Women's Health Research Day

Medical University of South Carolina  •  Charleston

Sponsored by the Specialized Center of Research (SCOR) on Sex and Gender Factors Affecting Women's Health, the Building Interdisciplinary Research Careers in Women's Health (BIRCWH) Program, and the South Carolina Clinical and Translational Research Institute (SCTR).
We would like to acknowledge and thank the Women’s Health Research Day 2015 Planning Committee:

Kathleen Brady, MD, PhD
Distinguished University Professor
Interim Associate Provost for Research
Director, South Carolina Clinical & Translational Research Institute
Medical University of South Carolina

Carol Feghali-Bostwick, PhD
Kitty Trask Holt Endowed Chair
Director, Center for ARROWS
Professor of Medicine
Division of Rheumatology & Immunology
Medical University of South Carolina

Sarah S. Gainey, MSW, LISW-CP
Women’s Research Center Coordinator, Department of Psychiatry
Medical University of South Carolina

Constance Guille, MD
Assistant Professor, Department of Psychiatry
Medical University of South Carolina

Jakie McGinty, PhD
Professor, Department of Neurosciences
Interim Dean, College of Graduate Studies
Director, Neuroscience Institute
Medical University of South Carolina

Aimee L. McRae-Clark, Pharm.D., BCPP
Professor, Department of Psychiatry
Medical University of South Carolina

Jennifer R. Peterson
Administrative Assistant, Department of Psychiatry
Medical University of South Carolina

Dayan Ranwala, PhD
Research Assistant Professor, South Carolina Clinical and Translational Research Institute
Medical University of South Carolina

Carmela Reichel, PhD
Assistant Professor, Department of Neurosciences
Medical University of South Carolina

Carol Wagner MD, FAAP
Professor, Department of Pediatrics- Neonatology
Medical University of South Carolina

Sharon Weissman, MD
Associate Professor of Clinical Internal Medicine
Program Director for the Infectious Disease Fellowship
University of South Carolina
## ORAL PRESENTATION ABSTRACTS

<table>
<thead>
<tr>
<th>Presenter</th>
<th>Abstract Title</th>
<th>Page Number</th>
</tr>
</thead>
</table>
| Melissa Cunningham, MD, PhD  
Department of Rheumatology and Immunology, MUSC | An Estrogen Receptor alpha Functional Mutant is Protective in Murine Lupus | 4 |
| Satomi Kohno, PhD  
Department of Obstetrics and Gynecology, MUSC | Developmental exposure to 17α-hydroxyprogesterone caproate used for clinical prevention of recurrent preterm birth suppressed estrogen-responsiveness in murine female reproductive tract | 4 |
| Andrea DeMaria, PhD, MS  
Department of Public Health, College of Charleston  
Beth Sundstrom, PhD, MPH  
Department of Public Health, College of Charleston | It’s Your Place: Development and evaluation of an evidence-based bystander intervention campaign | 5 |
| Jane Joseph, PhD  
Department of Neurosciences, MUSC | Sex differences in intrinsic functional brain connectivity in adult smokers | 5 |

## POSTER PRESENTATION ABSTRACTS

<table>
<thead>
<tr>
<th>Poster Number</th>
<th>Presenter</th>
<th>Abstract Title</th>
<th>Page Number</th>
</tr>
</thead>
</table>
| 1. | Emily Fanguy, BS  
Department of Psychiatry & Behavioral Sciences, MUSC | The Impact of PACE Parenting Program on Parental Stress and Locus of Control | 6 |
| 2. | Lisa T. Ross, PhD  
Department of Psychology, College of Charleston | Mental Health, Smoking, and Unpredictability Beliefs among College Women | 6 |
| 3. | Beth Sundstrom, PhD, MPH  
Department of Communication, Women’s Health Research Team, College of Charleston | 'It makes you rethink your choice of the Pill!' Theory-based formative research to design a contraceptive choice campaign | 7 |
| 4. | Lara Hewett, BS  
Department of Radiology, MUSC | Gender Bias in Radiology Resident Selection Process, Does it Exist? | 7 |
| 5. | Teresa Kelechi, PhD  
College of Nursing, MUSC | Sex-specific symptom differences in individuals with chronic venous disease | 8 |
| 6. | Qing Li, MD, DrPH  
Department of Obstetrics and Gynecology, MUSC | Birth settings and neonatal seizures recorded in birth certificates compared to Medicaid claims data and hospital discharge abstracts in South Carolina, 1996-2013 | 8 |
<table>
<thead>
<tr>
<th></th>
<th>Name</th>
<th>Department</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>Qing Li, MD, DrPH</td>
<td>Department of Obstetrics and Gynecology, MUSC</td>
<td>The South Carolina Cerebral Palsy Project, 1996-2013</td>
<td>9</td>
</tr>
<tr>
<td>8</td>
<td>Britney M. Cox, BS</td>
<td>Department of Neurosciences, MUSC</td>
<td>Greater cognitive flexibility in female rats relative to males in an automated set-shift task</td>
<td>9</td>
</tr>
<tr>
<td>9</td>
<td>Laura Kasman, PhD</td>
<td>Diagnostic Microbiology, MUSC</td>
<td>Sex differences in a mouse model of bladder cancer</td>
<td>10</td>
</tr>
<tr>
<td>10</td>
<td>Jennifer Scott, BS</td>
<td>Department of Microbiology and Immunology, MUSC</td>
<td>Estrogen receptor alpha deficiency modulates PDC-TREM expression in plasmacytoid dendritic cells impacting type I interferon production and response to TLR ligands</td>
<td>10</td>
</tr>
<tr>
<td>11</td>
<td>Sade Spencer, PhD</td>
<td>Department of Neurosciences, MUSC</td>
<td>Development of a rodent mode of THC self-administration</td>
<td>11</td>
</tr>
<tr>
<td>12</td>
<td>Kelly Barth, DO</td>
<td>Department of Psychiatry &amp; Behavioral Sciences, MUSC</td>
<td>A pilot trial of buprenorphine in women with chronic abdominal pain</td>
<td>11</td>
</tr>
<tr>
<td>13</td>
<td>Elizabeth Burnett, PhD</td>
<td>Department of Neuroscience, MUSC</td>
<td>The role of the rostromedial tegmental nucleus in sex-related differences in the negative effects of alcohol</td>
<td>12</td>
</tr>
<tr>
<td>14</td>
<td>Linnea Freeman, PhD</td>
<td>Department of Neuroscience, MUSC</td>
<td>Oxytocin attenuates conditioned cocaine seeking in males and females</td>
<td>12</td>
</tr>
<tr>
<td>15</td>
<td>Linnea Freeman, PhD</td>
<td>Department of Neuroscience, MUSC</td>
<td>Sex Differences in Demand for Highly Palatable Food Rewards: Role of Orexin Neurons</td>
<td>13</td>
</tr>
<tr>
<td>16</td>
<td>Andreana Benitez, PhD</td>
<td>Department of Radiology and Radiological Science, MUSC</td>
<td>Lose weight, gain brain? Microstructural alterations in brain white matter following weight loss in obese middle-aged women</td>
<td>13</td>
</tr>
<tr>
<td>17</td>
<td>Davy Vanderweyen</td>
<td>Department of Neuroscience, MUSC</td>
<td>Gender-based differences in functional connectivity of healthy subjects at rest</td>
<td>13</td>
</tr>
</tbody>
</table>
AN ESTROGEN RECEPTOR ALPHA FUNCTIONAL MUTANT IS PROTECTIVE IN MURINE LUPUS

Cunningham, Melissa\(^1\); Wirth, Jena\(^1\); Scott, Jennifer\(^1\); Eudaly, Jackie\(^1\); and Gilkeson, Gary\(^1\)

\(^1\)Division of Rheumatology and Immunology, Department of Medicine, Medical University of South Carolina

**Background:** Systemic lupus erythematosus is a disease that disproportionately affects females. The etiology of this sex bias is unclear. We previously showed that a functional knockout of estrogen receptor alpha (ER\(\alpha\)KO) resulted in significantly reduced renal disease and increased survival in murine lupus. Dendritic cell development, which requires both estrogen and ER\(\alpha\) is impacted, as is activation status and cytokine production. Due to altered hormonal feedback loops, ER\(\alpha\)KO mice have hypergonadism and partial endocrine sex reversal. Elevated estrogen (E\(2\)) and testosterone levels may have immunomodulating effects.

**Objectives:** To investigate the phenotypes of lupus-prone ER\(\alpha\)KO (functional ER\(\alpha\) mutant) vs. Ex3a (deletional ER\(\alpha\) mutant) following ovariectomy (OVX) +/- E\(2\) replacement to preserve a physiologic hormonal state.

**Methods:** ER\(\alpha\)KO and Ex3a strains were backcrossed onto the NZM2410 lupus-prone background. Mice underwent OVX or not, and were E\(2\)-repleted or not. Urine and blood were collected at 2 week intervals and mice were sacrificed at 32 weeks, or earlier if they had high proteinuria or >10% weight loss. Bone marrow was isolated and cultured for 7d with Flt3L to enrich for dendritic cells. Kidney and spleen single cell suspensions were generated and analyzed by flow cytometry.

**Results:** NZM ER\(\alpha\)KO mice were protected from lupus disease expression (no early deaths; no proteinuria) if they were unmanipulated, or if they were both ovariectomized and E\(2\)-repleted. These mice had fewer activated cDCs (CD11c+/CD11b+/MHCI+) isolated from Flt3L-cultured bone marrow, *ex vivo* spleen or kidney. Protection was lost after OVX if no E\(2\) pellet was administered, suggesting that the protective effect requires E\(2\) (despite the lack of a functional ER\(\alpha\)). A protective effect was not observed in NZM Ex3a mice (ER\(\alpha\)−/−) when they were similarly OVX and estrogen-repleted.

**Conclusions:** Surprisingly, OVX +/- E\(2\) repletion significantly changes the ER\(\alpha\)KO phenotype, which is also different from an ER\(\alpha\) null strain (Ex3a). These data suggest that it is the *presence* of the truncated ER\(\alpha\)KO mutant plus E\(2\), rather than the *absence* of full length ER\(\alpha\), that impacts DC development/function and modulates disease to confer protection in this lupus model.

DEVELOPMENTAL EXPOSURE TO 17A-HYDROXYPREGESTERONE CAPROATE USED FOR CLINICAL PREVENTION OF RECURRENT PRETERM BIRTH SUPPRESSED ESTROGEN-RESPONSIVENESS IN MURINE FEMALE REPRODUCTIVE TRACT

Kohno, Satomi\(^1\); Sato, Tomomi\(^2\); Miyagawa, Shinich\(^3\); Newman, Roger B.; Iuchi, Taisen\(^2\); Guillette, Louis J., Jr\(^1\)

\(^1\)Department of Obstetrics and Gynecology, Medical University of South Carolina, \(^2\)Graduate School of Nanobioscience, Yokohama City University, \(^3\)National Institute for Basic Biology, National Institutes of Natural Sciences

**Background:** The FDA has approved 17a-hydroxyprogesterone caproate (17OHPc) for prevention of recurrent preterm birth. However, the developmental effects of 17OHPc as an endocrine disruptor on developmental health have not been adequately explored.

**Objectives:** Altering the steroid hormone milieu during fetal development has potential long-term adverse consequences as observed with diethylstilbestrol exposure *in utero*. Our objective is to determine if developmental exposure to 17OHPc induces post-pubertal alterations in the female reproductive system.

**Methods:** Neonatal mice (C57BL/6J) were given daily SC injections (day 0-4) of 5 \(\mu\)g or 50 \(\mu\)g 17OHPc or a vehicle control (sesame oil), and were ovariectomized (OVX) as adults (8 wks). Ten-days after OVX, 17β-estradiol (E\(2\)) or the vehicle control (sesame oil) was injected IP at 5 \(\mu\)g/kg Body Weight. Six-hours after E\(2\) injection, transcriptomes of uterus and vagina were analyzed by microarray analysis.

**Results:** Neonatal exposure to 17OHPc skewed the estrus cycle pattern at 8-weeks of age. E\(2\) remarkably altered the uterine transcriptome (820 genes went up; 1063 down) in control mice, whereas significantly fewer genes were altered by E\(2\) in the uterus of mice exposed neonatally to 5 \(\mu\)g 17OHPC: 660 up/895 down or to 50 \(\mu\)g 17OHPC: 2 up/1 down. Altered sensitivity to E\(2\) following 17OHPc exposure was also observed in the vaginal transcriptome.

**Conclusions:** Neonatal mice are equivalent to 2\(^{nd}\) trimester human fetuses in terms of Müllerian duct development; thus, gestational treatment with 17OHPc between 16 and 36 weeks may result in similar altered estrogen sensitivity and reproductive function. This possibility demands further research.
IT’S YOUR PLACE: DEVELOPMENT AND EVALUATION OF AN EVIDENCE-BASED BYSTANDER INTERVENTION CAMPAIGN

DeMaria, Andrea1, Sundstrom, Beth2, Ferrara, Merissa2, Gabel, Colby1, Maja Grzjdziak1, Ellie Smith1, Jeri Cabot3

1Health and Human Performance, College of Charleston, 2Communication, College of Charleston, 3Office of the President, College of Charleston

Background: One in five women is sexually assaulted while in college. Bystander intervention offers a promising approach to change social norms and prevent sexual assault.

Objectives: This study presents formative research, implementation, and evaluation of a multi-media campaign to increase awareness of sexual assault and promote active bystander intervention. The goal of the campaign is to increase awareness and mastery of bystander intervention techniques in order to prevent sexual assault.

Methods: Rigorous formative audience research included eight focus groups with college women and men (n = 69) to assess knowledge, attitudes, and behaviors related to sexual assault and bystander intervention.

Results: Findings revealed the target audience’s perceived barriers, potential benefits, competing behaviors, and influence of important others on bystander intervention. Specifically, emergent themes included: 1) female participants’ experiences of sexism and misogyny; 2) the myth that rape is falsely reported; 3) complex understandings of consent and entitlement; 4) the reluctance to stop someone from having a “good time” and; 5) the role of alcohol as a moderating factor in sexual assault and bystander intervention.

Conclusions: These findings were used to segment target audiences and develop campaign strategies, communication channels, and messages, including “It’s your place to prevent sexual assault: You’re not ruining a good time.” The campaign fosters a culture of bystander intervention through peer-to-peer facilitation and training, as well as traditional and new media platforms to reach young adults. While campaign evaluation is ongoing, this evidence-based health communication campaign offers practical suggestions to promote active bystander intervention and reduce sexual assault on college campuses.

SEX DIFFERENCES IN INTRINSIC FUNCTIONAL BRAIN CONNECTIVITY IN ADULT SMOKERS

Joseph, Jane1; Vanderweyden, Davy1; Zhu, Xun1; Moran Santa-Maria2, Megan; McKee, Sherry3; Cosgrove, Kelly1; McRae, Aimee2, & Brady, Kathleen2

1Department of Neurosciences, Medical University of South Carolina, 2Department of Psychiatry, Medical University of South Carolina, 3Department of Psychiatry, Yale University

Background: Gender differences in addictive disorders are well established. A deeper understanding of gender differences may be advanced by including neuroimaging markers of functional brain organization, such as resting state connectivity.

Objectives: The goal of this study was to conduct a preliminary network analysis (using graph-theory measures) of sex differences in intrinsic functional connectivity in adult smokers.

Methods: Twenty-seven adult smokers (13 males; mean age = 35) completed a resting state fMRI experiment. Data analysis involved preprocessing, creation of correlation matrices using partial correlation, and computing a measure of functional connectivity (eigenvector centrality; Brain Connectivity Toolbox) that reflects the global influence of a region on the network.

Results: Independent samples t-tests conducted in each of the 264 brain regions revealed sex differences in 9 regions. Nodes that showed higher connectivity in female smokers included critical nodes of salience (insula and cingulate cortex) and dorsal attention (inferior parietal, dorsomedial prefrontal) networks. Nodes that showed higher connectivity in male smokers were associated with the default mode network.

Conclusions: The intrinsic connectivity profile of female smokers reflected stronger connectivity of attention networks, which continually monitor the external environment for relevant cues and ready the body for action. We suggest this profile may be associated with greater cue reactivity in female than male smokers. In contrast, the intrinsic connectivity profile of male smokers reflected stronger connectivity of the default mode network, which reflects internally directed thought processes. We speculate that this connectivity profile may be associated with the stronger reinforcing effects of nicotine.
THE IMPACT OF PACE PARENTING PROGRAM ON PARENTAL STRESS AND LOCUS OF CONTROL

Fanguy, Emily; Moreland, Angela

1Department of Psychiatry and Behavioral Sciences, University; 2Department of Psychiatry and Behavioral Sciences, University

Background: Parent-child interactions have been associated with parental stress (Begle & Dumas, 2011) and ways that parents perceive and react to situations impact these interactions; which is especially true for mothers (Matud, 2004). Mothers who adopt an external locus of control (PLOC) report poorer interactions with children (Rodriguez & Richardson, 2007), as they perceive the child’s behavior as willful and controlling. Mother-child interactions can be improved through parent management training (PMT) (Begle & Dumas 2011). It is essential to examine the link between PLOC and parent stress, and the impact of increased mother-child interactions (via participation in PMT) on PLOC and parent stress over time.

Objectives: We examine PLOC and parent stress in mothers who participated in an 8-week PMT program at baseline (T1) and completion (T2). It is hypothesized that (1) mothers with an external PLOC will report higher parental stress, and (2) higher program engagement will significantly decrease parental stress and PLOC from T1 to T2.

Methods: Parent reports PLOC, Parent Internalizing, Parent Stress and participation measures were collected from 598 mothers enrolled in the program.

Results: Using hierarchical multiple regression, results indicated that external PLOC was significantly associated with higher levels of parental stress (H1) and that higher program engagement significantly predicted changes in PLOC and parental stress from T1 to T2 (H2).

Conclusions: Both hypotheses were supported. Findings suggest that PLOC and parental stress are strongly associated and that engagement in PMT programs is effective in decreasing parent stress and in changing PLOC.

MENTAL HEALTH, SMOKING, AND UNPREDICTABILITY BELIEFS AMONG COLLEGE WOMEN

Ross, Lisa T; Hood, Caitlin

1Department of Psychology, College of Charleston; 2Department of Psychiatry and Behavioral Sciences, MUSC

Background: According to the National Alliance on Mental Health, the most common diagnoses among young adults are anxiety (12%) and depression (11%); people diagnosed with either are more likely to smoke (Murphy et al, 2003; Johnson et al., 2000). Limited research has examined how unpredictability beliefs relate to mental health and smoking.

Objectives: We hypothesized that current unpredictability beliefs would be positively related to mental health difficulties and higher rates of smoking.

Methods: College women (N = 260; ages 18-22; 72% Caucasian) answered questions from the Unpredictability Schema Scale (USS; Ross, under review), CES-Depression Scale (Radloff, 1977), Trait Anxiety (Spielberger, 1983), and from a brief Crown-Marlowe Social Desirability Scale (SD; Ballard, 1992). Participants were also asked if they had experienced anxiety or depression before age 18, and current smoking status.

Results: SD scores correlated with childhood anxiety and recent anxiety, so all analyses covaried SD. Current (but not childhood) mental health variables differed for smokers and nonsmokers, F(2,223)=3.278,p<.05. Follow-up ANCOVAs revealed smokers reported both more anxiety and depression symptoms. In addition, groups differed on unpredictability beliefs, F(2,244)=5.263,p<.01; smokers scored higher on USS Personal, Others, and Global subscales.

Among nonsmokers only, USS scores correlated with all mental health concerns; the strongest association was between USS-Personal beliefs and current anxiety (r=.51, p<.001). Among smokers, USS-Personal and USS-Global (but not USS-Others) correlated with current mental health, the strongest association being with anxiety (r=.72,p<.001).

Conclusions: This is the first demonstration of a relationship between unpredictability beliefs and illness symptoms. Future research is needed in more diverse samples and clinical samples. How unpredictability beliefs influence smoking initiation, maintenance, and relapse deserves further attention.
“IT MAKES YOU RETHINK YOUR CHOICE OF THE PILL”: THEORY-BASED FORMATIVE RESEARCH TO DESIGN A CONTRACEPTIVE CHOICE CAMPAIGN

Sundstrom, Beth1, DeMaria, Andrea2, Meier, Stephanie3, Jones, Annabel1, Moxley, Grace3, McInnis, Stephanie3.

1Department of Communication, Women’s Health Research Team, College of Charleston, 2Department of Health and Human Performance, Women’s Health Research Team, College of Charleston, 3Women’s Health Research Team, College of Charleston

Background: Half of all pregnancies in the United States remain unplanned despite improved access to highly effective long-acting reversible contraception (LARC), including the intrauterine device (IUD) and the implant.

Objectives: This study conducted theory-based formative research to develop a contraceptive choice campaign aimed at increasing LARC uptake by women ages 18-44 years old in Charleston, South Carolina. Researchers partnered with a local reproductive health care center to develop and test message concepts and designs.

Methods: Systematic theory-based formative research, including six focus groups (n=61), 18 interviews, and a web-based survey (n=547) was used to develop messages that resonate with women. The theory of planned behavior (TPB) and diffusion of innovations theory guided the development of campaign concepts and messages in this study.

Results: Qualitative data analysis revealed messages and designs that resonated with these women. Emphasizing LARC as the healthy option, highlighting LARC effectiveness, including relatable and trustworthy characters, and utilizing language of control emerged as themes. Women reported a preference for statistics illustrating effectiveness combined with empowering messages of control over contraceptive decision-making. A web-based survey was used to test and confirm the efficacy of these campaign messages. Reliability analyses were conducted on the theory of planned behavior (TPB) constructs to assess internal consistency. Structural equation modeling (SEM) affirmed the TPB’s fit as a predictor of LARC intention and uptake.

Conclusions: Findings from this study offer practical recommendations for developing contraceptive choice campaigns targeting LARC use and further the goal of reducing unintended pregnancy among women.

GENDER BIAS IN RADIOLOGY RESIDENT SELECTION PROCESS, DOES IT EXIST?

Hewett, Lara1; Lewis, Madeleine2; Collins, Heather3; Gordon, Leonie4.

1Department of Radiology, Medical University of South Carolina, 2Department of Radiology, Medical University of South Carolina, 3Department of Radiology, Medical University of South Carolina, 4Department of Radiology, Medical University of South Carolina

Background: Women continue to be underrepresented in Diagnostic Radiology, despite the increasing proportion of females graduating from medical schools. Previous studies have investigated degree of female medical student interest in Radiology, exposure to female faculty, and the influence of female mentorship as possible factors leading to lack of women entering the field. However, the presence or absence of bias in selection of residents has not been investigated.

Objective: To investigate whether there is a bias in the residency selection process influencing the proportion of females entering Diagnostic Radiology residencies.

Methods: A total of 2,752 US/Canadian applications to one Diagnostic Radiology residency program from 2009-2014 were analyzed. Invitations to interview were evaluated for each year, specifically looking at gender. Ranking of the applicants, especially those placed in the top 25% of the rank was also assessed. Data analyzed included USMLE Step 1 Board examination score (a proxy for academic performance), interview scores and final position on rank list.

Results: Females averaged 23% of the total applicant pool from2009-2014. Women comprised 30% of applicants invited to interview and 38% of the top 25% of ranked individuals. This trend was not attributable to superior academic performance by women.

Conclusions: Our findings suggest that although program directors aim to increase gender diversity, the number of females applying to Radiology residencies has decreased over the past five years. It appears the number of females pursuing Radiology is the limiting factor, and no bias against females in the resident selection process could be appreciated.
SEX-SPECIFIC SYMPTOM DIFFERENCES IN INDIVIDUALS WITH CHRONIC VEINOUS DISEASE

Teresa Kelechi¹, Martina Mueller¹, Mary Dooley¹

¹ College of Nursing, University of South Carolina

Background: Individuals with chronic venous disease (CVeD) experience multiple uncomfortable leg symptoms that negatively affect quality of life. The most severe forms of CVeD, skin damage and leg ulcers, affect men and women equally, however little is known whether these symptoms are different for women.

Objectives: To establish sex specific differences in uncomfortable leg symptoms in individuals with CVeD.

Methods: The VEINES/QoL questionnaire was used to measure 11 uncomfortable leg symptoms in individuals enrolled in an intervention study to test the efficacy of a leg cooling treatment to prevent venous leg ulcers. Chi square test was used to analyze symptoms by sex in two categories; high symptom burden defined as symptoms occurring every day or several times a week; or, low burden defined as occurring about once a week or less.

Results: Data were analyzed for 146 females (55%) and 120 males (45%), N=266. There were statistically significant differences between men and women for throbbing (p = 0.04), burning sensation (p = 0.02) and night cramps (p = 0.03). In women, the odds ratio (95% CI) for experiencing throbbing was 1.68 (1.02, 2.76) and burning sensation, 1.79 (1.09, 2.94). Controlling for body mass index, women experienced night cramps almost double, 1.83 (1.07, 3.15) compared to men.

Conclusions: Findings suggest there sex differences exist for uncomfortable leg symptoms in the presence of CVeD. Women report more burdensome neurological-type discomfort. It is important to understand sex specific differences in order to provide the most beneficial treatment to improve quality of life.

BIRTH SETTINGS AND NEONATAL SEIZURES RECORDED IN BIRTH CERTIFICATES COMPARED TO MEDICAID CLAIMS DATA AND HOSPITAL DISCHARGE ABSTRACTS IN SOUTH CAROLINA, 1996-2013

Li, Qing, M.D., Dr.P.H.¹; Newman, Roger, M.D.¹; Kirby, Russell, Ph.D., M.S.³; Kirby, Heather⁵; Kinsman, Stephen, M.D.⁵; Jenkins, Dorothea, M.D.⁶; Vena, John E. Ph.D.²

¹Department of Obstetrics and Gynecology, MUSC ²Department of Public Health Sciences, MUSC, ³University of South Florida, College of Public Health, Department of Community and Family Health, Tampa, Florida, ⁴SC Revenue and Fiscal Affairs Office, Health and Demographics Section, ⁵Division of Pediatric Neurology, MUSC, ⁶Department of Pediatrics, Division of Neonatology, MUSC

Background: Neonatal seizures have been recorded more frequently among home births compared to hospital births. However, available studies relied on birth certificates alone with low sensitivity in recording neonatal seizures.

Objectives: We designed this study to evaluate the reporting of neonatal seizures across birth settings in birth certificates compared to discharge abstracts and Medicaid claims.

Methods: We conducted a population-based study of the linked live birth, discharge abstracts, and Medicaid claims data from 1996 to 2013 in South Carolina. The discharge abstracts and Medicaid claims data were searched for ICD-9 code 779.0 (convulsions in newborn) and joined as gold standard. The sensitivity (Sen), positive predictive value (PPV), and the kappa statistic of birth certificates were evaluated.

Results: Among 558,307 births in hospital from 2004 to 2013, birth certificates had a sensitivity of 7% and a PPV of 64% (36% false positives) for neonatal seizures. The kappa statistic 0.12 indicated slight agreement between birth certificates and the joined source. Among 1,694 intended home births, both sensitivity and PPV were 0; the kappa statistic -0.0016 indicated the agreement worse than expected by chance. For births from 1996 to 2003, worse values (Sen 5%, PPV 32%, Kappa 0.09) were obtained for 404,577 hospital births and for 1,396 home births (Sen 0, PPV 0, Kappa -0.0012).

Conclusions: Compared to discharge abstracts and Medicaid claims, birth certificate in South Carolina under-reported neonatal seizures, suggesting it alone would not be an appropriate source to ascertain newborn neurological dysfunction at home or in the hospital.
THE SOUTH CAROLINA CEREBRAL PALSY PROJECT, 1996-2013

Li, Qing M.D., Dr.P.H.1,2; Newman, Roger M.D.1; Paneth, Nigel M.D., M.P.H.3; Kirby, Russell Ph.D., M.S.4; Kinsman, Stephen M.D.5; Jenkins, Dorothea M.D.6; Kirby, Heather B.S.7; Vena, John Ph.D.2

1Department of Obstetrics and Gynecology, MUSC, 2Department of Public Health Sciences, MUSC, 3Department of Epidemiology and Biostatistics, Michigan State University, East Lansing, Michigan, 4University of South Florida, College of Public Health, Department of Community and Family Health, Tampa, Florida, 5Department of Pediatrics, Division of Pediatric Neurology, Medical University of South Carolina, 6Department of Pediatrics, Division of Neonatology, MUSC, 7South Carolina Revenue and Fiscal Affairs Office, Health and Demographics Section, Columbia

Background: Cerebral Palsy (CP) is a relatively common and severe motor disability in which genetics, pregnancy and perinatal events play a role, and there is a suggestion of a higher prevalence in the US. A CP prevalence of 3.1 to 3.6 per 1,000 8-year old children was recently found by the CDC in Alabama, Georgia, Wisconsin and Missouri, figures much higher than the rate of 1.5–2 per 1,000 live births found in several European registries and older data from California.

Objectives: We attempted to ascertain all cases of CP diagnosed in South Carolina from 1996 to 2013.

Methods: We identified 2,641 children up to age 4 years with a CP diagnosis by searching linked records from the Department of Disabilities and Special Needs (DDSN 429 cases), Hospital Discharge Files (805 cases), and Medicaid files (2,510 cases) using the International Classification of Diseases, Ninth Revision, Clinical Modification codes 343.0 - 343.9. DDSN serves any South Carolina resident meeting the disability requirements, while a CP diagnosis qualifies a child for the Supplemental Security Income Program and the child is then eligible for the Medicaid program.

Results: The prevalence of CP was 2.7/1,000 live births. Among twins, CP prevalence was 6.0/1,000 births. Birth prior to 32 weeks was found in 28.1% (695) of 2,475 singletons and in 65.1% (69) of 106 twins. Birth below 1,500 g was found in 25.9% (641) of singletons and 67.0% (71) of twins.

Conclusions: This study joins recent CDC research in finding a CP prevalence in the US above 2.5/1,000 live births.

GREATER COGNITIVE FLEXIBILITY IN FEMALE RATS RELATIVE TO MALES IN A AUTOMATED SET-SHIFT TASK

Brittney M. Cox1, Helaina Regen-Tuero1, Stan B. Floresco2, Carmela M. Reichel1

1Medical University of South Carolina, Department of Neurosciences, Charleston SC, 2University of British Columbia, Department of Psychology, Vancouver, BC

Background: Deficits in cognitive flexibility are associated with a number of neuropsychiatric disorders, including schizophrenia and substance abuse, which rely on prefrontal cortical function. Furthermore, sex differences in cognitive flexibility have been identified in neuropsychiatric patients, although the neural mechanisms underlying these sex differences are unknown.

Objectives: We sought to identify baseline sex differences in cognitive flexibility of rats by assessing the ability to shift behavior in response to new information.

Methods: Cognitive flexibility was assessed using an Automated Set-Shift Task (ASST), in which male and female Sprague Dawley rats were placed in operant chambers (equipped with levers and lights) for daily sessions, and received a sucrose reward for correct trials. The rats completed ASST in phases: pre-training, visual cue discrimination, extra-dimensional shift (EDS), and a reversal. Estrous cycle was examined in females on all test days.

Results: Females out performed males during the early phases of the task, and also exhibited greater flexibility than the males in the EDS and the reversal learning tasks. Preliminary findings suggest that estrous cycle phase effects the performance of the females, but specific cycle effects are still being investigated. Fos expression (as an index of neuronal activity), will be presented from the prefrontal cortices.

Conclusions: As sex-specific rodent models of neuropsychiatric disorders are almost non-existent, these experiments may allow for the development of such models and subsequently facilitate a sex-specific approach to pharmacotherapies.
SEX DIFFERENCES IN A MOUSE MODEL OF BLADDER CANCER

White-Gilbertson, Shai2; Davis, Megan3; Voelkel-Johnson, Christina1, Kasman, Laura1.

1Department of Microbiology and Immunology, Medical University of South Carolina, 2Hollings Cancer Center Tumor Registry, Medical University of South Carolina, 3Diagnostic Microbiology at Medical University of South Carolina

Background: In humans, bladder cancer is one third as prevalent in women as in men, with a trend toward lower prevalence in parous compared to nulliparous women.

Objectives: To determine if a widely used murine model of bladder cancer (MB49) recapitulates the sex difference observed in humans, and to investigate a possible protective effect of pregnancy hormone, human chorionic gonadotropin (hCG).

Methods: Male and female C57BL/6 mice were implanted with syngeneic MB49 murine bladder cancer cells, treated with hCG or saline, and observed for tumor growth. Dose responses to hCG were determined for a panel of human bladder cancer cell lines and MB49 cells in vitro.

Results: MB49 tumor growth was significantly greater in male than female mice. Treatment of mice bearing MB49 cell xenografts with hCG resulted in a dramatic increase in tumor burden relative to saline treated controls in both sexes. In vitro dose--response studies indicated that the growth stimulation in vivo was most likely due to a mediator other than hCG itself, as MB49 cells treated with hCG in culture were not stimulated to grow and the functional receptor for gonadotropins was absent. Testosterone strongly stimulated growth of MB49 cells in vitro.

Conclusions: The MB49 murine model of bladder cancer does recapitulate the sex difference observed in humans. Our results suggest that testosterone may promote bladder cancer growth, which would explain the increased incidence of bladder cancer in men. Androgen inhibitors commonly used to treat prostate cancer may be useful in the treatment of bladder cancer.

---

ESTROGEN RECEPTOR ALPHA DEFICIENCY MODULATES PDC-TREM EXPRESSION IN PLASMACYTOID DENDRITIC CELLS IMPACTING TYPE I INTERFERON PRODUCTION AND RESPONSE TO TLR LIGANDS

Scott, Jennifer *†, Cunningham, Melissa †, Naga, Osama †, Wirth, Jena †, EuDaly, Jackie †, and Gilkeson, Gary †‡

Department of Microbiology and Immunology, College of Graduate Studies, Medical University of South Carolina, Charleston, SC 29425, USA*, Division of Rheumatology and Immunology, Department of Medicine, Medical University of South Carolina, Charleston, SC 29425, USA†; Medical Research Service, Ralph H. Johnson Veterans Affairs Medical Center, Charleston, SC 29403, USA‡

Background: Female lupus-prone estrogen receptor alpha knockout (ERαKO) mice are protected from renal disease and have prolonged survival compared to wild-type littermates, however the mechanism of protection is unknown. Plasmacytoid dendritic cells (pDCs) and type I interferon (IFN) can drive lupus pathogenesis, and estrogen via ERα enhances both the development and IFN production of pDCs.

Objectives: We hypothesize ERα deficiency impairs pDC function in lupus prone mice and this effect may contribute to disease protection.

Methods: We measured the effect of ERα deficiency on IFN activity and pDC frequency, number, maturation and activation state in the spleens of pre-disease lupus-prone mice (NZM2410). We also measured pDC activation after in vitro toll-like receptor (TLR) stimulation.

Results: Spleens from lupus-prone ERαKO mice expressed lower levels of IFN signature genes. ERα deficiency also reduced the frequency of pDC expressing MHCII and PDC-TREM in the spleens without altering the frequency, number, or maturation state of pDCs. In lupus-prone mice, pDCs can be activated by immune complexes, which function as stimuli for Toll-like receptor 9 (TLR9). After in vitro TLR9 stimulation, ERα deficiency reduced the percent of pDCs expressing PDC-TREM.

Conclusions: In this study we have identified an effect of ERα deficiency on pDCs and type I IFN activity in pre-disease lupus-prone animals. We believe this finding may represent a mechanism by which lupus-prone ERαKO mice are protected from disease. Additionally, we have identified PDC-TREM as a mediator of ERα’s impact on type I IFN production.
DEVELOPMENT OF A RODENT MODEL OF THC SELF-ADMINISTRATION

Spencer, Sade; Allen, Nicholas P; Scofield, Michael D; Kalivas, Peter W

1 Department of Neurosciences, Medical University of South Carolina

Background: Cannabis is the most frequently used illicit drug worldwide, but preclinical research on its effects has been hampered by lack of an animal model since rats will not maintain self-administration of purified Δ9-tetrahydrocannabinol (THC), the drug’s main psychoactive component. Self-administration of a synthetic cannabinoid receptor agonist (WIN55, 212-2) has revealed marked sex differences in drug taking and seeking with females showing enhanced physiological and behavioral responses, but this has not been tested with THC.

Objectives: The present study aims to extend these findings by establishing a reproducible rat model of THC self-administration. We hypothesize that THC vapor pre-exposure will promote acquisition of self-administering and that combining cannabidiol (CBD) with THC will reduce the drug’s aversive properties facilitating drug taking.

Methods: Adult male Sprague-Dawley rats were exposed to ten minutes of THC:CB vapor (ratios of 10:1 and 1:1, 10 mg THC per vapor pad) for 5 days. Following vapor exposure, rats transitioned to iv THC:CB self-administration (4μg/kg).

Results: Our THC vapor pre-exposure provided a physiologically relevant dose of THC as we were able to measure a decrease in core body temperature after exposure. During THC self-administration, clear lever discrimination was observed with greater than 2-fold preference for the drug-associated lever. The rats sustained low levels of responding with an average of 6 infusions per 2-hr session although there was high inter-individual variability.

Conclusions: We have established a rodent model of THC self-administration allowing us to evaluate THC-dependent brain changes relevant to addiction and sex differences in THC response.

IMPROVEMENT IN PAIN SCORES AFTER TRANSITION TO BUPRENOPHINE FOR WOMEN WITH CHRONIC PANCREATITIS PAIN

Barth, Kelly; Balliet, Wendy; Delaney, Kelley; Borckardt, Jeff; Back, Sudie; Owczarski, Stefanie; Adams, David; Morgan, Katherine; Brady, Kathleen

1 MUSC Department of Psychiatry & Behavioral Sciences; 2 MUSC Department of Surgery

Background: Pain is a prevalent issue in chronic pancreatitis (CP), with up to 95% of patients experiencing pain along the course of the disease. Although surgery is among the most effective treatments for CP, most patients still require chronic opioid therapy for pain (COT-P) after surgical intervention. In 2014, the Comprehensive Pain Management Program at MUSC started a clinical pilot trial of multi-disciplinary opioid medical management for 50 patients with post-surgical CP pain with the purpose of improving health outcomes. To date, 22 patients have engaged in the program, 21 of them females. Of those, 5 have had indications for opioid cessation and were transitioned to buprenorphine, a partial opioid agonist, as a first step in opioid cessation.

Objectives: To describe the characteristics and outcomes for 5 female patients transitioned from COT-P to buprenorphine.

Methods: Case series of 5 females transitioned from COT-P to buprenorphine.

Results: Average Morphine Milligram Equivalent (MME) was 236mg. Average duration on opioids was 7.2 yrs. Average COMM score was 12. All 5 patients tolerated transition from COT-P to buprenorphine. Average pain scores (1-10) were 7.9 pre-buprenorphine and 6.2 post-buprenorphine.

Conclusions: Buprenorphine is a promising agent to assist patients in tapering off COT-P when an indication exists. These preliminary results show that patients on COT-P can tolerate transition to buprenorphine and that their average pain scores trend down after transition to buprenorphine. The majority of patients with post-surgical pancreatic pain requiring COT-P are females, and more research is needed to examine this gender difference.
THE ROLE OF THE ROSTROMEDIAL TEGMENTAL NUCLEUS IN SEX-RELATED DIFFERENCES IN THE NEGATIVE EFFECTS OF ALCOHOL

Burnett, Elizabeth J; Chandler, L Judson

Department of Neuroscience, Medical University of South Carolina, Charleston, SC 29425

Background: Few studies have examined the neurobiological mechanisms underlying sex differences in the sensitivity to alcohol’s negative properties. Recent work suggests that a midbrain region known as the rostromedial tegmental nucleus (RMTg) may be involved in signaling the aversive properties of drugs and alcohol.

Objectives: To investigate the role of the RMTg in sex differences in the negative effects of alcohol.

Methods: Using a standard conditioned taste aversion assay, a novel saccharin solution was conditioned to an i.p. injection of either 1.5 g/kg 20% ethanol, 20 mL/kg 0.15M lithium chloride (LiCl) or saline in adult male and female rats. Rats were sacrificed 90 minutes following final saccharin exposure and brains processed for immunohistochemistry to measure RMTg cFos expression.

Results: Ethanol and LiCl produced significant CTA of equal magnitude in males and females compared to saline. The magnitude of ethanol-induced CTA was more variable, however, in females than males with some females exhibiting substantial resistance to ethanol-induced CTA. Both ethanol and LiCl-induced CTA significantly enhanced cFos expression in the RMTg. While no sex differences in cFos expression were uncovered, we observed a negative correlation between RMTg cFos and CTA magnitude that trended toward significance.

Conclusions: These data demonstrate a role for the RMTg in signaling the aversive properties of alcohol. The absence of significant sex differences in CTA magnitude and associated cFos expression may be due to increased variability among females. The involvement of estrous cycle in this variability is currently being investigated.

OXYTOCIN ATTENUATES CONDITIONED COCAINE SEEKING IN MALES AND FEMALES

Linnea R. Freeman, Shannon M. Ghee, Carol Berini, Carmela M. Reichel

Medical University of South Carolina, Charleston, SC 29425

Background: Oxytocin has gained increasing attention as a possible treatment for multiple neuropsychiatric disorders, including addiction. Oxytocin impacts natural and drug reward due to extensive innervation of central reward pathways. Sex differences clearly exist in psychostimulant addiction patterns. However, the underlying neurobiology and potential addiction therapies have typically only been studied in males. The oxytocin system is sexually dimorphic with a greater number of oxytocin receptors expressed throughout the addiction circuit in males relative to females. Here, we examined whether oxytocin would alter reinstated cocaine seeking in males and females following systemic oxytocin treatment. We have begun to identify key brain regions involved in this effect.

Methods: Male and female rats underwent 2 weeks of cocaine self-administration followed by extinction and reinstatement tests after systemic (1 mg/kg, i.p.) oxytocin or vehicle treatment in the presence of conditioned cues. Following testing, rats were perfused and the brains were processed for c-fos staining and c-fos/oxytocin double-labeling. A separate group of rats received oxytocin treatment during extinction and were tested with vehicle or oxytocin in response to cocaine-conditioned cues.

Results: An acute oxytocin injection (i.p.) reduced reinstated cocaine seeking in both males and females. Likewise, repeated oxytocin during extinction also reduced responding on a cue test in males and females. However, oxytocin during extinction had no lasting impact on a cued reinstatement test. Currently, we are double labeling c-Fos and oxytocin cell bodies in the periventricular nucleus to determine whether oxytocin reduced reinstated cocaine seeking via similar mechanisms. Additionally, we are quantifying c-Fos expression in terminal areas.

Discussion: Oxytocin impacted reinstated cocaine seeking similarly in both sexes. This similarity is in contrast to the well-known sex differences in the role of oxytocin on peripheral organ sites of actions and the sexually dimorphic distribution of central oxytocin receptor cites in females, relative to males. This study will determine if similar behavioral outputs may be mediated by a different underlying neurobiology.
SEX DIFFERENCES IN DEMAND FOR HIGHLY PALATABLE FOOD REWARDS: ROLE OF OREXIN NEURONS

Linnea Freeman, Brandon Bentzley, and Gary Aston-Jones

Medical University of South Carolina, Charleston, SC 29425

Background: Demand is a measure of reward consumption as a function of reward price – the effort required to earn a reward. Recent studies (including ours) have found that orexin signaling is involved in responding for highly salient rewards, particularly during high effort (Cason & Aston-Jones 2012). Furthermore, orexin is sexually dimorphic: female rats have higher pre-pro orexin mRNA, orexin A protein and orexin-1 receptor mRNA in hypothalamus than males (Johren et al 2001; Johren et al 2002; Taheri et al 1999).

Methods: Here we used a within-session behavioral economics (BE) approach recently developed in our laboratory (Bentzley et al, Psychopharmacology 2013) to evaluate the role of orexin signaling in demand for a highly palatable food reward (HPF). With this method, an entire demand curve (consumption as a function of effort) is generated in each session, allowing for comparisons of demand following different manipulations.

Results: In the current study, demand for a low-fat, a high-fat, and a sucrose HPF were evaluated in male and female rats. Female Sprague-Dawley rats revealed increased motivation (lower demand elasticity) for the low-fat, high-fat and sucrose (chocolate-flavored) HPF compared to males. Furthermore, administration of an orexin 1 receptor antagonist SB 334,867 (SB) prior to the BE session resulted in decreased demand for all three rewards in male and female rats.

Conclusions: These results indicate sex differences in mechanisms that drive reward motivation for high fat and sucrose rewards that should be evaluated in future studies.

Supported by PHS grants R37-DA006214, T32-DA07288-22 and F30-DA035065.

LOSE WEIGHT, GAIN BRAIN? MICROSTRUCTURAL ALTERATIONS IN BRAIN WHITE MATTER FOLLOWING WEIGHT LOSS IN OBESE MIDDLE-AGED WOMEN

BENITEZ, Andreana¹; CHAN, Clifford¹; FALANGOLA, Maria Fatima¹; BROWN, Joshua²; JENSEN, Jens¹; HELPERN, Joseph¹; O’NEIL, Patrick²

¹ Department of Radiology and Radiological Science, MUSC, ² Department of Psychiatry and Behavioral Sciences, MUSC

GENDER-BASED DIFFERENCES IN FUNCTIONAL CONNECTIVITY OF HEALTHY SUBJECTS AT REST

Vanderweyen, Davy¹; Zhu, Xun¹; Moran Santa-Maria²; Megan; McKee³, Sherry; Cosgrove, Kelly³; McRae, Aimee², Brady, Kathleen²; & Joseph, Jane¹

¹ Department of Neurosciences, Medical University of South Carolina, ² Department of Psychiatry, Medical University of South Carolina, ³ Department of Psychiatry, Yale University

Background: Differences in functional brain activation patterns between males and females have been observed in the past. Further investigation of gender differences during resting state may help us to better understand heterogeneities inherent to fMRI.

Objectives: In this study we used resting state fMRI to investigate the differences in functional connectivity network structure based on gender in healthy subjects.

Methods: Sixty five subjects (31 males) completed a resting state fMRI experiment. Data analysis involved preprocessing, parcellation of data into 264 functionally defined regions of interest, generation of correlation matrices using partial correlation, and computing three measures of functional connectivity (eigenvector centrality, betweenness centrality, and clustering coefficient; Brain Connectivity Toolbox) that reflect global properties of the network.

Results: Independent samples t-tests conducted in each of the 264 brain regions revealed sex differences in multiple regions, including the motor cortex, insula, fusiform gyrus, prefrontal cortex, and precuneus.

Conclusions: Our results hint to the presence of gender-dependent cognitive differences like sensory perception, emotion processing, resting state dynamics, and homeostasis regulation.