Women's Health Research Day
4.18.2013
8 a.m. - 6 p.m.
Institute of Psychiatry

Medical University of South Carolina • Charleston, SC
Specialized Center of Research (SCOR) on Sex and Gender Factors Affecting Women's Health
Building Interdisciplinary Research Careers in Women's Health (BIRCWH)
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Investigation of Epidemiological Factors As Barriers To Indicated Radiation Therapy in Post-Mastectomy Breast Cancer Patients in South Carolina

Rhome R1, Walquist AE2, Cooper SL3, Hill E2, Garrett-Mayer E2, Harper JL3
1MUSC College of Medicine, 2 MUSC Division of Biostatistics and Epidemiology, 3 MUSC Department of Radiation Oncology

**Background:** Three large prospective randomized trials have demonstrated increased survival and loco-regional control in women with intermediate and high risk breast cancer receiving post-mastectomy radiotherapy (PMRT).

**Objective:** To investigate the frequency of utilization and potential barriers to receipt of adjuvant PMRT in SC.

**Methods:** Using SCCR data, simple and multiple regression models were used to estimate the odds OR of receiving PMRT in each risk group and for the epidemiologic factors age, race, median household income and distance to the nearest radiation therapy facility. SCCR PMRT utilization rates were compared to SEER rates using a Chi square test.

**Results:** The SC rates of PMRT utilization were 4% (low), 23% (intermediate) and 44% (high risk). The SC rates of PMRT utilization were significantly lower than the national rates only for the high risk group (44% vs. 55%) (p=0.027). Only, age at diagnosis was significantly associated with receipt of PMRT in intermediate and high risk. Specifically, for every year increase in age there is a 3% reduction among intermediate risk (OR = 0.97, 95% CI = 0.951 to 0.992; p = 0.01); and 2% decrease in the odds of receiving PMRT among high risk patients (OR = .98, 95% CI = 0.966 to 0.998; p = 0.03).

**Conclusions:** The SC rate of PMRT utilization for high risk patients is lower than national rates, despite prospective randomized data to support its efficacy. Age at diagnosis was the only patient-specific characteristic associated with a decreased OR for receipt of PMRT in this SCCR analysis.

Molecular Basis for Racial Disparity in Preeclampsia

Kyu-Ho Lee, MD-PhD1, Christopher J Robinson, MD2, Elena Rivers1, Anthony J Horton1 and Christopher D Clark, BS1.

1Pediatrics, Medical University of South Carolina, Charleston, SC, United States and 2Obstetrics and Gynecology, Medical University of South Carolina, Charleston, SC, United States.

**Background:** Preeclampsia (PE) affects 5-8% of pregnancies and is a significant source of perinatal morbidity and mortality. PE results in hypertension and proteinuria after 20 weeks of pregnancy whose increasing severity leads to premature delivery. Mechanisms underlying PE are poorly understood as are risk factors mediating observed racial disparity. The developmental gene Nkx2.5 is expressed in trophoblast cells and abnormal amnions are observed in mice bearing null Nkx2.5 mutations. We assessed Nkx2.5-related gene expression in placenta from normal and PE pregnancies.

**Objective:** To examine expression levels of Nkx2.5/Nkx2.5 target genes in placenta of normal vs PE patients. Design/Methods: IHC assay of Nkx2.5 and target gene expression and qPCR of mRNA from normal term and PE placenta.

**Results:** Nkx2.5 and its targets are expressed in syncytiotrophoblast of human placenta with a strong correlation between early onset severe PE (EOSPE) and high levels of placental Nkx2.5 expression more prevalent among whites vs. blacks (n=32). A highly significant correlation was found between high Nkx2.5 and sFlt-1 mRNA expression levels (Pearson’s r=.73). Nkx2.5/sFlt-1 levels were also highly correlated to levels of Nkx2.5 target gene Sam68 (Pearson’s r=.64). Sam68 regulates mRNA splicing of the type generating sFlt-1 mRNA, suggesting a functional link between Nkx2.5 and induction of PE via sFlt-1, an inducer of PE. Expression of two other Nkx2.5 targets, Ccdc117 and the stress response factor Xbp1 is elevated in white (Ccdc117) or black (Xbp1) PE patients with high Nkx2.5 levels.

**Conclusions:** Nkx2.5 and its target genes represent novel and racially disparate biomarkers for EOSPE.
Gender Effects on Biologic Measures of Stress and Bonding in Mother-Infant Pairs

Eve Spratt, MD, MSCR¹, Paul J Niertet², PhD, Amy Wahlquist, MS², Courtney Marsh³, Carrie Papa¹, Kathleen Brady, MD, PhD³ and Carol Wagner, MD¹

¹MUSC Department of Pediatrics, ²MUSC Department of Biostatistics and Epidemiology, ³MUSC Department of Psychiatry

Background: Examination of the Hypothalamic Pituitary Adrenal (HPA) axis response to stress as measured by salivary cortisol and serum levels of the posterior pituitary hormone oxytocin (OT) associated with bonding improves our understanding of physiologic mechanisms present in early development and influenced by mother-infant interactions.

Objective: The goals of the study were (1) to explore correlations between mother and baby cortisol levels; (2) to explore gender differences in infant serum OT and HPA responses after a blood stick stressor in infants.

Methods: 42 infant-mother pairs provided baseline biologic samples and clinical data on behavior and mood. The mother and infant pairs provided a sample of salivary cortisol to measures HPA response, followed 10 minutes later by a blood draw to collect serum including oxytocin, and 10 minutes post the stress of a blood draw, a second sample of salivary cortisol was collected.

Results: (1) Higher baseline cortisol measures for the mother were related to higher baseline cortisol measures for the infant (rho=0.68, p=<0.0001). (2) Girls had a larger positive change in cortisol than boys, after adjusting for the baseline cortisol value (adjusted difference = 0.58ug/dL, p=0.05). (3) OT was not statistically different between male and female infants or in those that breast-fed and bottle-fed.

Conclusions: Mothers and infants have similar patterns of HPA response to a stressor as measured by salivary cortisol. In response to the stressor, female infants had a greater peak response in cortisol levels than male infants. OT levels between male and female infants and those that breast fed or not were similar.

Acknowledgments: This research project was supported by Award Number UL1RR029882 from the National Center for Research Resources and from grant K23 NIH/NIMH K25MH064111 (PI: Eve G. Spratt) and additional resources were obtained from grant NIH/NIDA K24DA00435: Midcareer Investigator Award in Patient-Oriented Research (PI: Kathleen T. Brady). This study was supported by the South Carolina Clinical & Translational Research Institute, Medical University of South Carolina’s CTSA, NIH/NCATS Grant Number UL1TR000062.

Results of NICHD Two-Site Maternal Vitamin D Supplementation Randomized Controlled Trial during Lactation

Carol L Wagner, MD¹, Cynthia R Howard, MD², Thomas C Hulsey, ScD¹, Myla Ebeling, RA¹, Judy R Shary, MS¹, Pamela G Smith, RN¹, Cynthia Childs, BS¹, Martha Murphy, BS¹, Sarah N Taylor, MD¹, Ruth A Lawrence, MD² and Bruce W Hollis, PhD¹.

¹Pediatrics, Medical Univ of SC, Charleston, SC, United States and ²Pediatrics, Univ of Rochester, Rochester, NY, United States.

Background: AAP recommends all breastfed (BrF) infants receive vitamin D supplementation (vitD-S) starting within 1st few days after birth. Could maternal vitD-S at higher doses provide adequate levels in breast milk without toxicity to mother, effectively treating both mother and her BrF infant?

Objective: To assess safety and effectiveness of maternal vitD-S of 6400 IU/day alone compared with maternal and infant vitD-S of 400 IU/day.

Design/Methods: Fully BrF women and their infants at 4-6 wks postpartum living in Charleston, SC and Rochester, NY participated. Women randomized to 1 of 2 tx grps substratified by race: Control (400 IU vitD/day) or 6400 IU/day. Infants of Control mothers received 400 IU/day while infants of 6400 IU grp received placebo. 1o outcome measure: serum 25(OH)D at 7 mos postpartum in both mother and infant.

Results: 405 mother/infant dyads enrolled into 2 tx grps: 206 in 400 IU and 199 in 6400 IU grp. Maternal vitD status at
baseline differed by race/ethnicity, education, SES and by latitude, but not by tx: maternal 29.1±13.9 (Control) vs. 30.2±12.8 ng/mL (6400 IU) (p=0.1). N=177 mothers continued fully BrF through 7 mos (n=83 400 IU; n=94 6400 IU grp). By 2 mos tx, maternal 25(OH)D differed between groups sustained to 7-mos postpartum (p<0.0001); however, no differences in infant 25(OH)D by tx: 45.2±12.4 (400 IU grp) and 43.2±14.3 (p=0.4).

Conclusions: Maternal vitD supplementation w/6400 IU/day alone safely improved maternal vitD status during 6-mos of full BrF and was equivalent to maternal/infant vitD-S of 400 IU/d in achieving infant vitD sufficiency. These findings have implications for vitD recommendations during lactation.

Altered Th-1/Th-2 Cytokines in Pregnancy and Risk for Postpartum Anxious Depression

Constance Guille, MD1, Leah Fryml, BA2, Roger Newman, MD 3, Neill Epperson, MD 4, Laura Goetzl, MD, MPH5

Medical University of South Carolina, Department of Psychiatry and Behavioral Sciences1; College of Medicine2; Department of Obstetrics and Gynecology3, University of Pennsylvania, Department of Psychiatry4, Temple University School of Medicine, Department of Obstetrics and Gynecology5

Background: Alterations in Th-1/Th-2 cytokines represent a promising biomarker for risk of major depression but findings have been inconsistent owing to disease heterogeneity. Further, cross-sectional studies preclude inference regarding directionality of cytokines and depression. Depression with comorbid anxiety is common during the postpartum period and likely represents a distinct subclass of depressive symptoms (anxious depression). Moreover, the postpartum period can be anticipated, allowing prospective assessment of cytokine levels.

Objective: To determine if cytokines in pregnancy are associated with subsequent postpartum anxious depression (ppAD).

Methods: Medical records were reviewed to identify cases of depression and anxiety during pregnancy and the year postpartum in participants in a prospective study of cytokines in pregnancy. Signature Th-1/Th-2 cytokines (7 in total) were measured at 34-42 weeks gestation. Logistic regression methods were used to assess the relationship between individual cytokines and ppAD.

Results: 231 women with a complete cytokine profile were included in the analysis. After controlling for potentially confounding variables, women were more likely to experience ppAD with lower Interferon-gamma (IFN-γ)(OR 0.78; 95%CI 0.61-0.99), higher Interleukin (IL) 6(OR1.6; 95%CI 1.002-2.79) and higher IL-10(OR1.2; 95%CI 1.01-2.79).

Conclusions: We report a novel temporal relationship between altered Th-1/Th-2 cytokine profile in pregnancy and subsequent risk of ppAD. One therapeutic mechanism of selective-serotonin reuptake inhibitors is upregulation of IFN-γ, therefore our finding of an association between lower IFN-γ and increased ppAD has biologic validity. Higher IL-6/IL-10 levels suggest that maternal inflammatory response to pregnancy may mediate mood and/or anxiety symptoms. Further prospective evaluation of these relationships are needed.

Exploring the neural correlates of psychosocial stress in cocaine dependent women: Implications of ovarian hormones

M.M. Moran-Santa Maria, K. Johnson, J. Pfeiffer and K.T. Brady

Department of Psychiatry and Behavioral Sciences, Medical University of South Carolina, Charleston, SC, 29425
Department of Anesthesia, Stanford University, Stanford CA, 94035

Background: A convergence of evidence suggests that ovarian hormones mediate negative affect and drug craving in cocaine dependent women. Despite these data the role of ovarian hormones in mediating the neural correlates of psychosocial stress have yet to be explored in clinical populations.

Objectives: The purpose of the study was to explore the impact of ovarian hormones on psychosocial stress related brain activity in cocaine dependent women and healthy control women.

Methods: Blood oxygen level dependent (BOLD) functional magnetic resonance imaging data were collected from cocaine-dependent (n=13) and control (n=13) women during the Montreal Imaging Stress Task (MIST). Plasma estrogen
and progesterone data were collected. Subjective stress, anxiety and craving were measured at baseline and after the MISt.

**Results:** During psychosocial stress, cocaine dependent women exhibited significantly greater limbic brain activity than controls (p<0.05). During mental arithmetic, healthy controls exhibited greater brain activity than cocaine dependent women (p<0.05). There were no group differences in ovarian hormone levels.

**Conclusion:** These data support the extant literature demonstrating stress related hyperactivity in limbic brain regions of cocaine dependent women. Moreover, future studies examining the impact of changes in ovarian hormone status on stress related brain activity across the menstrual cycle are warranted.

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**Oxytocin differentially decreases methamphetamine intake and reinstatement to methamphetamine seeking in male and female rats**

Reichel, Carmela M; Cox, Brittney M; Young, Amy B; and See, Ronald E.

Department of Neurosciences, Medical University of South Carolina, Charleston, SC, USA

**Background:** Sex differences exist in methamphetamine (meth) addiction patterns; however, meth effects and potential therapeutic treatments are typically studied in males. Here, we determined whether oxytocin impacted motivation for meth and sucrose self-administration as well as its efficacy at reducing reinstatement in males and females.

**Methods:** Rats self-administered meth or sucrose pellets. Following stable daily intake, rats were tested on a progressive ratio after acute oxytocin (1 mg/kg) or saline. Lever responding was then extinguished and rats underwent a series of conditioned cue, meth, and yohimbine primed reinstatement tests with oxytocin (1 mg/kg) or saline.

**Results:** On the progressive ratio test, females had higher lever responding, drug infusions, and break points relative to males. Oxytocin effectively decreased responding on these measures in females. Sucrose intake in males and females did not differ on any measure, nor did oxytocin impact responding. Females reinstated more than males to meth-conditioned cues and oxytocin decreased this responding. Females had greater meth-primed reinstatement and oxytocin decreased meth seeking in both sexes. Oxytocin did not affect reinstatement of sucrose seeking under any conditions.

**Discussion:** The combined pattern of results suggests that oxytocin may be a potential treatment for prevention of relapse in meth addiction for males and females with more extensive benefits in females. These studies were conducted in accordance with the Guide for the Care and Use of Laboratory Animals, as adopted and promulgated by the National Institutes of Health. This research was supported by NIH grants P50DA016511, K12HD055885.

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**The Association of NMDA Receptor Antibodies and Neurocognitive Dysfunction in Pediatric Lupus Patients**

Ruth NM, Kral MC, Slan S, Nowling TK, Passo MH, and Gilkeson GS

Division of Pediatric Rheumatology, MUSC, Charleston, SC

**Background:** Activation of the NMDA receptor is critical in learning and memory and is expressed on neurons throughout the hippocampus and cortex.

**Objectives:** To measure the prevalence of anti-NMDA-NR2 receptor antibodies in patients with cSLE and JIA; to assess the association between elevated anti-NMDA-NR2 receptor antibodies and neurocognitive dysfunction in cSLE and patients with JIA.

**Methods:** Patients diagnosed with SLE prior to age of 18 were recruited. Each underwent formal neurocognitive testing. The test battery included a comprehensive assessment of cognitive domains. The patients also underwent NMDA receptor-NR-2 subunit antibody testing by ELISA.

**Results:** JIA patients performed better than SLE patients in full scale IQ (p<.05), single word reading skills (p<.01) and math calculation skills (p<.05). There was a trend toward significance for a measure of inattention (CPT-II Omission
score, the JIA group made more omission errors than the SLE group, p=.06). Spearman correlations between NMDA receptor antibodies and neurocognitive testing for the entire group (SLE and JIA) showed a strong correlation between NMDA receptor antibodies and math fluency (0.49, p=.02). Spearman correlations between NMDA receptor antibodies and neurocognitive testing for the SLE group only showed correlations for working memory (0.43, p=.07) and for math fluency (0.65, p=.003). Spearman correlations for SLEDAI and all cognitive measures in the SLE group showed that none of the correlations were strong (none>0.4).

Conclusions: The findings of this study seem counterintuitive and demonstrate the difficulties in finding biomarkers in patients with NP-SLE. Further studies will be necessary to make more definitive conclusions.

Abstracts – Poster Presentation

Poster 1.
Number of Breastfed Babies Inversely Related to Mother’s Development of Systemic Lupus Erythematosus (SLE) Compared to Controls
April Barnado*, Lee Wheless, Anna Meyer, Gary S. Gilkeson, Diane L. Kamen
1Division of Rheumatology and Immunology, Department of Medicine, Medical University of South Carolina
2Department of Public Health Sciences, Medical University of South Carolina

Background: Given the female predominance in Systemic Lupus Erythematosus (SLE), hormonal factors may play a role. Studies on breastfeeding and development of SLE have been inconsistent. Objectives: From a longitudinal study of Gullah African Americans, we examined the impact of parity and breastfeeding on development of SLE.

Methods: Cases and controls with at least one live birth were selected. We collected demographic, socioeconomic, and reproductive data. Differences between cases and controls were tested using t-tests or chi-square tests. Logistic regression was used to calculate odds ratios and 95% confidence intervals, adjusting for age and education.

Results: Compared to controls (n = 207), cases (n = 120) had significantly fewer mean live births. Cases were as likely as controls to have breastfed with similar mean weeks of breastfeeding and mean number of babies breastfed. Number of live births was not associated with risk of developing SLE (p for trend=0.70). There was a non-significant trend for a decreased risk of SLE with longer duration of breastfeeding (p for trend=0.20). The number of babies breastfed was associated with a lower risk of SLE (p for trend= 0.02).

Conclusions: Number of live births was not associated with risk of developing SLE. The number of babies breastfed was protective against developing SLE. Duration of breastfeeding was not associated with risk of SLE, possibly because prolactin levels peak early in lactation and may offer a protective role that is less significant as levels decline. Early breastfeeding may be protective against autoimmune disease, which warrants further investigation.

Poster 2.
Gender differences in the effects of sleep disruption on pain – A pilot study
Kelly S. Barth, DO*, Jeffrey Borckardt PhD, Kathleen Brady, MD PhD
Medical University of South Carolina

Background: Females are more likely to suffer with both chronic pain disorders and sleep disturbances than males. The reasons for these gender differences are not understood. As poor sleep and pain are strongly inter-related, one possible explanation is that females may be more sensitive to the effects of sleep disturbance on pain.

Objectives: This pilot study explored gender differences in the role of sleep disruption on laboratory measures of pain
in four healthy men and women. The purpose of the pilot study was to inform the application for a larger grant using this protocol in 52 subjects.

**Methods:** Utilizing a within-subjects design, we examined pain laboratory measures in four subjects (two male and two female) before and after one night of sleep disruption. The method of sleep disruption was unique and imitates sleep disturbances seen in those with chronic pain.

**Results:** Preliminary data analysis reveals that pain inhibition (measured by Descending Noxious Inhibitory Control Index), was decreased in female subjects after sleep disruption, while it was slightly increased in male subjects after sleep disruption.

**Conclusion:** These preliminary findings suggest that females may be more likely than males to demonstrate a breakdown of central pain inhibition mechanisms following sleep deprivation. This data will inform a larger study that will measure gender differences in pain, somatic symptoms and stress reactivity following sleep disruption. This data will ultimately inform the study of gender-specific treatment interventions for those that suffer with painful conditions that are more prominent in females, such as fibromyalgia.

**Poster 3.**

**Gender differences in neural response to mesolimbic stimulation: an interleaved TMS-BOLD imaging study**

Melanie Canterberry, William DeVries, Joseph J Taylor, Mark S George, Colleen A Hanlon

Medical University of South Carolina, Department of Psychiatry

**Background:** The medial prefrontal cortex (MPFC) is the primary cortical hub of mesolimbic circuitry which governs emotional and reward processing. Disruptions in this circuit are associated with disordered affect and substance-dependence. Preliminary evidence suggests women may be particularly responsive to mesolimbic stimulation, which may be related to their high levels of stress-induced substance abuse.

**Objective:** To determine whether the MPFC stimulation has a greater effect on mesolimbic circuit activity in women than men through the use of interleaved transcranial magnetic stimulation (TMS)-BOLD imaging.

**Methods:** Functional neuroimaging data (BOLD) was acquired from 20 healthy participants (45% women) and a small cohort of cocaine users (n=12, 58% women). Single TMS pulses were applied to their MPFC while the participants lay still in the scanner. The BOLD response to MPFC stimulation was modeled as events using standard voxel-based analyses and compared between genders within groups.

**Results:** Among controls, women had significantly more BOLD activity than men the MPFC and caudate. Men had significantly more activity in the inferior parietal cortex and the lateral frontal cortex (BA 9). As with the controls, female users had significantly more activity in the prefrontal cortex than men. There were no areas in which male users had a larger response to MPFC stimulation than women.

**Conclusions:** These preliminary data suggest that both healthy and substance-dependent women have an elevated baseline mesolimbic response to stimulation compared to men. Understanding these gender differences may be critical to understanding individual differences in acquisition of and treatment of limbic-related disorders, including addiction.

**Poster 4.**

**Role of orexin/hypocretin in conditioned sucrose-seeking: a comparison between female and male rats**

*Angie M. Cason* and Gary Aston-Jones. Department of Neurosciences, Medical University of South Carolina, Charleston, SC 29425

**Background:** Accumulating evidence implicates the orexin/hypocretin system in reward-seeking for highly salient food rewards. Increased reward-seeking leads to the overconsumption of palatable foods that in turn contributes to obesity. Like other eating disorders, obesity affects more women than men. Our findings indicate that signaling at the orexin 1 receptor (OxR1) is involved in sucrose reinforcement and cue-induced reinstatement of extinguished sucrose-seeking ,
particularly in food-restricted subjects (Cason & Aston-Jones, Psychopharmacology 2012).

**Objectives:** Here we investigated the role of OxR1 activation in sucrose reinforcement, and in cue-induced reinstatement of extinguished sucrose-seeking, in female and male rats.

**Methods:** Food-restricted and ad lib-fed rats were trained to self-administer sucrose pellets, and the OxR1 receptor antagonist SB 334867 (SB) or vehicle was administered 30 min prior to a self-administration session or prior to a cue-induced reinstatement session.

**Results:** In females, SB (20-30 mg/kg) decreased responding during self-administration, but not during reinstatement behavior. In males, SB decreased responding for sucrose (10-30 mg/kg) and the number of reinforcers earned (20-30 mg/kg) during self-administration. Furthermore, SB attenuated cue-induced reinstatement of sucrose-seeking. In both sexes, the effects of SB were greatest in food-restricted subjects.

**Conclusions:** These results indicate that signaling at the OxR1 receptor is involved in sucrose reinforcement, and lead us to consider that conditioned activation of Orx neurons may increase motivation for food reward especially during food restriction. Moreover, the findings that SB is less effective at inhibiting responding for sucrose in females suggest that signaling at the OxR1 receptor is sexually specific. Supported by PHS grants DA016511, DA006214, DA023354.

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**Poster 5.**

**Role of corticotropin releasing factor (CRF) receptors in cocaine seeking during the initiation of abstinence: a comparison between female and male rats**

*Angie M. Cason* and Gary Aston-Jones. Department of Neurosciences, Medical University of South Carolina, Charleston, SC 29425

**Background:** After repeated daily cocaine self-administration, responding on the previous active lever on the first day of extinction (ED1) is reported to be greater in female than in male rats. We hypothesized that brain CRF stress systems are engaged to promote drug seeking because of the absence of expected drug reward, and that antagonism of CRF receptors at that time would attenuate the increase in drug-seeking on ED1.

**Objectives:** The focus of the present study was to determine the role of CRF1 receptors in ED1 drug seeking in males and females.

**Methods:** Rats were trained to make an active lever press on a fixed-ratio 1 schedule of reinforcement. Active lever presses resulted in a single infusion of cocaine (3.0 mg/ml), paired with a compound light+tone stimulus and followed by a 20 second time-out. Each animal met a criterion of 10 sessions with at least 10 infusions per session. On the following day, rats were subjected to an extinction test (ED1). Rats received an injection of the selective CRF1 receptor antagonist CP 154,526 (10 or 20 mg/kg) or vehicle 20 min prior to the ED1 session. During the ED1 test, active lever presses resulted in no programmed consequence (no stimulus light, tone, or infusion).

**Results:** Females exhibited slightly higher responding on ED1 compared to males, as previously reported. Pretreatment with CP 154,526 significantly decreased ED1 responding (drug seeking) in both males and females.

**Conclusions:** These findings indicate that females have an elevated stress response to cocaine abstinence, and that the CRF system is involved in drug seeking during the initiation of abstinence in both males and females. Future studies will identify the neural sites where CRF is involved. Supported by PHS grants DA016511, DA006214, DA023354.
Faculty of Medical Sciences, University of the West Indies at Mona, Jamaica 3Bureau of Disease Control, SC DHEC 4South Carolina College of Pharmacy/University of South Carolina Campus, Columbia, SC.

**Background:** Female breast cancer (BC) mortality rates in South Carolina (SC) are 40% higher among African-Americans (AAs) than European-Americans (EAs). Proposed reasons include race-associated variations in tumor characteristics and/or care, which may be subject to income effects.

**Objective:** To describe race-associated differences in tumor biologic phenotype and stage among low-income participants in the Best Chance Network (BCN), a government-funded screening program, and compare them with disparities in the general SC BC patient population.

**Methods:** BCN data for participants aged 47-64 years during 1996-2006 were linked with SC Central Cancer Registry. Race-specific case proportions and incidence rates based on estrogen receptor (ER) status and histologic grade were estimated.

**Results:** Among 33,880 BCN participants, 607 BCs were diagnosed (53% among AAs). Proportionally, stage did not differ by race, with about 40% advanced stage. Invasive tumors in AAs were 67% more likely (proportions) to have poor-prognosis phenotype (ER-negative and high-grade) than in EAs; this was more due to the 46% lesser AA incidence (rates) of better-prognosis (ER+ lower-grade) cancer than the 32% greater incidence of poor-prognosis disease (p-values <0.01). Compared to the general SC population, racial disparities in poor prognostic features within the BCN population were attenuated, due to more frequent adverse tumor features in EAs rather than improvements for AAs.

**Conclusions:** Rates and proportions give different, but complementary, perspectives on BC racial disparities. For low-income women, closing racial and income mortality gaps requires improved early diagnosis, addressing causes of racial differences in tumor biology, and improved care for cancers with poor-prognosis biology.

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**Poster 7.**

**Gender Differences in Stroke Recognition**

**Charles Ellis,** Health Sciences and Research, College of Health Professions, MUSC

**Background:** Studies suggest gender differences exist in recognition of early warning signs of stroke. Poor recognition of stroke warning signs is associated with negative treatment seeking behaviors which can result in poor stroke-related outcomes.

**Objective:** To examine gender differences in recognition of traditional early warning signs of stroke and first action to initiate treatment in a sample of stroke survivors.

**Methods:** We compared demographic (age, stroke age, education, usual source of care, and insurance) and clinical (health literacy and stroke knowledge) variables along with stroke survivor’s recognition of traditional stroke warning signs and appropriate first action to initiate treatment.

**Results:** Seventy-one stroke survivors participated in this pilot study. Females in the sample were significantly older than males at time of stroke (62 years vs. 55 years; \( p < 0.05 \)). The two groups did not differ in clinical variables. Recognition of traditional individual stroke warning signs ranged from approximately 60% to 90%. There were no significant gender differences in the recognition of individual warning signs. Females were more likely to recognize all five traditional warning signs compared to men (67% vs. 42%; \( p = 0.04 \)). Similarly, 58% of female participants recognized all five traditional stroke warning signs collectively and would call 9-1-1 as a first action compared to only 29% of males (\( p = 0.02 \)).

**Conclusions:** Females recognized traditional stroke warning signs more often than males. Educational programs should emphasize both traditional and non-traditional stroke warning signs among females and address these differences with their healthcare providers.
Serum inflammatory markers and preeclampsia in type 1 diabetes: a prospective study

Mei Du1, Arpita Basu2, Dongxu Fu1, Mingyuan Wu1, Michael Centola3, Alicia J. Jenkins1, 4, Kristian F. Hanssen5, 6, Satish K. Garg7, Samar M. Hammad8*, James A. Scardo9, Christopher E. Aston10, and Timothy J. Lyons1

1Harold Hamm Diabetes Center & Section of Endocrinology and Diabetes, University of Oklahoma Health Sciences Center (OUHSC), Oklahoma City, Oklahoma, USA 2Department of Nutritional Sciences, Oklahoma State University, Stillwater, Oklahoma, USA 3Arthritis and Immunology, Oklahoma Medical Research Foundation, Oklahoma City, Oklahoma, USA 4The University of Melbourne, Department of Medicine, St. Vincent's Hospital, Melbourne, Australia 5Department of Endocrinology, Oslo University Hospital, Oslo, Norway 6Department of Obstetrics and Gynecology, Oslo University Hospital and Faculty of Medicine, University of Oslo, Oslo, Norway 7Barbara Davis Center for Childhood Diabetes, University of Colorado Health Sciences Center, Aurora, Colorado, USA 8Department of Regenerative Medicine and Cell Biology, Medical University of South Carolina, Charleston, South Carolina, USA 9Spartanburg Regional Medical Center, Spartanburg, South Carolina, USA 10Harold Hamm Diabetes Center, Clinical and Translational Research Unit & Department of Pediatrics, OUHSC, Oklahoma City, Oklahoma, USA

Background: Inflammation and endothelial dysfunction have been associated with the immunobiology of preeclampsia (PE), a significant cause of adverse pregnancy outcomes. The prevalence of PE is elevated several fold in the presence of maternal type 1 diabetes (T1DM). While cross-sectional studies in non-diabetic pregnancies have shown altered inflammatory markers in the presence of PE, longitudinal studies in T1DM women are lacking. Objective: In maternal serum samples, we examined the temporal associations of markers of inflammation with the subsequent development of PE in T1DM women.

Methods: We conducted longitudinal analyses of serum C-reactive protein (CRP), adhesion molecules, and cytokines at first (12.2±1.9 weeks [means ± SD]), second (21.6±1.5 weeks) and third (31.5±1.7 weeks) trimesters of pregnancy (‘visits 1-3’ respectively). All study visits took place before PE onset. Covariates were BMI, HbA1c, age of onset and duration of diabetes, and mean arterial pressure.

Results: In T1DM women who developed PE vs. those who remained normotensive, CRP tended to be higher at visit 1 (p=0.07) and was significantly higher at visits 2 and 3 (p<0.05); soluble E-selectin (sE-selectin) and interferon-γ-inducible protein-10 (IP-10) were significantly higher at visit 3, and interleukin-1 receptor antagonist (IL-1ra) was higher at visit 2 (all p<0.05). These conclusions persisted following adjustment for covariates.

Conclusions: In pregnant women with T1DM, elevated CRP, sE-selectin, IL-1ra, and IP-10 were associated with subsequent PE. The role of inflammation as a marker and potential mechanism for the high prevalence of PE in T1DM merits further investigation. Manuscript in press in Diabetes Care

Female Radiologists: Pregnancy Policies and Perceptions

Madeleine Lewis, MD¹, William J Rieter², PhD, Leonie Gordon, MBChB¹

¹MUSC Department of Radiology, ²MUSC Department of family Medicine

Background: The number of females entering radiology remains discrepantly low. Women enter residency during their childbearing years, and radiation safety during pregnancy and lack of written policies may be one of the reasons why women are hesitant in choosing radiology as a profession.

Objectives: Our objectives were to determine how many female radiologists were provided formal maternity policies and radiation safety counseling during pregnancy.

Methods: An anonymous electronic survey was emailed to active American Association of Women Radiologists members. Data concerning birth trends, institutional policies and perceptions were analyzed.

Results: A total of 1128 female radiologists received an online survey with a response rate of 25%. The average age of
delivery for the first child was 31.2 years. Assisted reproductive technology utilization was ten times more likely than the national average. Less than half (47%) were provided written pregnancy policy. Only 33% received counseling about radiation exposure. Fluoroscopy and interventional radiology time was restricted by 66% and 72%, respectively. A maternal lead apron was not available to 64%. Approximately half (55%) wore a second dosimeter badge. Respondents were split over concerns about occupational radiation exposure to the fetus. Perceptions of co-workers’ attitudes were generally positive (51%).

**Conclusions:** The majority of pregnant radiologists do not receive formal maternity policies or radiation safety counseling. Improvements can be made with the formation of written policies and radiation safety counseling for all pregnant radiologists. These improvements will likely make radiology a more attractive field for female medical students.

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**Poster 10.**

**Trichomonas vaginalis in HIV positive women: a risk factor for high risk human papillomavirus**

Ellen M. Maher¹, Emma Kennedy², MPH, and Gweneth B. Lazenby³, MD MSCR

¹College of Medicine, ²Department of Medicine, Division of Infectious Diseases, and ³Department Obstetrics and Gynecology

**Introduction:** Women with Trichomonas vaginalis (TV) are twice as likely to have a high risk human papillomavirus (HR HPV) infection. TV is more common in HIV positive women and is associated with HIV transmission. The aim of this study was to describe the association between TV and HR HPV infection in HIV positive women undergoing cervical cancer screening.

**Methods:** We reviewed the records of HIV positive women presenting for cervical cancer screening from 2006-2012 to determine rates of HR HPV, vaginitis, sexually transmitted infections, and HIV immunosuppression. Chi-squared statistics were used to compare proportions of disease in women with and without HR HPV. Univariate and multivariate logistic regression analyses were used to determine factors associated with HR HPV infection.

**Results:** Over 6 years, 302 HIV positive women presented for cervical cancer screening. The majority of subjects were of black race (241/302, 80%). Of the 218 women screened for lower genital tract infection, one quarter had TV (51/218, 23%). Of women screened for HR HPV, over half were infected (95/183, 52%). When controlling for women screened for both TV and HR HPV, TV vaginitis was associated with a 3-fold increase risk of HR HPV infection (OR, 2.7; 95% CI 1.1-6.5), but advanced HIV/AIDS was the most significant risk factor (OR, 18.1; 95% CI 4.1-79.7).

**Conclusions:** TV and HR HPV are common infections among HIV positive women. In addition to immunosuppression, TV was a significant risk factor for HR HPV infection. The consequence of this association may be persistent HR HPV infection and risk of possible genital squamous cell carcinoma.

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**Poster 11.**

**A role for estrogen receptor alpha (ERalpha) and estrogen receptor beta (ERbeta) in collagen biosynthesis in mouse skin**

M.Markiewicz¹*, S.Znoyko², L.Stawski³, Gary Gilkeson⁴, A.Ghatnekar¹, Maria Trojanowska³.

¹Division of Rheumatology and Immunology, Medical University of SC. Charleston, SC, ²Moscow State University, Moscow, Russia, ³Arthritis Center, Department of Medicine, Boston University School of Medicine

**Background:** Sex steroid hormones are among the factors that have been shown to influence skin changes. We have demonstrated that estrogen plays a critical role in regulating the organization and stability of collagen fibrils (Markiewicz et al. 2007).

**Objective:** The goal of this study was to investigate the role of ERAlpha and/or ERbeta on collagen biosynthesis in the skin using unique genetic models: ERKO-alpha and ERKO-beta female mice.
Methods: We first investigated whether ERalpha and ERbeta influence collagen accumulation in the skin using the hydroxyproline assay. Furthermore, we examined the amounts of newly made soluble collagens that are not yet incorporated into the large fibrils using acetic acid extraction method. Using qRT-PCR technique we measured mRNA levels of small leucine-rich proteoglycans (SLRP’s) contributing to this process.

Results: The hydroxyproline content was two times higher in ERKO-alpha mice while in ERKO-beta mice was decreased (~30%) as compared to control animals. In ERKO-alpha mice, the soluble collagen was slightly elevated (1.6 fold increase) most likely reflecting increased synthesis of collagen. Alterations in collagen solubility have suggested changes in the expression level of SLRPs involved in fibrillogenesis. In ERKO-alpha mice, expression levels of Lumican and Decorin were significantly elevated (9.9 folds and 1.9 folds respectively) while in ERKO-beta of Lumican and Decorin was diminished (2.3 folds and 7.7 folds respectively).

Conclusions: Our data indicate that ERalpha plays an inhibitory role in collagen synthesis and fibrillogenesis, while data from ERKO-beta mice suggest that ERbeta may play an opposite role in these processes.

Poster 12.
Trauma, PTSD, and Related Sleep Disturbances Among Women
Melissa E. Milanak, Ph.D.*, Heidi Resnick, Ph.D., & Dean G. Kilpatrick, Ph.D.
Department of Psychiatry & Behavioral Sciences, National Crime Victims Research & Treatment Center, Medical University of South Carolina, Charleston, SC, USA

Background: Individuals with posttraumatic stress disorder (PTSD) report sleep disturbances such as insomnia and nightmares. Sleep disturbances soon after a traumatic event are positive predictors of PTSD a year later.

Objectives: (1) To examine gender differences in trauma-related sleep disturbances among those exposed to traumatic or other stressful events; and (2) to determine whether traumatic or other stressful event exposure plus PTSD diagnosis changes prevalence.

Methods: The National Stressful Events Survey (NSES), a structured online interview, was conducted with a large sample recruited from a probability-based online panel of U.S. adults, and assessed exposure to stressful events, as well as proposed DSM-5 PTSD symptoms. Of the 2721 adults who reported exposure to at least one traumatic or other stressful event and provided gender information, 51.6% were women.

Results: Among adults exposed to traumatic or other stressful events, women reported higher prevalence than men’s (p’s < .001) of trauma-related nightmares (32.6% vs. 19.2%) and trauma-related insomnia (37.4% vs. 22.3%). When restricting analyses to the 250 participants who met lifetime DSM-5 PTSD diagnostic criteria, overall prevalence of trauma-related sleep disturbances increased substantially. Interestingly, among individuals with PTSD, women still reported higher prevalence of trauma-related nightmares (71.2% vs. 58.0%) but no longer significantly differed from men on trauma-related insomnia (78.7% vs. 81.2%). Effects of traumatic event type on prevalence and associations between other demographic variables and sleep disturbances controlling for gender were also examined.

Conclusions: Significant gender differences exist, and PTSD diagnosis increases prevalence of trauma-related insomnia and nightmares. Implications are discussed.

Poster 13.
Vitamin D in Lactating Women and Serum Levels of TGF-β2
Patrick Orgel¹, Frank S Shary¹, Judy R Shary, MS¹, Renee Washington, MS¹, John E Baatz, PhD¹, Bruce W Hollis, PhD¹ and Carol L Wagner, MD¹.
¹Pediatrics, Medical University of SC, Charleston, SC, United States.

Background: Vitamin D has been shown to have effects on immune regulation and function. Transforming growth factor-beta 2 (TGF-β2) is a cytokine that plays a role in immune cell differentiation and regulation.
**Objective:** Investigate the relationship between serum concentrations of TGF-β2 and vitamin D status in fully breastfeeding mothers and their infants.

**Design/Methods:** Serum samples were obtained from lactating women and their infants in Charleston, SC and assayed for 25(OH)D (RIA) and TGF-β2 (ELISA). Primary outcomes were TGF-β2 concentration as a function of vitamin D status and the difference in TGF-β2 concentrations at baseline by race. Data were analyzed using Spearman for non-parametric and ANOVA.

**Results:** 104 subjects participated in the study, with 57 mothers [18 Hispanic (H), 18 Caucasian (C), 21 African American (AA)] and 47 babies (23 Hisp, 11 Cauc, 12 AA). Maternal 25(OH)D differed by race at baseline: 20.2 ng/ml AA, 25.7 ng/ml H, and 42.9 ng/ml C (p<0.0001). There was a negative correlation between 25(OH)D and TGF-β2 (p=0.0467) and a significant difference in mother’s TGF-β2 by race with highest concentrations in African American (441.5 pg/mL) compared with Caucasian (200.3 pg/mL) and Hispanic (293.2 pg/mL) women. While maternal and infant vitamin D status were highly correlated (p<0.0001), infant vitamin D status and TGF-β2 did not appear to be associated.

**Conclusions:** Vitamin D status during lactation appears to be independently associated with maternal circulating TGF-β2. Race also appears to be an independent predictor of TGF-β2. A mechanism by which vitamin D deficiency impacts health may be through elevated circulating TGF-β.

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**Poster 14.**

**Determining Human papillomavirus genotyping to evaluate for racial differences in type distribution**

*Jennifer Young Pierce, MD, MPH, Jeffrey Korte, PhD, Kim Creek, PhD, J. Graham Theisen, BS, Lisa B. Spiryda, MD, PhD, Lucia Pirisi-Creek, MD*

1Department of Obstetrics and Gynecology, Medical University of South Carolina, 2Department of Public Health Sciences, Medical University of South Carolina, 3Department of Pharmaceutical and Biomedical Sciences, University of South Carolina, 4Department of Pathology and Microbiology, University of South Carolina

**Background:** Epidemiology studies document that 70% of cervical cancer is caused by HPV 16 and 18. However, African-American (AA) women are underrepresented in studies of HPV type distribution. The Creek/ Pirisi-Creek lab documented racial differences in type of HPV infection, rate of HPV persistent, and rate of cervical dysplasia between European Americans (EA) and African Americans (AA).

**Objective:** To determine the HPV type associated with cervical cancer in EA women compared to AA women.

**Methods:** Thirty cervical cancer patients, 15 EA and 15 AA women, will be recruited from the Hollings Cancer Center. Two Pap tests are collected, one placed in a ThinPrep transport media and the second specimen is placed directly in RNAlater. Specimens are tested for HPV type using the same INNO-LIPA assay. Histograms of HPV type by race will be used to compare high risk HPV type among AA women compared to EA women. Chi-square and Fischer’s exact analyses will assess any racial differences in percent prevalence of specific HPV types in the tumor specimens.

**Results:** We are currently at 40% enrollment for this study. Of the 12 samples collected, 9 were evaluable for HPV genotyping. Of these, 44% tested positive HPV 16 alone. Two tested positive for HPV 31 and 2 for HPV 35. Our racial distribution in these samples does not allow for determination of racial differences at this time. Final results will be available by mid April.

**Conclusions:** We anticipate racial differences in HPV genotype distribution.

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**Poster 15.**

**Breastfeeding and oral Mutans streptococci in mother-infant pairs**

*Susan G. Reed, DDS, MPH, DrPH, Thao N. Latham, BA, Joan E. Cunningham, PhD, Susannah C. Shirer, DDS, Judy R. Shary, MS, Pamela G. Smith, RN, Martha L. Murphy, BS, Myla D. Ebeling, Thomas C. Hulsey, ScD, Bruce W. Hollis, PhD, Carol L. Wagner, MD*
MUSC Department of Pediatrics, COM, MUSC College of Dental Medicine, MUSC Department of Medicine/Biostatistics & Epidemiology, COM

Background: Early Childhood Caries (ECC) is a communicable disease that impacts about 27% of US children. Mutans streptococci (MS) bacteria are an initiator in ECC and MS transmission from mother to child is known. Recent studies found oral MS more likely in lactating mother-infant pairs compared to non-lactating mother-infant pairs. Our study investigates the potential contribution of the maternal oral MS status among lactating and non-lactating mother-infant pairs.

Objective: To evaluate the association of feeding method (lactation vs non-lactation) and maternal oral MS status with infant oral MS status.

Methods: Cross-sectional baseline data from mother-infant pairs at 4-6 weeks postpartum included mother and infant oral MS presence, feeding method (lactation vs non-lactation), race/ethnicity, delivery method, maternal insurance, and maternal dental treatment during pregnancy. Oral MS levels were determined by Dentocult®SM Strip mutans test.

Results: Mother and infant oral MS status were available for 104 mother-infant pairs: 68 in lactation group and 36 in non-lactation group; 12% of infants (n=12) and 31% (n=32) of mothers were MS positive. Infant oral MS status was significantly associated with oral SM status of the mother in the lactation group (Fisher’s exact p-value=0.039; OR 5.97, p=0.043), but not in the non-lactating group (Fisher’s exact p=1.000; OR 0.72, p=0.782). Breastfeeding alone did not predict infant oral MS status (p=0.748).

Conclusions: We found the oral MS status of the infant to be predicted by the mother’s oral MS status, but only if the infant was breastfed. Breastfeeding itself was not associated with infant oral MS status.

Poster 16.

Absence of Estrogen Receptor Alpha Reduces the Number and Function of Bone Marrow derived PDCA1+ cells in Lupus Prone Mice

Jennifer Scott1, Melissa Cunningham2,3, Osama Naga2, Gary Gilkeson2,3

1College of Graduate Studies, Department of Microbiology & Immunology. Med. Univ. of South Carolina, Charleston, SC, 2Division of Rheumatology & Immunology, Department of Medicine. Med. Univ. of South Carolina, Charleston, SC, 3Ralph H. Johnson VA Medical Center, Charleston, SC

Background: Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease that affects women at a 9:1. Estrogen receptor alpha (ERα) deficient lupus-prone mice have increased survival and less renal disease compared to wild type lupus-prone mice.

Objective: We would like to understand the mechanism by which ERα deficiency improves SLE.

Methods and Results: We hypothesize that ERα deficiency improves SLE by limiting dendritic cell (DC) development and function. PDCA1+ cells make up less than 5% of the bone marrow derived mDCs from B6 mice. Using the same mDC culture conditions, PDCA1+ cells account for 60% of mDCs from lupus prone NZM 2410 mice. Moreover, PDCA1+ DCs from NZM 2410 mice lacking ERα account for only 35% of DCs. The PDCA1 marker denotes plasmacytoid dendritic cells (pDCs), the body’s major producer of type I interferon (IFN), a critical cytokine in the pathogenesis of SLE. ERα deficient mDCs express lower levels of IFN response genes when stimulated with TLR7 and 9 agonists compared to the wild type cells. To further characterize these cells, the traditional pDC culture system was used to obtain pDCs from bone marrow progenitors. Using this culture system, ERα deficient bone marrow from NZM 2410, MRL/lpr, SLE1,3, and B6 mice showed a similar decrease in PDCA1+ cells seen with the cDC culture system.

Conclusion: This data indicates that ERα plays a role in altering the number and function of PDCA1+ cells cultured under both mDC and pDC culture conditions.
Poster 17.

**Bone Mineral Density Changes during Lactation for Women Participating in a RCT of Vitamin D Supplementation**

Judith R Shary, MS¹, Betsy D Anderson¹, Pamela G Smith, BSN¹, Martha Murphy¹, Bruce W Hollis, PhD¹, Cynthia R Howard, MD², Ruth Lawrence, MD², Myla Ebeling¹ and Carol L Wagner, MD¹.

¹Pediatrics, Neonatology, Medical University of SC, Charleston, SC, United States and ²Pediatrics, University of Rochester, Rochester, NY, United States.

**Background:** It has been reported that lactating women lose bone mineral density (BMD) at the rate of 1.25% per month, with a plateau at 7 months.

**Objective:** To measure BMD during lactation in a large cohort of women of diverse racial/ethnic background.

**Design/Methods:** A prospectively enrolled cohort of healthy women recruited for a multicenter randomized controlled trial (RCT) of vitamin D supplementation during lactation (400 or 6400 IU/daily for six months, beginning at one month postpartum) underwent BMD measurement of spine and hip. 171 women completed the study with BMDs at 1-, 4- and 7-months after delivery. 25(OH)-vitamin D [25(OH)D] was measured at the same time points by RIA. Women were either Caucasian (C, n=90), African-American (AA, n=33) or Hispanic (H, n=48) and treatment groups were evenly distributed. BMD was expressed as rate of change per subject (g/cm²). Data were analyzed using t-test with Welch’s correction.

**Results:** Women randomized to the 6400 IU group had a significant increase in 25(OH)D from 1- to 7- months, regardless of race (p<0.0001). Compared to the 400 IU group, there was a general trend observed in Caucasians and Hispanics for less bone loss at the spine and hip during the study in those randomized to 6400 IU, but the mean differences did not reach significance.

**Conclusions:** Supplementation of exclusively lactating mothers with 6400 IU vitamin D/day preserves maternal bone mineral density.

Poster 18.

**Role of Deoxysphingolipids In Paclitaxel-induced Peripheral Neuropathy In Breast Cancer Patients**

Rita Kramer¹, Jacek Bielawski², Drew Kornhauser¹, Thorsten Hornemann³ and Stefka Spassieva¹*

¹Department of Medicine, ²Department of Biochemistry and Molecular Biology, Medical University of South Carolina, Charleston, SC, USA, Institute for Clinical Chemistry, University Hospital Zurich, Zurich, Switzerland

**Background:** Paclitaxel is an effective chemotherapy agent against breast cancer. However, 40% of the patients develop a distal axonopathy with sensory neuropathic pain and abnormal sensations. Paclitaxel-induced neuropathy has clinical similarities to the hereditary sensory and autonomic neuropathy type 1, which is associated with increased levels of deoxysphingolipids. Deoxysphingolipids are an atypical class of sphingolipids produced when L-alanine is used as a substrate for the first step of sphingolipid biosynthesis rather than L-serine. Importantly, deoxysphingolipids been shown to be neurotoxic in vivo.

**Objective:** In this work we are testing whether paclitaxel exposure alters sphingolipid metabolism resulting in increased levels of neurotoxic deoxysphingolipids in cells and in the plasma of breast cancer patients.

**Methods:** Deoxysphingolipids in cells treated with paclitaxel and in the plasma of breast cancer patients receiving standard adjuvant paclitaxel are measured by mass spectrometry. Patient samples are collected prior, during and at the end of therapy. The levels of deoxysphingolipids will be correlated with the development of neuropathic symptoms. 26 patients are currently enrolled in the study.

**Results:** Our data in cells showed that paclitaxel treatment resulted in a significant increase of deoxysphingolipids.

**Conclusions:** These results suggest that deoxysphingolipids could be the underlying cause for paclitaxel-induced peripheral neuropathy.
Poster 19.

Gender and Biologic Markers in Autism: An Exploratory Study

Eve G. Spratt, MD, MSCR, Ann-Charlotte Granholm, PhD/DDS, Humera Chaudhary, Sarah-Wade Boatwright, Carrie Papa, Laura Carpenter, PhD, and Kathleen Brady, MD, PhD.

College of Medicine, Medical University of South Carolina, Charleston, SC 29425, USA

Background: Autism Spectrum Disorder’s (ASD’s) are up to 4 times more common in males but research examining biologic gender differences is sparse. An improved understanding of neurobiological factors may lead to more effective therapeutic interventions and improved understanding of the etiology of the disorder. Brain-Derived Neurotropic Factor (BDNF) is a peptide that plays a role in the regulation of neuronal cell survival, differentiation, and plasticity and may influence neurotransmitter systems such as the dopaminergic, cholinergic, and serotonergic by moderating gene expression.

Objective: The goals of the study were 1) to explore if biologic measures (serum BDNF) known to be associated with Autism have an associated behavioral phenotype; 2) to explore whether this neurobiologic marker is influenced by gender or severity of illness.

Design and Methods: 35 children were participants, including 7 females and 28 males ages 5 to 12 recruited for a biologic intervention study that included baseline serum BDNF and an Autism severity measure.

Results: A statistical analysis revealed BDNF to be evenly distributed between ethnic groups with a significantly higher serum level in females compared to males (p<0.05). BDNF levels corresponded significantly to hyperactivity in females (p<0.0003) but not in males (p=0.948). BDNF did not correlate with severity of disease in either gender. There were no gender differences in terms of severity of illness or hyperactivity and hyperactivity did not correlate with severity of disease.

Conclusions: Although a small sample, these results suggest that further examination of gender differences related to BDNF as well as the relationship to hyperactivity, severity, exercise and overall activity level is warranted.

Acknowledgements: This research project was supported by Award Number UL1RR029882 from the National Center for Research Resources. Control participants were from grant K23 NIH/NIMH K25MH064111: Neurodevelopmental Biology of Neglected Children (PI: Eve G. Spratt). This study was supported by the South Carolina Clinical & Translational Research Institute, Medical University of South Carolina’s CTSA, NIH/NCATS Grant Number UL1TR000062 and Autism Speaks Grant #2934.

Poster 20.

Gender Differences in Composite Control of Cardiovascular Risk Factors among Patients with Type 2 Diabetes

Strom JL, Lynch CP, Winchester R, Egede LE

Medical University of South Carolina and Ralph H. Johnson VAMC

Background: Women with type 2 diabetes (T2DM) have greater risk of developing cardiovascular disease (CVD) and worse outcomes than men; differences in simultaneous control of CVD risk factors in T2DM are less clear.

Objective: This study examined the difference in composite control by gender in patients with T2DM.

Methods: Data were collected from 678 participants with T2DM at 3 clinics. Data for the primary outcome, composite risk factor control (glycosylated hemoglobin, HbA1c ≤7%; systolic and diastolic blood pressure, SBP/DBP ≤130/80mmHg; low-density lipoprotein cholesterol, LDL ≤100mg/dL) were obtained from medical records. Logistic regression analyzed the independent effect of gender on composite control using STATA v11.

Results: Males had better control than women of BP, cholesterol, and composite factors. After adjusting for covariates, males were 1.7x more likely than females to have control of BP (95% CI 1.16, 2.37; p<0.001) and cholesterol (95% CI
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1.17, 2.48; p<0.001). Blacks were half (odds ratio, OR 0.47, 95% CI 0.32, 0.69; p<0.001) as likely as whites to have BP control. Compared to uninsured, those with governmental insurance showed nearly twice the odds of BP (OR, 1.9, 95% CI 1.17, 3.11; p<0.001) and cholesterol (OR, 2.0, 95% CI 1.22, 3.29; p<0.001) control. Overall, males were >three-fold (OR 3.14, 95% CI 1.70, 5.79; p<0.001) odds of composite control compared to females.

Conclusions: Findings indicate females had worse composite control of CVD risk factors. Research and clinical efforts require a multi-factorial approach that targets underlying behavioral and psychosocial factors to improve adverse CVD outcomes among females with T2DM.

Poster 21.

Participant Distress in Traumatic Stress Research: A Comparison of Male and Female Adolescents

*Zajac K¹, Ruggiero KJ², Smith DW², Saunders BE², Kilpatrick DG²

¹MUSC Family Services Research Center, ²MUSC National Crime Victims research and Treatment Center

Background: Only a small minority (<10%) of adult research participants report distress in response to questions about trauma. Less is known about distress among adolescent participants. In addition, given the high rates of certain types of trauma among female adolescents (e.g., sexual assault), an exploration of gender differences in responses to traumatic stress research is warranted.

Objectives: The study aims to examine: a) prevalence of participant distress in response to questions about trauma; b) gender differences in rates of distress; c) relations between distress and study attrition; and d) relations between endorsement of traumatic events and distress.

Method: As part of the National Survey of Adolescents-Replication, a nationally representative sample of 3,614 youth ages 12-17, adolescents were interviewed by phone about traumatic experiences and mental health. Following the interview, participant distress was assessed. Participants were contacted for a one year follow-up.

Results: Overall, 204(5.7%) adolescents found questions distressing, with only 8(0.2%) still feeling upset by the end of the interview, and 2(< 0.1%) requesting to speak to a counselor. Females were more likely than males to report distress (7.5% versus 3.9%; χ²=21.23, p<.05). Distress did not predict attrition at follow-up. Adolescents who endorsed any type of trauma were more likely to report distress.

Conclusions: Findings suggest that females have more frequent negative responses to traumatic stress interviews than males. Nevertheless, questions about traumatic stress pose minimal risk to adolescent participants and do not increase attrition rates. Results have implications for the ethical conduct of traumatic stress research with adolescents.

Poster 22.

Sex differences in oxytocin-induced attenuation of cocaine self-administration and reinstatement of cocaine seeking in rats

Luyi Zhou*, Amy B. Young, Ronald E. See

Department of Neurosciences, Medical University of South Carolina

Background: Previous studies have shown that female rats exhibit different patterns of cocaine seeking during multiple phases of cocaine addiction when compared with males. However, the neurobiological mechanisms for these sex differences remain to be determined. Recent findings suggest that central oxytocin may be a critical modulator of drug reward. However, oxytocin has not been studied in a self-administration/reinstatement model, and its role in sex differences in cocaine addiction is not known.

Objectives: In the current study, we examined oxytocin-mediated cocaine seeking during self-administration and reinstatement in male and female rats using acute, systemic oxytocin treatment.

Methods: Age-matched male and female Sprague Dawley rats were trained to self-administer intravenous cocaine, paired with light+tone conditioned cues. Once cocaine intake was stabilized, all animals received oxytocin (0.1, 0.3, 1, 3
mg/kg, IP) or vehicle prior to cocaine self-administration in a counterbalanced manner. Another set of rats received oxytocin or vehicle prior to discrete reinstatement trials for conditioned cue-induced or cocaine-primed reinstatement of cocaine seeking.

**Results:** Oxytocin equally reduced cocaine seeking and intake during self-administration in males and females. Oxytocin also dose-dependently reduced cocaine seeking induced by cocaine-conditioned cues or a cocaine prime in both sexes. However, females showed significantly greater reductions in cocaine-primed reinstatement at lower doses than males.

**Conclusions:** These data suggest that increased oxytocin reduces the primary and secondary reward properties of cocaine in both sexes. Thus, oxytocin may act as an anti-relapse medication in both men and women. However, women may be more sensitive to oxytocin effects on relapse triggered by renewed drug intake.

**Poster 23.**

**Higher blood estradiol reduces functional brain asymmetry in mental rotation processing**

Xun Zhu¹, Christine R. Corbly², Thomas E. Curry Jr.³, Thomas H. Kelly⁴, Jane E. Joseph²*

¹Department of Neurosciences, College of Medicine, Medical University of South Carolina, Charleston, SC 29425, USA, ²Department of Anatomy and Neurobiology, College of Medicine, University of Kentucky, Lexington, KY 40506, USA, ³Department of Obstetrics and Gynecology, Endocrinology, College of Medicine, University of Kentucky, Lexington, KY 40506, USA, ⁴Department of Behavioral Sciences, College of Medicine, University of Kentucky, Lexington, KY 40506, USA

**Background:** Mental rotation is a visual-spatial task has associated with significant sex difference and is affected by gonadal hormones such as testosterone and estradiol.

**Objectives:** To better understand the neural substrates of hormonal modulation of mental rotation, the present study examined the influence of estradiol using functional magnetic resonance imaging.

**Methods:** Ten pre-menopausal women were tested on a 3D mental rotation task during the early follicular (EF) and late follicular (LF) phases of the menstrual cycle.

**Results:** The between-phase estradiol concentration difference was confirmed by hormone assays. Although brain activation patterns were similar across the two phases, the most striking pattern that emerged was that estradiol had different associations with the two hemispheres. Better performance in the LF than the EF phase was associated with a pattern of reduced recruitment of the right-hemisphere and increased recruitment of the left-hemisphere in the LF compared to EF phase.

**Conclusions:** We speculate that estradiol interferes with right-hemisphere visuo-spatial processing in the higher estradiol phase, and facilitates left-hemisphere processing. Given that the right hemisphere is the dominant hemisphere in visuo-spatial processing, our results suggest that estradiol is associated with reduced functional asymmetry, consistent with contemporary accounts of hormonal modulation of neurocognitive function.