,527) = 4.18$ ,  $p < 0.001$ . Older children also completed the task in significantly fewer trials, less time, and perseverated less than younger children. Girls had a higher success rate than boys, but there was no interaction between age and sex. The STP task was developmentally appropriate across a wide age range but also sufficiently difficult to detect age-related changes, sex differences, and limits to VSWM during early childhood. Overall these findings provide further support for rapid acquisition of working memory during early childhood.

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