UK College of Public Health Research Day
ORAL and POSTER ABSTRACTS

Thursday, March 27, 2014 **Lexington Convention Center**

#1 Abstract Title: **Working Together, Working Apart: A Bayesian Time-Utilization Analysis**

Author(s): D. R. Bardach, Departments of Epidemiology and Biostatistics, U of Kentucky

Abstract: Background: In 2011, the University of Kentucky opened two new patient floors of its inpatient hospital. Each floor has four units; two Intensive Care Units and two Acute/Progressive Care Units. Each unit has approximately 600 square feet designated as a "Team Station" for interdisciplinary collaboration. Hospital administration was interested in assessing whether these large sections in the current design were being used for their intended purpose. Methods: Over a three week period a trained observer collected data along a predetermined route through the two floors 75 times. The route was made up of 259 ordered points at which he recorded the approximate number of staff present, the disciplines represented, and whether the work being done was solo or collaborative. Data was analyzed using Bayesian logistic regression with diffuse Cauchy priors. Results: Intensive Care Team Stations were used for interdisciplinary collaboration 4.6% of the time, with a 95% credible interval of (3.7%, 5.6%). Acute/Progressive Care Team Stations were used for interdisciplinary collaboration 3.5% of the time, with a 95% credible interval of (2.7%, 4.4%). The relative risk for collaboration occurring in the Team Station as opposed to near the patient rooms in the Intensive Care setting is 1.154 (0.901, 1.449) and in the Acute/Progressive Care setting is 1.156 (0.900, 1.455). Conclusion: The Team Station space is not often used for its intended purpose. Collaboration does not convincingly happen there over other more essential spaces. The allocation of space for Team Stations should be revisited before future floors are constructed.

Supported by: None

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Thursday, March 27, 2014 **Lexington Convention Center**

#2 Abstract Title:	**Coronary Artery Disease in Women with and without Rheumatoid Arthritis in Kentucky Women's Health Registry.**
Author(s):	H. Mousa, Dept of Preventive Medicine & Environmental Health, U of Kentucky D. Mannino, Dept of Preventive Medicine & Environmental Health, U of Kentucky W. Sanderson, Dept of Epidemiology, U of Kentucky

Abstract: Abstract:The objectives of this project were to determine the relationship between rheumatoid arthritis (RA) and the reporting of coronary artery disease (CAD) and to measure the prevalence and incidence of CAD in women with and without RA using the Kentucky Women's Health Registry. Data was analyzed on 7944 women over 18 years of age who responded to survey questions on rheumatoid arthritis, angina, and heart attack. Coronary artery diseases included in the analysis were angina and heart attack. Analyses controlled for age, obesity, diabetes, smoking, alcohol consumption, general health, education level, race, hypercholesterolemia, and hypertension. Results showed that women with RA were more likely to report CAD than women without RA (adjusted odds ratio [aOR] = 1.90 and 95% confidence interval [CI] 1.20, 2.90). The prevalence of CAD was 11.1% among women with RA while it was 4.0% among women without RA. The incidence of CAD among women with RA was 10.0% while it was 2.2% among women without RA.

Supported by: N/A

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Thursday, March 27, 2014 **Lexington Convention Center**

#3 Abstract Title:	**The Effects of Giving Some Form of Breast Milk to Preterm Infants while in the NICU**

Author(s):	H.M. Flannagan, College of Public Health, U of Kentucky W. Sanderson, College of Public Health, U of Kentucky L. Chesnut, College of Public Health, U of Kentucky S. Browning, College of Public Health, U of Kentucky H. Bada, Div of Neonatology, U of Kentucky

Abstract: It is known that breast milk can offer numerous benefits, such as immunologic benefits, to term infants, however not much research has been done on the benefits for preterm infants. This study examined the benefits of infants receiving breast milk while in the neonatal intensive care unit (NICU). The study included preterm infants from the University of Kentucky NICU who were participating in the Vermont Oxford Network. Many variables and outcomes were examined, specifically, the effects of gestational age, post-delivery interventions, and APGAR score on length of stay, positive developmental outcomes, and common health issues of premature infants. After adjusting for potential confounders, receiving breast milk in the NICU had a significant effect on infant's length of stay, by decreasing length of stay by an average 6.06 days ($p<0.0001$) and significantly reducing the odds of needing supplemental oxygen at 28 days and 36 weeks post birth. Breast milk was not found to be significant in decreasing the odds of developing necrotizing enterocolitis and intestinal perforation or respiratory distress syndrome, and it showed that those who did not receive breast milk had a more significant percent change in weight. This study has proven that receiving breast milk has some benefits for preterm infants, however more studies need to be done to determine if the most benefit comes from giving preterm infants both breast milk and fortified formula.

Supported by: MPH Capstone

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Thursday, March 27, 2014 **Lexington Convention Center**

#4 Abstract Title: **Appalachian Breastfeeding Disparities: A Literature Review**

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Abstract: Background: The health advantages of breastfeeding (BF) have been well documented and reported for both mothers and infants. In the last 15 years breastfeeding initiation rates in the nation have increased from 60% to 74%. Kentucky reports one of the lowest rates of breastfeeding nationwide (56%), specifically around the Appalachian area, where rates range from 22% to 42%. The objective of this systematic literature review is to examine studies related with breastfeeding in Appalachia in order to: a) describe current level of scientific evidence about barriers to BF for Appalachian women; and b) suggestion of future research needed to define strategies for promoting positive breastfeeding behaviors in this population. Methods: A search of peer-reviewed publications on Pub Med and CINAHL databases was performed using the search terms “breastfeeding” and “Appalachia”, of which six relevant publications were identified. Results: Low BF rates in this area correlate with smoking, young age, being unmarried, uninsured, inadequate prenatal care, low education levels, and low income of the mother. In addition, lack of support from employers, family, community, and healthcare professionals further impacts the cultural norms resulting in a decreased likelihood to breastfeed. Conclusions: The Appalachian region lags behind the rest of the nation in breastfeeding rates, which in turn contributes to poor health outcomes. Future research should include further evaluation of successful interventions with an emphasis on determining the optimal type and source of support that Appalachian women need to establish successful breastfeeding.

Supported by: Start fund College of Nursing, University of Kentucky

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Thursday, March 27, 2014 **Lexington Convention Center**

#5 Abstract Title: **An Evaluation of Three Positive Parenting Practices and Their Combined Impact on Developmental, Social, or Behavioral Delays in Children Ages 1-5 in the United States**

Author(s):
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Abstract: Objectives: (1) Determine whether three individual positive parenting practices (PPP) – reading to children, engaging in storytelling or singing, and eating meals together as a family – decrease the risk of developmental, behavioral or social delays among children between the ages of 1-5 years in the United States. (2) Determine if a combination of these parenting practices has an additive effect on the outcome. Methods: Multiple logistic regression and chi-square analyses were used to analyze data from the National Survey of Children's Health 2011/2012 in regards to the relationship between each of the three individual PPP as well as a total PPP score and the child's risk of being developmentally, socially, or behaviorally delayed. These analyses controlled for poverty and parental education. The sample included 24,875 participants and all analyses were completed using SAS Version 9.3. Results: A strong correlation was found between each of the three PPP as well as the total PPP score and the child's risk of developmental, social, or behavioral delays ($p<0.05$ for each test). These associations were found to have a dose-response relationship ($p<0.05$ in all but one analysis). Conclusions: This study found that parents engaging in daily PPP could possibly reduce the risk of delay in young children. Furthermore, we found that engaging in all three PPP daily has an additive effect in reducing risk of delays. Limitations of this study include its cross-sectional design, as well as potential recall and social desirability biases.

Supported by: NA

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Thursday, March 27, 2014 **Lexington Convention Center**

#6 Abstract Title: **The Impact of Perceived High Levels of Stress on Non-usage of Condoms During Sex Among College Students**

Author(s): S. Bearman, College of Public Health, U of Kentucky

Abstract: Introduction: There is a paucity of research that specifically examines the non-use of condoms during sexual encounters as a maladaptive coping strategy for stress among college students; therefore, the purpose of this study is to determine if there is an association between perceived high levels of stress and the decreased likelihood of condom use during sex among undergraduate students attending a large university in the southeastern U.S. Method: Data for this secondary analysis originate from a larger study assessing the health behaviors of more than 7,000 undergraduate students enrolled in fall 2013 courses. For the purposes of this analysis, we focused on gaining a detailed understanding of students who choose sex as an unhealthy coping method for perceived high levels of stress, and the likelihood of condom use. The variables of interest are perceived stress, coping methods used to relieve stress, sexual behaviors, and contraception use; perceived stress is the predictor variable, and condom use is the outcome variable. Analyses are restricted to those respondents who have been sexually active within the last 30 days, excluding responses from sexually naïve respondents. The moderating covariates are gender and sexual orientation. Conclusion: Results are pending; analyses will be finalized in April 2014 as part of a public health capstone research project. Study findings have the potential to inform university health service initiatives aimed at helping undergraduate students adopt adaptive coping strategies for perceived high levels of stress and practice safe sexual behaviors, including condom use.

Supported by: University of Kentucky University Health Services provided the survey which provided the data used.

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Thursday, March 27, 2014 **Lexington Convention Center**

#7 Abstract Title: **Community Health Workers: Implementing a System in Kentucky**

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J. Chamness, Montgomery County Health Department
C. White, Kentucky Department of Public Health
S. Mayfield Gibson, Kentucky Department of Public Health

Abstract: Disparities and access to healthcare are not improving in the United States. Socioeconomic, environmental and cultural barriers, especially for rural and low-income populations, continue to impede access to equitable care and add to rising healthcare costs. In Kentucky, overall inequities including education, income, and chronic disease burden, are getting worse especially in the rural eastern Kentucky. The growing number of Medicaid enrollees and aging baby boomers population is more than likely to create significant healthcare workforce shortage which, if left unchecked, will only worsen the existing health disparities and healthcare costs. Healthcare providers, while highly trained, often lack the time, cultural competency and community knowledge to engage and empower low-income patients, adversely affecting their care. Community Health Workers (CHWs) are lay health workers known to effectively connect at-risk communities to healthcare and human services and promote better health. CHWs play a significant role in reducing and/or managing chronic illnesses, reducing healthcare costs, and improving the overall health of the population. Evidence gathered over the years makes it clear that support for, and development of a CHW workforce is a wise investment. This presentation will educate the audience about the evidence, opportunities, barriers, and plan of action towards implementation of a system for the CHW Workforce in Kentucky.

Supported by: None

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Thursday, March 27, 2014 **Lexington Convention Center**

#8 Abstract Title: **Community Health Workers: Contributing to the Triple Aim**

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Abstract: The US health care system is the most costly in the world, accounting for 17% of the gross domestic product with estimates that percentage will grow to nearly 20% by 2020. Triple Aim is a framework developed by the Institute for Healthcare Improvement and later adopted by Centers for Medicare and Medicaid Services that describes an approach to optimizing health system performance by improving the patient experience of care (including quality and satisfaction); improving the population health; and reducing the per capita cost of healthcare. The Community Health Worker (CHW) is a frontline public health worker who is a trusted member of and/or has an unusually close understanding of the community served. This trusting relationship enables the CHW to serve as a liaison/link/intermediary between health/social services and the community to facilitate access to services and improve the quality and cultural competence of service delivery. This presentation examines how the CHW effectively contributes to the achievement of the Triple Aim of Healthcare Reform. The audience will gain clarity on how CHWs improve quality of care, understand how utilizing a CHW as a member of the team benefits population health, and increase awareness of potential cost savings from averted complications and reduced readmissions.

Supported by: None

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Thursday, March 27, 2014 **Lexington Convention Center**

#9 Abstract Title:	**Listening to the winds of change: characterizing local health department (LHD) leaders' openness to change**
Author(s):	E.D. Jadhav, Dept of Health Management &Policy, U of Kentucky J. W. Holsinger, Dept of Health Management & Policy, U of Kentucky G. P. Mays, Dept of Health Management and Policy, U of Kentucky D. Fardo, Dept of Biostatistics, U of Kentucky

Abstract: Background: During the recent economic recession Kentucky's local health departments (LHDs) leaders used innovative approaches to maintain or grow their budgets. Providing an opportunity to glean valuable insights into top executive behavior and LHD financial performance. Research Objective: 1. Identify variation in socio-demographic characteristics of LHD leaders by their openness to change (ACQ) score, 2. Characterize association between LHD characteristics and leader demographic and experiential attributes with openness to change score. Data Sets: The unit of analysis are Commonwealth of Kentucky LHD leaders. Actual expenditures and revenues are from the state health department and county level population estimates are from the national census website. Study Design: A cross-sectional survey of KY LHD leaders. To identify differences in mean ACQ score by leader and LHD characteristics we used Wilcoxon-Mann-Whitney non-parametric test and the Kruskal Wallis test and the Spearman rank correlations test to determine correlations between leaders' ACQ score and leader and LHD characteristics. Principal Findings: Approximately 45% of LHD leaders had a high ACQ score with mean rank of 20.46 (SD 2.70). The spearman correlation test for the LHD characteristic, preceding year revenue was statistically significant with a negative relationship. The Mann-Whitney U - tests for gender and race, and the Kruskal-Wallis test for highest degree obtained were statistically significant. Implications for Public Health Practice and Policy: There are strong underlying relationships between leader experiential and demographic attributes and their openness to change. Since change oriented behaviors have strong implications on agency effectiveness formal public health leadership development programs will benefit from preparing leaders to modify their leadership behaviors.

Supported by: not applicable

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#10 Abstract Title: **Indexing the Availability of Health Care Services and Resources for Kentucky Seniors**

Author(s): M. Wallace, Dept of Health Services Management, U of Kentucky

Abstract: The availability of health care resources is often dependent on where one lives within the commonwealth of Kentucky. This occurrence can also be observed with senior services for the elderly. This study aims to measure the availability of services and resources for elderly persons by creating an index that quantifies the number of senior centers, nutrition sites, assisted living facilities, home health care agencies, adult day care centers, nursing homes, and family care homes in each of 120 counties in Kentucky. The results show that the Appalachian region and southern part of Kentucky is limited in the availability of senior services and resources when compared to western and northern Kentucky, especially Jefferson, Fayette and the Tri-county areas. This research increases the evidence-base that the limited availability of resources and services for Appalachian elderly decreases their opportunity for optimal health, thereby further demonstrating the health disparities for Appalachian residents when compared to non-Appalachian county residents. Future studies should investigate the overall accessibility of health care services and resources by this population by considering the probable challenges of distance, transportation and affordability.

Supported by: There is no financial support for this research

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#11 Abstract Title: **Psychosocial Change in Old Age: An Assessment of Beliefs and Values**

Author(s): A. I. Hoogland, Graduate Center for Gerontology, U of Kentucky

Abstract: Introduction: The majority of aging research focuses on deficits and decline, with few studies addressing positive change in late life. Current research points to a positive developmental change experienced by many older adults as a product of experience and time lived, but it is not clear how one's personal paradigm can shift with age. Research Aims: Identify contributors and predictors of beliefs and values in old age, and explore how older adults' beliefs and values have changed or stayed constant over time. Procedures: Eighteen participants over the age of 60 (aged 62-85; 14 females) in good health were recruited into three focus groups and assigned by age (60s, 70s, and 80s). In each 90-minute session, participants were asked to explore and articulate their core beliefs, influences on their beliefs, and change/continuity in beliefs over time. Interviews were digitally recorded and transcribed using a constant comparative method following initial code determination by the PI. Findings: Three primary themes emerged from the data: continuity of the self; change in core beliefs as pertains to the self and relations with others; and increased acceptance/nonjudgment over time. Conclusions: Older adults experience a continuity of the self over time, but with life experience there is a shift towards an increased focus on issues related to the welfare of others, and general harmony. Future Directions: These findings are being used to inform a quantitative study on beliefs and values that will incorporate a larger sample and age range.

Supported by: none.

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Thursday, March 27, 2014 **Lexington Convention Center**

#12 Abstract Title:	**Not-for-Profit Hospitals and Community Benefits: A Comprehensive Analysis**

Author(s): A. Parks, College of Medicine, U of Kentucky
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G. Mays, College of Public Health, U of Kentucky

Abstract: Purpose: The provision of community benefits in exchange for tax-exemption status for Not-for-Profit hospitals has been the topic of scrutiny for decades; mainly the adequacy of benefits provided relative to the amount of foregone governmental tax revenue. In light of recent policy enactments, most notably the Affordable Care Act, there has been a resurgence of this issue back into the healthcare agenda due to the predicted subsequent decline of uninsured persons within the U.S. It is the purpose of this study to analyze the patterns of community benefits focusing on traditional measures as well as new measures that many believe should be included such as Medicare Shortfalls and Bad Debt. In addition, this study will attempt to interpret environmental factors that are believed to also contribute to community benefit provision relating to the theory of Organizational Legitimacy. These levels will then be compared against For Profit and Government Owned hospital's benefit levels to determine the definitive factors that lead to community benefit provision as well as their true adequacy. Methods/Data/Results: This study analyzes a unique longitudinal dataset derived from the Form CMS-2552-96 Cost Report Data files of the Centers for Medicare & Medicaid Services (CMS). The dataset contains 8 years of observations covering fiscal years 2003-2010 on various individual hospital characteristics, costs, and ownership type. Panel regression methods will be used to evaluate the determinants of hospital community benefits. Results will be presented and discussed.

Supported by: The project described was supported by the Professional Student Mentored Research Fellowship and the Center for Clinical and Translational Science.

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Thursday, March 27, 2014 **Lexington Convention Center**

#13 Abstract Title:	**Establishing Pre-Season Self-Reported Functional Outcomes Scores for Athletes**

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Abstract: Hypotheses: Upper limits of self-reported functional questionnaires will not be reached by athletes during pre-season physicals and perceived function will vary based on past injury and sex. Participants: 875 high school and collegiate athletes (Age 18±2 years, 598 males/276 females). Procedures: Athletes with and without a history of shoulder, elbow, or knee injury were administered questionnaires (Knee Injury and Osteoarthritis Outcome Score Sports and Recreation Function (KSR) and Knee-Related Quality of Life (KQOL) subsections and Kerlan-Jobe Orthopaedic Clinic Shoulder and Elbow Score (KJOC)) after receiving medical clearance to participate in sport. All questionnaires were scaled 0-100, low to high function. Non-parametric analysis was performed to determine if scores differed within and between sexes and history of injury. Results: The mean score for all athletes was ≥93/100 for all 3 questionnaires. 513 of 875 athletes reported a history of injury. Within the sexes, outcomes scores were significantly lower for athletes with a history of injury for all 3 joints surveyed (range 8-20 points, $p<.001$). Female athletes with history of injury had significantly lower scores for the KJOC and KQOL compared to previously injured males (range 7-9 points, ≤.007). Conclusions: The pre-season functional value for an athlete's shoulder, elbow, or knee is just below upper thresholds. Although athletes were medically cleared, a history of injury negatively impacted self-perceived function in athletes with females faring less favorably than males. Prospective collection of preseason perceived function may provide clinicians relative "normal" values and is recommended to compliment and possibly enhance routine physical exams.

Supported by: Not applicable

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#14 Abstract Title: **Getting to the Core of the Matter: Does Trunk and Hip Strength Really Matter?**

Author(s): C. Oswald, Biology, U of Kentucky
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Abstract: The addition of a trunk and hip (core) strengthening program has become a popular component for Cross Country teams in order to help prevent injury. Despite this popularity, little evidence exists that such programs can reduce injuries or improve strength. Purpose: As a first step to assess core programs we sought to define if a core training program in Division I Cross Country athletes improves trunk and hip strength. Methods: eight Division I Cross Country athletes, with a mean age of 18.5 ± 1.1 years completed the protocol. Before starting the core exercise program, peak isometric hip abduction, external rotation, extension strength, v-up ability, and trunk control were evaluated. After a thirteen week core strength and stability program, these tests were re-measured. Results: There was a significant improvement in plank time (pre: 398±107.8, post: 615 ± 154.5 seconds, p= 0.000),) trunk stability error (pre: 17.75±8.6 , post:7.625 ± 6.07 errors, p-value= 0.003), and a trend towards hip abduction (pre: 12.60±3.0, post:15.82±3.15 0 N*m/kg, p-value= 0.06. There was no significant difference for v-ups (pre: 16.1±1.6, post: 18.75±3.4, p-value= 0.1) and hip external rotation (pre: 7.26±4.00 , post: 6.58± 1.5 0 N*m/kg, p-value= 0.6) Conclusions: The results of this study suggest a core program helps improve some measures of core strength. While the errors significantly decreased on the trunk stability test, the error rate is still high as compared to normative data . Incorporating exercises that target these areas which did not improve may help to maximize results of the core program.

Supported by: The project describe was supported by the University of Kentucky BioMotion Laboratory.

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Thursday, March 27, 2014 **Lexington Convention Center**

#15 Abstract Title: **The effects of sex and age on lower extremity joint coupling and loading during running.**

Author(s): P. W. Kline, Dept of Rehabilitation Sciences, U of Kentucky
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Abstract: Purpose: The purpose of this study is to explore kinetic and kinematic changes during running that occur between the sexes, between age groups, and the interaction between age and sex. Methods: Forty-one subjects were placed in 4 groups: young males (13 subjects), young females (6 subjects), old males (16 subjects), old females (6 subjects). Young runners were between 20-34 years old while old runners were between 60-74 years old. 10 running trials were collected and analyzed for each subject. Kinematic data were collected and reconstructed using a 9-camera motion analysis system and Qualisys software. Visual 3-D software was used to determine kinetic and kinematic variables for each subject. Analysis was performed using a 2-factor ANOVA (Sex X Age) to determine differences between groups for stance phase of running gait. Results: Significant differences were seen between age groups in initial vertical ground reaction force (iGRF) ($p < 0.01$) and loading rate (LR) ($p < 0.01$) with older subjects demonstrating higher iGRF and higher LR than younger subjects. No significant differences were seen between sexes and no interactions were found. Conclusions: Older runners experience greater iGRF and LR. These variables are related to bone loading and stress fractures and suggest that older runners may be at a greater risk for bony injury as compared to younger runners. Key Words: LOADING RATE, GROUND REACTION FORCE, MOMENT, INJURY

Supported by: No funding sources to report.

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Thursday, March 27, 2014 **Lexington Convention Center**

#16 Abstract Title:	**To Return or Not Return? A Qualitative Investigation of Factors Influencing Return to Sport Following ACL Reconstruction.**

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Abstract: Background: Return-to-sport criteria following anterior cruciate ligament(ACL) injury is often based on “satisfactory” functional and patient-reported outcomes. However, an individual’s decision to return to sport is likely multifactorial; psychological and physical readiness to return-to-sport may not be synonymous. Purpose: To determine the various psychosocial factors that influence decision to return-to-sport post ACL reconstruction(ACLR). Design: Qualitative study. Methods: A total of 12 participants (6 male, 6 female; ages 16-44) a minimum of 1-year post-surgery who had previously participated in sports were purposefully chosen from a larger cohort. Data was collected through semi-structured interviews. Qualitative analysis using a descriptive phenomenological process called horizonalization was used to derive themes that best represented the data. Results: Interviews revealed 6 predominant themes that describe and represent participant experiences following ACL reconstruction: hesitation and lack of confidence leads to self-limiting tendencies, athletic participation reinforces intrinsic characteristics, expectations about the recovery process influences the decision to return-to-sport, coming to terms with ACL injury causes re-evaluation of priorities, heightened knee awareness leads to anxiety and fear when considering return-to-sport, strong support systems are important in building a patients confidence. Conclusions: Following ACLR, the decision to return was largely influenced by psychosocial factors. Some factors, including hesitancy, lack of confidence, or fear of re-injury, are directly-related to knee function and have the potential to be addressed within the rehabilitation setting. Other factors, such as changes in priorities or expectations, may be independent of physical function, but remain relevant to the patient-clinician relationship and should be considered during post-operative rehabilitation.

Supported by: NATA Research and Educational Foundation District 2 Research Grant Endowment: Master's Research 'Understanding Return-to-Sport Factors Following Anterior Cruciate Ligament Reconstruction: A Mixed-Methods Study.'

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Thursday, March 27, 2014 **Lexington Convention Center**

#17 Abstract Title: **Longitudinal Myoelectrical and Architectural Adaptations in Distal Hindlimbs of Rats Following Experimentally-induced Proximal Muscle Weakness: Preliminary Findings**

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Abstract: Background: Weakness of the hip abductors and knee extensors is traditionally linked to the onset and progression of knee osteoarthritis. Proximal muscle weakness(PMW) has been reported to increase joint contact forces at the knee by altering lower extremity(LE) kinematics. However, the neuromuscular adaptations behind these altered kinematics remain unknown. The purpose of this study is to investigate the longitudinal effects of botulinum toxin-A(BTX-A)-induced PMW on muscle activity and architectural adaptations in the LE of rats. Hypothesis: Distal LE muscle activation patterns will shift and a transition in muscle fiber-type will occur within the proximal muscles. Subjects: Two 16-week old male Long-Evans rats. Procedures: BTX-A was injected into the left gluteus medius(GM) and vastus lateralis(VL) of both rats and ipsilateral measurements were performed 4 weeks post-injection. Prior to injection, indwelling electromyography(EMG) electrodes were implanted into the vastus lateralis, semimembranosus, tibialis anterior, and gastrocnemius to measure EMG amplitudes and onset intervals during treadmill walking. EMG data were collected simultaneously with video to sync paw-strike and toe-off kinematics. At 4 weeks, rats were euthanized and both GM were harvested and flash frozen to compare fiber-type composition and cross-sectional area(CSA) bilaterally. Results: EMG amplitude during stance phase and onset duration was increased in tibialis anterior but decreased in all other muscles at 4 weeks. The injected GM demonstrated a lower percentage of type-I fibers and decreased CSA compared to its non-injected, control GM. Conclusion: Adaptations in LE muscle activity and fiber-type due to PMW may explain altered kinematics and the etiology of knee osteoarthritis.

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UK College of Health Sciences Research Day
ORAL and POSTER ABSTRACTS

Thursday, March 27, 2014 **Lexington Convention Center**

#18 Abstract Title: **Experiences of Individuals in Upper Extremity Rehabilitation with Incongruence between their QuickDASH and GROC Scores: A Phenomenological Study**

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Abstract: Study design: Qualitative phenomenological Background: Patient's perception of treatment success in acute hand therapy has been found to be multifactorial. Two subjective forms often used in hand therapy to capture these factors are the Quick Disabilities of the Arm Shoulder and Hand (QuickDASH) and the Global Rate of Change scale (GROC). However, it is not uncommon for there to be directionality incongruence between the two forms, which may indicate patient dissatisfaction with care or a lack of progress. Purpose: To describe the experiences and expectations of rehabilitation of patients who demonstrated incongruence between their QuickDASH and GROC forms, in addition to their decisions to adhere and comply with their treatment plan. Method: Participants were patients in an outpatient hand therapy clinic who demonstrated incongruence between their QuickDASH and GROC forms beyond measurement error. Semi-structured interviews were recorded and transcribed, and analyzed using Colaizzi's phenomenological method until attaining saturation. Results: From 10 participants, 151 significant statements were extracted yielding five themes: 1) Desire to return to normal, 2) Anticipation of a brief recovery, 3) Trust or mistrust of therapist impacts recovery, 4) Can't stop living because of injury or rehabilitation, 5) Feelings of ambivalence towards the recovery process. Conclusion: Interventions where patients viewed therapists as dedicated tended to improve patient adherence. Early therapist and patient agreement of what was minimally clinically important may improve patient adherence. Teamwork at three levels was essential, between: therapist and patient, therapist and staff, and therapist liaising with the healthcare system.

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#19 Abstract Title: **The relationship between trunk power, rotation and muscle endurance**

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Abstract: Dysfunction of the muscles that make up the core is thought to influence the mechanics of the lower extremities and result in injury. Core function is dependent on forces generated by hip, pelvis, and trunk musculature. As joint power is dependent on both muscle force and joint motion, it may provide valuable insights into potential injury mechanisms. However, trunk power and its relation to joint motion and muscular endurance remains understudied in literature. Therefore, the goal of this study was to investigate the association between trunk power, trunk motion during running, and core endurance. Fifteen subjects with no history of lower extremity injury participated. To assess core endurance, each subject held a side plank to fatigue and the duration was recorded. An instrumented gait analysis was then conducted. From this, the range of trunk rotation and maximum trunk power were extracted. Our primary finding was that greater trunk power was correlated with greater side plank time ($r=.528$, $p=.043$). These results indicate that a side plank performed to fatigue may be a useful clinical tool to predict a patient's trunk power and hence trunk function during running. Because of the large mass of the trunk and its proximal location, trunk power may have important implications for lower extremity function. However, the relation between trunk power and injury needs further investigation.

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UK College of Health Sciences Research Day
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Thursday, March 27, 2014 **Lexington Convention Center**

#20 Abstract Title: **Risk Factors of Anterior Cruciate Ligament Injury: A Meta-Analysis**

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Abstract: Context: Anterior cruciate ligament(ACL) injury risk factors have been investigated at length; however, it was hypothesized that few studies have prospectively assessed risk factors prior to an actual ACL injury. Objective: To systematically review the literature to determine which modifiable risk factors are directly linked to ACL injury. Procedures: Search words were “anterior cruciate ligament” and “risk factor”. Criteria for inclusion were: (1)prospective, (2)evaluated risk factors of ACL injury regarding body composition or neuromuscular/biomechanical function, and (3)provided means and standard deviations for injured and non-injured cases. Three primary categories of modifiable risk factors were identified: (1)body mass index(BMI), (2)biomechanical alterations(BIOMECHANICAL), and (3)knee muscle function(MUSCLE). The quality of evidence was assessed using the Centre for Evidence-Based Medicine(CEBM)–Levels of Evidence. Bias-corrected Hedges g was used to calculate the effect size(ES) for each variable within each category. A separate random-effects meta-analysis was performed on each category. Results: Inclusion criteria were met by 7 studies with 20 separate data points. Two studies were classified as Level 3, five were classified as level 2. The overall summary effect was moderate (ES=0.58[0.33,0.81]) demonstrating more risk factor-related deficits for individuals subsequently injured compared to those who were not. BMI demonstrated a strong effect (ES=0.87[0.54,1.21]). BIOMECHANICAL also yielded a strong effect (ES=0.70[0.18,1.22]). A weak effect was observed for MUSCLE (ES=0.31[0.06,0.56]). Conclusions: While ACL risk factors are heavily investigated, there are very few studies that provide that direct link. Even commonly accepted risk factors such as knee flexion and abduction have not been evaluated extensively.

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UK College of Health Sciences Research Day
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Thursday, March 27, 2014 **Lexington Convention Center**

#21 Abstract Title: **The Relationship between Hip Strength and the Y Balance Test**

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Abstract: Performance on the Y Balance Test is used in rehabilitation as a marker of improved lower extremity function. Hip strength may play an important role in maintaining stability. PURPOSE: The aim of this study was to assess the relationship between hip strength and the composite Y Balance Test score. METHODS: Fifty healthy subjects (22 female, 28 male, age of 26.06 ± 5.6 years) participated. Subjects completed the composite Y Balance Test. Isometric strength of the hip abductors, external rotators, and extensors was assessed using a hand-held dynamometer. Pearson product moment correlations were used to determine the association between variables and significant values. RESULTS: Mean values for hip abductor, external rotation, and extension strength were 19.9 ± 4.7, 7.4 ± 2.2, and 22.1 ± 8.0 Nm/kg, respectively. The mean value for the Y balance composite score was 98.2 ± 9. The results of the linear regression showed hip abductor strength to be the only significant predictor of Y Balance Test performance (r=0.40, p=0.004). CONCLUSION: A greater Y Balance Test score was significantly related to greater hip abductor strength. This may be one factor that allows the person to maintain balance and thus reach further; therefore, poor performance on the Y Balance Test could be due in part to hip abductor weakness. However, the relationship to hip abductor strength was moderate, which suggests that other factors such as knee and ankle control may play a larger role in performance.

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UK College of Health Sciences Research Day
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Thursday, March 27, 2014 **Lexington Convention Center**

#22 Abstract Title: **The Effect of Tennis Play on Glenohumeral Rotation**

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Abstract: Background: Glenohumeral internal rotation deficits increase the risk of shoulder injury. Research agrees that as external rotation increases internal rotation decreases, which may result in upper extremity pathology. Glenohumeral rotational measurements have been reported in the baseball population following activity; however, limited information has been reported amongst tennis athletes. Purpose: The purpose of this study was to objectively quantify short-term Glenohumeral rotational changes within a group of tennis athletes. Methods: Shoulder internal and external rotation was evaluated on eighty-one professional women's tennis players during four tournaments. Measurements were taking at three different time points: before match play (baseline), after match play (time point 2), and 24 hours later (time point 3). Glenohumeral joint total arc of motion was determined by combining shoulder internal and external rotation. Results: There was a decrease in glenohumeral internal rotation from baseline (42±11) to time point two (39±9) (p=0.005) and three (38±10) (p=<0.001). There was a decrease in total arc of motion from baseline (144±11) to time point two (141±13) (p=0.013). Neither internal rotation nor total arc of motion returned back to baseline 24 hours following baseline measurements. Conclusions: Both shoulder internal rotation and total arc of motion is reduced after a tennis match. Potential interventions such as post match stretching may help to increase rotation following tennis play. Clinical Relevance: These data provide implications for clinicians on the importance of stretching following tennis. It is recommended that therapist establish a method of flexibility training following overhead activity.

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Thursday, March 27, 2014 **Lexington Convention Center**

#23 Abstract Title:	**Angiopoietin 1 gene expression is increased in metabolic syndrome and decreased with aerobic exercise training**

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Abstract: Poor skeletal muscle capillarization is associated with obesity and results in decreased oxygen consumption, decreased glucose tolerance, and insulin resistance. Exercise training stimulates capillary growth and reverses many of these metabolic defects. In the presence of VEGF-A, a central determinant of angiogenesis is the ratio of the secreted glycoproteins Angiopoietin 2 (Ang2) and Angiopoietin 1 (Ang1), with greater Ang2:Ang1 ratios promoting angiogenesis. We sought to determine whether exercise training normalizes muscle capillaries in metabolic syndrome (MetS) patients, resulting in improved VO2 Max and insulin sensitivity (SI). 20 subjects (11 MetS, 9 healthy) had muscle biopsies (vastus lateralis) before and after 12 weeks of aerobic exercise training (cycle ergometer). Using immunohistochemistry and Nanostring gene expression analysis, we examined mechanisms of angiogenesis in healthy versus MetS subjects at baseline and following exercise training. Baseline BMI was inversely correlated to Si and VO2 Max. Capillary density was positively correlated to VO2, but was not related to BMI or SI. VEGF-A gene expression was not correlated with any physiological measures. Baseline Ang1 (which is anti-angiogenic) was increased in MetS versus healthy, positively correlated with BMI, and inversely correlated with capillary density and VO2 Max. Similarly, baseline Ang2 (an antagonist of Ang1) was inversely correlated to capillaries at baseline. Following exercise training, both capillary number and VO2 increased, with no changes in BMI or Si. Exercise training did not affect mean VEGF-A or Ang2 gene expression. However, Ang1 gene expression was decreased and the Ang2:Ang1 ratio was increased following exercise. Interestingly, individual changes in Ang2 were inversely correlated to baseline VO2 max, with the most “unfit” subjects displaying the largest increases in Ang2 gene expression. Based on these data, we conclude that VEGF-A expression is not impaired in MetS, nor is it changed following exercise. However, expression of Ang1 is increased in MetS, and is reduced following exercise, leading to an improved Ang2:Ang1 ratio, thereby promoting increased capillarization.

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UK College of Health Sciences Research Day
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Thursday, March 27, 2014 **Lexington Convention Center**

#24 Abstract Title:	**Strength and Endurance in Shoulder Musculature is Enhanced with 5 minute Exercise Programs.**

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Abstract: Context: The Advanced Throwers 10 protocol has been suggested to increase shoulder muscular strength; however, no empirical data exists to support this statement. Objective: We hypothesize that the Advanced Throwers 10 program will produce greater increases in shoulder muscular strength and endurance compared to a traditional training program. Design: Randomized clinical trial. Setting: Clinical Laboratory. Patients or Other Participants: Twenty Five healthy subjects volunteered to participate (age=26±9 years, MARCs Activity Level=10±4, Mass=75±14 kg). Investigators allocated participants into 2 groups using concealed envelopes. Interventions: Traditional 3x15 and Advanced Throwers 10 which requires the use of sustained holds for a similar number of repetitions were compared. Starting with 15% of participant's baseline average force, resistance was increased 25% per week. Main Outcome Measures: At pre and post testing each subject performed 2 repetitions of maximal isometric arm elevation 90° for 30 seconds bilaterally. The average force and angular impulse were measured with a load cell and was converted to torque. The average torque and average angular impulse generated from the two trials represented the pre and post strength and endurance values. Repeated measure ANOVAs with one between-factor (group) and one within-factor (time) was performed for each arm data. Results: The only significant finding was that average force and average angular impulse significantly increased from pre to post testing in both groups ($p<.001$). The overall increase was 15% for both measures. Conclusions: These findings reject our hypothesis and support that either the Traditional or the Advanced Throwers 10 program can be used to increase muscular strength and endurance.

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UK College of Health Sciences Research Day
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Thursday, March 27, 2014 **Lexington Convention Center**

#25 Abstract Title: **Assessing Responsiveness to RET by Individuals with Chronic Non-fluent Aphasia: A Clinical Perspective**

Author(s): R. S. Husak, Dept of Communication Disorders, U of Kentucky
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Abstract: Introduction: Response elaboration training (RET) is a “loose training” program designed to increase the amount of information contained in the spoken utterances of patients with aphasia. Numerous studies showed patients respond robustly to RET. One difficulty faced by clinicians seeking to use RET is participants in research studies have been treated for a duration that far exceeds standard clinical practice. The aim of this study is to examine RET from a “clinical perspective” by carrying out a selective meta-analysis that focused on a “treatment window” commensurate with standard clinical practice. Methods: Thirteen participants with nonfluent aphasia from six RET studies were included in the study. Participants were separated into two groups based on their aphasia severity level (moderate and severe). Effect sizes from studies employing multiple-baseline single-subject designs were estimated using a variation of a d statistic. The magnitude of change from (1) pretreatment to posttreatment and (2) after 10 treatment sessions was calculated. Results: Positive treatment effects were seen for virtually all participants on trained and untrained items. Larger effect sizes were seen in participants with severe aphasia. Overall, the effect sizes estimated after 10 treatments were larger than the improvements seen from the tenth treatment to the final treatment. Discussion: Results from this study provide support for use of RET with patients with a limited number of treatments. Moreover, the study introduces a novel approach for evaluating treatment effects within a timeframe that is conducive to the constraints of today’s healthcare climate.

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UK College of Health Sciences Research Day
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Thursday, March 27, 2014 **Lexington Convention Center**

#26 Abstract Title:	**Factors that Influence Patient Expectations for Recovery Following Cartilage Repair of the Knee**
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Abstract: Context: Patient expectations have been shown to be a major predictor of outcomes. Expectations may be influenced by a variety of factors, including patient characteristics, pre-operative function, or disease characteristics. However, it is currently unknown what factors and to what degree they may influence patient expectations prior to knee surgery. Design: Cross-sectional. Participants: Seventeen patients undergoing cartilage repair of the knee, including autologous chondrocyte implantation, osteochondral allograft transplantation, or meniscal transplant were included. Procedures: During their pre-operative visit, patients were asked to complete a survey regarding their expectations. Expectations were assessed using the Hospital for Special Surgery(HSS) Knee Surgery Expectations Survey. Additionally, self-report measures and demographic information were obtained at this visit, including, surgical procedure, sex, age, activity level, and time from onset to surgery. The KOOS was used to assess pre-operative functional ability. The KOOS produces separate scores within five sub-domains(pain, symptoms, ADL, sport-and-recreation, and QOL), with lower scores representing worse function in each area. Pearson correlation coefficients were used to determine relationships between expectations and patient characteristics or KOOS scores. Results: There was a significant positive relationship between patient expectations and the KOOS sub-domains of ADL's(r=0.48, p=0.05) and QOL(r=0.52, p=0.03). Conclusions: Patient expectations appear to be a separate construct that should be captured independently. Patient self-reported symptoms do not appear to influence patient expectations. Patients with higher scores on the KOOS sub-domains of QOL and ADL had higher expectations for recovery suggesting that QOL may influence patient expectations and therefore must be assessed independently from self-report measures evaluating pain, symptoms, and physical function.

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UK College of Health Sciences Research Day
ORAL and POSTER ABSTRACTS

Thursday, March 27, 2014 **Lexington Convention Center**

#27 **Abstract Title:**	**Impact of obesity on bone marrow stem cell progenitor cell (BMSPC) mobilization in the setting of acute myocardial infarction (AMI)**

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Abstract: Obesity is approaching epidemic levels in the western world and increases the risk for acute myocardial infarction (AMI), specifically in the state of Kentucky and surrounding states. Paradoxically, while obesity is a risk factor for AMI, it appears to confer protection from complications of ischemic heart disease (IHD). The molecular mechanisms underlying the protective effects of obesity are not known. Cardiomyocyte renewal following ischemic injury is a dynamic process, facilitated by bone marrow (BM)-derived stem/progenitor cells (SPCs). Our previous data indicates that that bioactive lipid sphingosine-1 phosphate (S1P) is a potent chemoattractant for BMSPCs and thereby contributes to BMSPC mobilization in the setting of AMI. Obesity and the associated metabolic syndrome cause alterations in bioactive lipid metabolism. Thus, alterations in S1P levels, BMSPC mobilization, or both may contribute to the protective effect of obesity on development and complications of IHD. Our human studies demonstrated temporal correlation between elevated plasma bioactive lipids and stem cell mobilization after AMI. Interestingly, obese individuals had higher plasma levels of bioactive lipids and BMI correlated with the number of circulating BMSPCs after AMI. Our data strongly suggests that the role of bioactive lipids in stem cell mobilization during the events of AMI is enhanced with moderate obesity and could therefore contribute to cardiac regeneration and the protection noted in this state. Plasma isolated from AMI patients was capable of chemoattracting enriched BMSPCs in vitro in an S1P-dependent manner. And finally, we were able to replicate these data in an in vivo murine model. These data suggest presence of obesity-associated pathways responsible for the mobilization and homing of BMSPCs following AMI and ultimately their regenerative capacity.

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UK College of Health Sciences Research Day
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Thursday, March 27, 2014 **Lexington Convention Center**

#28 Abstract Title: **Variation in Minimal Clinically Important Difference Values Among Knee Surgical Patients**

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Abstract: Background: Determining patient improvement is a fundamental necessity in clinical practice. Minimal clinically important difference (MCID) criteria determine the smallest change in outcome scores that can be deemed meaningful to the patient. A single MCID value is typically determined for a patient-reported-outcome measure (PROM) without regard for baseline function. The Lysholm Knee Scale is a (PROM) that is commonly used to document treatment outcomes in a variety of knee patients. Hypothesis: It was hypothesized that MCID values would vary based on patient severity. Procedures: This study utilized data from an existing knee surgical patient outcomes registry. Data from 77 patients one year post-surgery were examined. A Global Rating of Change scale (GROC) at one year post-surgery was used as a measure of overall treatment success. Based on pre-operative Lysholm scores, patients were divided into tertiles. Analyses using a receiver-operator characteristic (ROC) were performed for all patients combined, and for patients placed in tertiles. The pre-post Lysholm change scores with the highest combined sensitivity and specificity were identified as the MCID values. Results: The Area-Under-the-Curve was significantly greater than 0.5 ($p<.05$) for all ROCs. The MCID for all patients combined was 20 (sensitivity=0.81, specificity=0.71). MCID for the upper tertile was 20 (sensitivity=0.60, specificity=0.90). MCID for the middle tertile was 35 (sensitivity=0.81, specificity =0.78). MCID for the lower tertile was 26 (sensitivity=0.91, specificity=0.87). Conclusions: MCID values varied across the spectrum of patient severity. The largest change needed for a patient to improve was 35 for patients in the middle tertile. Using a generalized MCID value for all patients without regard to baseline functionality may result in the misclassification of patients as treatment successes or failures.

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UK College of Health Sciences Research Day
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Thursday, March 27, 2014 **Lexington Convention Center**

#29 Abstract Title: **Can core strength influence the knee valgus angle during a step down test?**

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Abstract: The frontal plane projection angle (FPPA) is a valuable clinical tool for measuring knee valgus in females who may be at risk for injury. The FPPA is unable to determine the specific deficits leading to greater knee valgus. Weakness of the core may result in a lateral trunk lean and subsequently greater knee valgus collapse to maintain stability. Whether trunk strength influences the FPPA has yet to be formally evaluated. Purpose: To assess whether plank and side plank performance is related to knee valgus as measured on the FPPA. Methods: Thirty females (age of 24.8±4.4 years) completed a single-leg step down. The FPPA was calculated and a timed plank and right-side plank were performed. Pearson product correlations were used to analyze the relationship between FPPA and plank and side plank times. Results: Mean values for plank and right-side plank times were 112.8±69.8 and 61.9±33.6s, respectively. The mean frontal plane projection angle was 0.11±10.8º. There was a significant correlation between FPPA and side plank time (r=.37, p=.042) but not plank time (r=.33, p=.075). Conclusion: Greater side plank times were significantly related to a smaller FPPA, suggesting that core strength is one factor related to the performance on the FPPA. The correlation between side plank and FPPA was stronger than that between FPPA and plank times as the side plank utilizes just the right side muscles and the plank uses both sides equally. Clinicians should consider emphasizing core exercises in injury prevention to reduce knee valgus angle and potential risk of injury.

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UK College of Health Sciences Research Day
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Thursday, March 27, 2014 **Lexington Convention Center**

#30 Abstract Title:	**Well-being and Coping Strategies of Military Veterans Transitioning to Academia**

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Abstract: Background: Military student veterans are at-risk for disruptions of daily occupations due to combat exposure. Following discharge from active duty service, numerous veterans begin their transition from the military to academic institutions, utilizing the post the 9/11 GI Bill entitlement. Many students with veteran status exist at the University of Kentucky experiencing transition challenges. Awareness and support are required to assist military veterans advancing their aspirations in higher education. Purpose: To survey attitudes on community reintegration and psychosocial wellness concerns for student veterans at the University of Kentucky. Investigation of their attitudes on the transition from military service to academia will identify intrinsic and extrinsic factors perceived as barriers and/or supports and further intervention. Subjects: Recruitment of approximately 100 respondents via the UK Veterans Resource Center Listserv. Inclusion criteria: males and females between the ages of 20-45, no more than 3 years removed from combat service and ability to speak, write and understand the English language. Methods and Materials: Following recruitment for study enrollment, eligible participants will receive an electronic mail notification with URL to an anonymous online survey. A 40-item Qualtrics™ questionnaire composed of 27-Likert scale questions and 13 demographic/open-ended questions will collect the attitudes and perceived behaviors of respondents. Results will be tabulated into frequency data. Expert review will establish content validity. Internal consistency will be calculated for reliability. Discussion: The benefit of this survey study will be its focus on coping with life transitions for student veterans thus; defining concerns for practical consideration and prompt intervention.

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33rd Annual Symposium in Reproductive Science and Women's Health
POSTER ABSTRACTS

Thursday, March 27, 2014 **Lexington Convention Center**

#31 Abstract Title: **An analysis of leukocyte populations at the time of ovulation in the human: A potential role for CCL20**

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Abstract: The LH surge sets in motion a chain of events that culminates in ovulation. One of these is the presence of an inflammatory reaction characterized by leukocyte influx. Chemokines are known in other systems to attract leukocytes. We previously explored the expression of Chemokine ligand 20 (CCL20) in the dominant follicle from women throughout the periovulatory period. CCL20 mRNA and protein are massively induced in the Granulosa-cells (GC) and Theca-cells (TC) during the early and late ovulatory stage. Our hypothesis is that the LH surge stimulates CCL20, resulting in leukocyte recruitment that impacts ovulation. To determine the regulation of CCL20, an in vitro model using granulosa-lutein-cells (GLC) from IVF patients was utilized. This culture model was validated and signaling pathways involved in CCL20 regulation were explored. Preliminary studies revealed that a MEK1/2 inhibitor decreases CCL20 expression. Since patients expressed varying CCL20 levels, ongoing studies aim to Correlate CCL20 with patient diagnosis. We next determined the percentage of leukocytes containing the CCL20 receptor CCR6 using flow-cytometry in GLCs. GLCs were processed and stained for CD45 and CCR6 and analyzed. CD45+/CCR6- cells accounted for ~40% and ~5% were CD45+/ CCR6+. The remaining 55% of cells are CD45-. Flow-cytometry was used to determine leukocyte subtypes: NK-cells (CD56) accounted for ~2%, T-cells (CD3) and neutrophils (CD66b) for ~38% each, monocytes (CD14) for ~27% and B-cells (CD19) for ~13%. Leukocytes that express CCR6 were analyzed to delineate which types of leukocytes are recruited by CCL20. CCR6+/CD45+ cells were primarily NK-cells (41%), the remaining were neutrophils (10%), monocytes (9%), B-cells (12%), and T-cells (11%). In summary, CCL20 expression is dramatically increased in human GC and TC prior to ovulation and is possibly recruiting primarily NK-cells to aid in the breakdown of the follicular wall.

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Thursday, March 27, 2014 **Lexington Convention Center**

#32 **Abstract Title:**	**Predictors of receiving guideline-recommended antiretroviral treatment: role of physician specialty, sex, age and education**

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Abstract: Background: Randomized clinical trials of combination antiretroviral therapy (cART) inform the use of specific antiretrovirals (ARV) and their combination for optimizing therapeutic efficacy. Therefore, it is critical that patients have access to and receive the most appropriate first-line treatment. We aimed to examine factors that impact receiving initial guideline-recommended cART within a cohort of commercially insured patients in the United States (US). Methods: We established an employed, commercially insured, population-based cohort of HIV patients receiving a new ARV prescription throughout the US between January 2007 and December 2009. The primary outcome was defined as a claim for a prescription containing recommended cART consisting of two nucleoside reverse transcriptase inhibitors and either a non-nucleoside reverse transcriptase inhibitor, protease inhibitor, or an integrase strand transfer inhibitor. Logistic regression models evaluated predictors of receiving recommended cART. Results: There were 2,316 HIV patients that received a new ARV prescription. The population was 57% white, 79% male with a median age of 42 years (Interquartile Range:35-49). Overall, 66% of the population received recommended cART. Receiving care from an infectious disease specialist was the strongest predictor of receiving recommended cART (Odds Ratio (OR):1.47, 95% Confidence Interval (CI):1.38, 1.56). Men were also more likely to receive recommended cART (OR:1.34, 95% CI:1.22, 1.48). Age and education also influenced receiving recommended cART ($p<0.02$) Conclusions: We found that many HIV-infected patients that are in clinical care are not prescribed recommended cART. Provider specialty and sex influence receipt of optimum treatment. Increased communication and training of healthcare providers is necessary to insure patients receive the most durable first-line regimen.

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Thursday, March 27, 2014 **Lexington Convention Center**

#33 Abstract Title:	**Dehydroepiandrosterone sulphate (DHEA-S) concentrations in mares with experimentally induced ascending placentitis**
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Abstract: Dehydroepiandrosterone is utilized by the equine placenta as a precursor for oestrogen. DHEA is conjugated and appears in the maternal circulation as DHEA-S. We hypothesized that DHEA-S is elevated in mares with placentitis. The objective of this study was to compare plasma concentrations of DHEA-S in mares with experimentally induced placentitis and control mares. Pregnant mares (260-280d of gestation) were assigned to a control group (n=17) and to a group with experimentally induced placentitis (n=17). As part of another study, within each group, 7 mares had ultrasound-guided foetal fluid sampling (FFS) at 0, 5 and 12 days post inoculation (DPI) or until abortion. Placentitis was induced via intracervical inoculation of Streptococcus equi spp zooepidemicus (5x106 cfu). Blood was collected at inoculation/initial FFS (day=0) and daily until abortion or for 12 DPI. DHEA-S was determined by immunoassays (CV's; intra-assay 6.5% and inter-assay 10.3%). Data were log-transformed and analysed using a mixed model for changes up to 6 DPI. Mares with experimentally induced placentitis aborted within 5-25 DPI with (mean 9.4 ± 1.3). There were no group differences or effects of FFS. There was significant effect of DPI ($p<0.05$), but not time by group interaction. In conclusion, DHEA-S did not change following experimental induction of placentitis.

Supported by: The funds for this project were provided by the Kentucky Thoroughbred Association and University of Kentucky (Albert Clay Endowment and Geoffrey Hughes Fellowship).

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#34 Abstract Title: **Effects of Ischemia in Astrocytes**

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Abstract: Astrocytes are one of the crucial cells in the central nervous system. They are the most abundant type of cells in the brain and they provide neurons with structural and metabolic support, modulate synaptic transmission, and possibly play a role in vasomodulation. Astrocytes are thus, an important target cell population to study in response to brain injury, such as ischemia caused by stroke. Previous studies in our laboratory have shown that in mixed neuron and glial cells the female hormone estrogen is neuroprotective against ischemia-induced cell death. In the present study, we will examine the direct effects of ischemia on astrocytes and determine the effect of estrogen. A mouse astrocyte cell line will be culture under normal conditions and then exposed to a chemically induced-ischemia using 2-deoxyglucose and potassium cyanide for thirty minutes. Uninjured cultures will serve as a control. These two groups will be compared to determine if there are any differences in cell death, and whether or not estrogen has a protective effect. Additionally we will determine if the effects are mediated by estrogen receptors. The proposed experiments include immunocytochemical staining, western blots, and quantitative RT-PCR for potential mediators of estrogen's actions. By examining the ability of estrogen to regulate the astrocytes response to ischemia, it may help us identify therapeutic targets as well as elucidating mechanisms that may be involved in the astrocyte/neuron interaction in female brains.

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Thursday, March 27, 2014 **Lexington Convention Center**

#35 Abstract Title: **Intraperitoneal administration of lipopolysaccharide induces differential expression of mRNA encoding inflammatory mediators in the oviducts of mice.**

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Abstract: Infection with gram-negative bacteria is a major cause of aberrant inflammation in the oviduct; consequences can include tubal infertility and/or ectopic pregnancy. Understanding inflammatory responses due to bacterial infection is necessary for the development of novel treatment options that specifically target inflammatory responses. Our objective was to test the hypothesis that intraperitoneal (IP) administration of E. Coli -derived lipopolysaccharide (LPS) induces the expression of inflammatory mRNAs in the mouse oviduct. On the day of estrus, 6-8 week old CD1 mice (n=4/treatment) were treated IP with 0 (control), 2 ug (low dose) or 10 ug (high dose) of LPS from E. Coli serotype 055:B5 in 100 ul PBS. Mice were killed 24 h later and the oviducts collected for determination of inflammatory gene expression by a targeted nanostring approach using the nCounter GX Mouse Inflammation Kit (Nanostring Technologies, Seattle, Wa). Real-time PCR was used to validate selected mRNAs. The effect of LPS was evaluated by one-way ANOVA and treatment means of differentially expressed mRNA ($P<0.05$) were separated using a post-hoc LSD test. 56/179 targeted genes were affected by treated ($P<0.05$). Pairwise comparison revealed 8 mRNA differentially expressed in control vs low dose, 50 mRNAs in control vs high dose and 43 mRNAs in low vs high dose ($P<0.05$). These results indicate that systemic treatment with LPS induces inflammation in the oviducts of mice; this study providing evidence of a new model to investigate the regulation of oviductal inflammation in the future.

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Thursday, March 27, 2014 **Lexington Convention Center**

#36 Abstract Title: **Endocrine and molecular changes in the equine follicle associated with ageing in mares**

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Abstract: Reproductive ageing in mares is an important process that is associated with reduced fertility. The objective of this study was to examine age-related differences in follicular dynamics, hormone concentrations, and gene expression in granulosa cells of growing and dominant follicles. Young (n=10), middle-aged (n=16), and old (n=17) mares were examined using transrectal ultrasonography over 2 to 3 estrous cycles. Progesterone and FSH concentrations were measured using an ELISA and RIA, respectively. The expression of the FSH receptor (FSHR), LH receptor (LHR), and estrogen receptor β (ERβ) in granulosa cells of growing and dominant follicles was examined by qRT-PCR. The influence of age on reproductive parameters and mRNA transcripts was examined using a mixed model. Old mares had a significantly longer interovulatory interval and follicular phase, lower number of antral follicles, and the day of deviation occurred later than in young mares. The diameter of the preovulatory follicle had a tendency to be smaller in old mares. Concentrations of FSH were significantly higher during the follicular phase in old mares, while progesterone concentrations had a tendency to be higher in old and middle-aged mares. The expression of FSHR, LHR, and ERβ within growing or dominant follicles was not significantly influenced by mare age. In contrast, FSHR and ERβ were significantly upregulated in growing follicles compared to dominant follicles whereas the LHR was upregulated in dominant follicles. In conclusion, ageing is associated with reproductive and endocrine changes, whereas molecular changes within the equine follicle are related to the stage of follicular development.

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Thursday, March 27, 2014 **Lexington Convention Center**

#37 Abstract Title: Effects of a third-generation GnRH antagonist on reproductive parameters in the stallion

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Abstract: Numerous investigators have attempted to suppress the hypothalamic-pituitary-gonadal axis in the stallion with varying results. We hypothesized that the GnRH antagonist Acyline would lead to such down regulation. The objective of the current study was to evaluate the effect of Acyline on testis volume, peripheral testosterone concentration, seminal parameters and reproductive behavior in stallions. Stallions (n=4) were treated (330 µg/kg Acyline IM every 5 days) for 57 days, and vehicle-treated stallions (n=4) served as controls. Semen was collected and evaluated daily on alternate weeks; time to erection and ejaculation were recorded; and testis volume was measured weekly by ultrasonography. Serum testosterone concentrations were measured by EIA. Data were analyzed using a random-effects mixed model. There was a significant time by treatment interaction ($P<0.05$) on serum testosterone concentration (Day 3), testis volume (Week 5), total sperm number (Week 1), and total sperm motility (Week 2; with the first significant decline in each parameter noted in treated stallions in parentheses). There was no effect of Acyline treatment on time to erection or ejaculation. Following cessation of Acyline treatment, serum testosterone concentrations, testis volume, total sperm number and sperm motility appeared to recover their pretreatment values. Overall, this study demonstrates that administration of Acyline to the stallion results in a rapid suppression of the hypothalamic-pituitary-gonadal axis with recovery following cessation of treatment. Interestingly, measured behavioral parameters were not different in treated stallions compared to controls.

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Thursday, March 27, 2014 **Lexington Convention Center**

#38 Abstract Title: **Effects of low progesterone concentrations on endometrial transcription at Days 8 and 12 of the estrous cycle in mares**

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Abstract: Changes in the endometrial transcriptome under the influence of progesterone (P4) have been reported in horses. However, there is little information available concerning relative changes in endometrial gene expression associated with low P4. The objective of this experiment was to evaluate changes in gene expression in mares with normal or low P4 concentrations. Mares (n=12) were bled and scanned via rectal ultrasound on a daily basis during two cycles; control and treated cycle (125 □g of cloprostenol IM on Days 0 through 3). In one group (n=6) uterine biopsies were collected on day 8 (D8) post-ovulation and on day 12 (D12) in the second group (n=6). P4 concentrations were measured via ELISA and expressed as area under the curve (AUC). For gene expression analysis, ten relevant target transcripts were analyzed by qRT-PCR (□□Ct method using B2M as a reference). Changes between control and treated cycles were compared with a paired t-test. P4 concentrations between Days 0 and 8 were lower in mares that received cloprostenol (D8: 33.5±1.8 & D12: 19.6±1.0 ng/day/mL-1±SEM) compared to control mares (D8: 98.8±7.2 & D12: 94.7±4.3) ($p<0.0001$). Quantitative RT-PCR demonstrated a down-regulation of PTGES ($p=0.015$) and of P19 ($p=0.08$) in mares with low P4 at Day 8. At Day 12, there was an up regulation of ESR1, ($p=0.001$), PGR ($p=0.003$), SCGB1A1 ($p=0.009$) in the mares with low P4;. This study indicates that low concentrations of P4 have an effect on the endometrial transcriptome.

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Thursday, March 27, 2014 **Lexington Convention Center**

#39 Abstract Title: **Effects of seminal plasma proteins CRISP-3 and lactoferrin on the immune response of the equine uterus.**

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Abstract: The equine uterus undergoes a transient innate immune response to breeding in preparation for embryo implantation, also known as mating-induced endometritis. The deposition of spermatozoa triggers the expression of pro-inflammatory cytokines which recruit polymorphonuclear neutrophils to migrate from the lumen. Select seminal plasma proteins, specifically Crisp-3 and lactoferrin, have been shown to affect the activity of the PMNs, either by suppressing (Crisp-3) or promoting (lactoferrin) the phagocytosis of spermatozoa based on their viability in vitro. Our objective of this study was to determine if these select proteins effect the mRNA expression of cytokines after insemination. Six mares resistant to post-mating induced endometritis were bred at estrous during four consecutive estrous cycles in randomized order of treatment with 1mg/mL Crisp-3, 150 ug/mL lactoferrin, 10 mL seminal plasma, or 10 mL lactated ringer's to a total volume of 10mL fluid combined with 1x109 live spermatozoa pooled from two stallions. Six hours after treatment, an endometrial biopsy was taken for qPCR. No differences were found for the mRNA expression of IL-1β, IL-6, IL-8, IL-10, TNFα, and IFNG, while lactoferrin was seen to significantly suppress the mRNA expression of IL-1RN when compared to lactated ringer's. In conclusion, the seminal plasma proteins Crisp-3 and lactoferrin have minimal effect on the expression of these cytokines at 6 hours post breeding.

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Thursday, March 27, 2014 **Lexington Convention Center**

#40 **Abstract Title:**	**Beclin-1 , A New Regulator of Progesterone Synthesis During Pregnency**

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Abstract: Progesterone is the essential hormone for the maintenance of pregnancy in all mammals studied. Recent studies have implicated a role for autophagy in lipid metabolism of macrophages and hepatocytes through the targeted degradation of lipid droplets. Autophagy is an evolutionarily conserved mechanism for sequestering and delivering cytosolic material to the lysosome for degradation and recycling of the components within a cell. Thus, we hypothesized that autophagy is necessary for lipid metabolism in steroidogeneic tissue, which use cholesterol as a substrate. We utilized a conditional knockout approach to generate mice with conditional alleles for two autophagy genes, Beclin-1 and Atg7, that will be deleted in the granulosa cells of growing ovarian follicles which will terminally differentiate to form the corpus luteum after ovulation. The corpus luteum is an endocrine gland that is responsible for synthesizing the necessary progesterone for the entire murine pregnancy. Beclin-1 cKOs fail to maintain pregnancy and by modulating the number of Beclin-1 alleles, either abortion or preterm birth can be achieved. Beclin-1 cKOs have reduced circulating progesterone from mid-pregnancy and onward and the shortened gestation can be rescued through exogenous progesterone administration. Furthermore, Beclin-1 cKO luteal cells do not accumulate lipids and are found full of undigested endosomes. On the other hand, Atg7 cKO mice do not exhibit pregnancy problems and produce nearly twice as much progesterone throughout pregnancy. We performed rt-PCR on genes associated with lipid metabolism and progesterone synthesis as an attempt to understand how Beclin-1 might be regulating the phenotype. There is a slight decline in prolactin receptor at mid-pregnancy in Beclin-1 cKO corpus luteum that might account for the reduced synthesis beyond this point. Interestingly, the Atg7 cKO corpus luteum have elevated expression for all progesterone synthesis genes, corroborating the progesterone levels and suggesting that Atg7 is a negative regulator of these gene. Overall, this data shows for the first time a differential result from two autophagy genes, suggesting that they have different functions. Progesterone synthesis is a rising issue during pregnancy in humans and this data indicates a new avenue for treatment.

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Thursday, March 27, 2014 **Lexington Convention Center**

#41 Abstract Title: **TSC1 is a Novel Interacting Partner of Beclin1, and Essential for Terminal Differentiation of the Murine Mammary Gland**

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Abstract: Tsc1 is one of the causal genes for tuberous sclerosis complex (TSC) a diverse multi-symptomatic autosomal dominant disease characterized by hamartoma formation that affects 1 in 6,000 births to varying degrees. It has been well characterized that TSC1 (also known as hamartin), in a heterodimer with its primary binding partner TSC2, inhibit MTOR signaling via inhibition of RHEB. The Tsc1 traditional knockout is embryonic lethal and investigation using the floxed model has revealed many functions for TSC1, however the role of TSC1 has not yet been investigated in the mammary gland. The mammary gland is stimulated by pregnancy hormones to rapidly proliferate and prepare to lactate then remodels after lactation primarily via programmed cell death to resemble a resting-like state. Our lab has previously shown that autophagy is critically important for development of the mammary gland, so we hypothesize that since TSC1/2 is an inducer of autophagy it follows that it will also have importance for proper mammary gland development. Furthermore, we posit that Tsc1 and Becn1 are interacting partners. We generated a mammary gland specific Tsc1 conditional knockout (cKO) and found that these mice phenocopy the Becn1cKO mice, including a gross lactation failure. Tsc1cKO mammary glands have altered glandular morphology, retained lipid droplets in secretory epithelia, and an overall increase in MTOR signaling, as measured by increased total MTOR and p4EBP1 protein levels. We show that TSC1 and BECN1 are interacting partners, and when autophagy is chemically inhibited these interactions are reduced. Taken together these results demonstrate a novel protein-protein interaction and an important link between regulation of MTOR pathway and regulation of autophagy in a developmental context.

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Thursday, March 27, 2014 **Lexington Convention Center**

#42 Abstract Title: Pubertal Hormone Associations with Psychopathology: Dynamic Cyclic and Moderated Effects

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Abstract: Introduction. Puberty is an extremely important activational and perhaps organizational developmental period characterized by dynamic changes in gonadal hormone levels and a rapid increase in the prevalence of many types of psychopathology (Sisk & Zehr, 2005). Many depressive and anxiety disorders, eating disorders, substance-related and addictive disorders, and personality disorders such as borderline personality disorder, exhibit peak rates of onset during or following puberty (APA, 2013), and many types of behavioral impulsivity, such as aggression and suicide attempts, become prominent during this time (Spear, 2009). Further, rapid changes and surges in many types of gonadal hormones have been associated with psychopathological symptoms with small to moderate effect sizes (Martel et al., 2009). Yet, these hormonal effects likely operate in part by instantiating individual differences in temperament and environmental sensitivity to context (Del Giudice, Ellis, & Shirtcliff, 2011). The current study examined this idea empirically across several samples using different designs and in relation to several different types of psychopathology. Methods. Study designs were two cross-sectional studies and two longitudinal studies. For the cross-sectional studies, participants were 312 adolescents (134 females; age M=13.31) over-recruited for clinically-significant attention problems and 60 female freshman undergraduate students (age M=18.03). For the longitudinal studies, participants were 50 female college students (age M=18.89) and 40 female college students (age M = 18.23). Symptoms associated with psychopathology were assessed using well-validated questionnaire or interviews, and hormones were measured using established and sensitive assays. Results. Key cross-sectional findings were that higher levels of circulating testosterone during adolescence were associated with decreased inattention in females (β=-.22, $p<.01$), but not in males (β=.02, $p>.05$). Further, higher levels of binge eating in females were apparent during the luteal phase of the menstrual cycle (β=.13, $p<.05$), a period that is characterized by higher levels of ovarian hormones. However, longitudinal results suggested that the dynamic effects of hormones were moderated by key trait individual differences. For example, high ovarian hormones during the luteal phase were associated with increased depressive symptoms, but only for those with high trait perspective taking (interaction γ=.05, $p<.01$). Further, within-person cyclical increases in estradiol (i.e., at ovulation) were associated with reduced borderline personality disorder symptoms, but only for those individuals characterized by high neuroticism (interaction γ=-.13, $p<.01$) or exposed to high levels of sexual abuse (interaction γ=-.15, $p<.01$; see figures). Discussion. Therefore, hormonal effects on behavior appear dynamic, exhibiting both longitudinal within-person change, as well as between-person variation based on constitutional traits and exposure to life stressors. Evolutionary theory suggests that such hormone-based effects instantiate environmental influences and shape dispositional functioning in such a way as to increase risk for psychopathology (Ellis et al., 2011; Martel, 2013). Understanding dynamic associations between hormones and psychopathology have utility for assessment and intervention that could be targeted to key developmental periods such as adolescence.

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Thursday, March 27, 2014 **Lexington Convention Center**

#43 Abstract Title: **A Longitudinal Assessment of Omentin in Pregnancy**

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Abstract: Objective: Omentin is an adipokine which modulates an anti-inflammatory pathway and is strongly expressed by the placenta. The function of omentin during pregnancy is unknown. The purpose of this study was to define the natural history of omentin longitudinally in human pregnancy and correlate observation with inflammatory cytokines. Study Design: This is a secondary analysis from a prospective study of pregnant women with repeated measures design. Women with a singleton gestation were recruited for specimen collection in three periods: 1) 5-13 weeks; 2) 14-26 weeks; and 3) 27-36 weeks gestation. At each collection point, serum concentrations of omentin-1 and markers of inflammation were determined by ELISA. Statistical analysis was performed by paired t-test and regression analysis. Results: Serum samples were available for 74 women in the first trimester, 64 in the first and second trimesters, and 61 in all three trimesters. Omentin averaged 17.3 ± 11 ng/ml in the first trimester, 14.0 ± 9 ng/ml in the second trimester, and 15.2 ± 9 ng/ml in the third trimester. In paired specimen comparison, omentin concentration was significantly higher in the first trimester than in the second ($p=<0.0001$) or third ($p=0.0005$) trimesters. Omentin was negatively correlated with BMI in the first ($p=0.017$) and third trimester ($p=0.0035$), and negatively correlated with CRP in the second trimester ($p=0.0369$). Omentin concentrations were not correlated with TNF alpha, IL-6, IL-8, or IL-10 at any time point. Conclusion: Omentin is significantly higher in the first trimester than in the remainder of pregnancy. Further study is needed to elucidate the significance of this finding and its potential correlation to the inflammatory state in pregnancy.

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33rd Annual Symposium in Reproductive Science and Women's Health
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Thursday, March 27, 2014 **Lexington Convention Center**

#44 Abstract Title: Bladder Antimuscarinics Use by Older Women Enrolled in the National Alzheimer's Coordinating Center Cohort

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Abstract: OBJECTIVES: Cognitive impairment and urinary incontinence (UI) in women, a prevalent combination, creates a complex situation in which medication for one condition (i.e., UI) can reduce treatment effectiveness, or worsen the other condition. We evaluated bladder antimuscarinics (BAM) use by levels of cognitive function in women enrolled in the National Alzheimer's Coordinating Center (NACC) cohort. METHODS: We used NACC Uniform Data Set (2005–2013) for patients 65+ with complete medication information. We identified BAM use and determined prevalence/incidence by cognitive status, treatment discontinuation, and concomitant use of other drugs. We used logistic regression to calculate odds ratios (OR) and 95% confidence intervals (CI) to evaluate factors associated with BAM use. RESULTS: 13,072 (45%) of the enrollees were women 65+. At enrollment, 2,674 (20%) reported active UI and 17% (N=452) were treated with BAM. 3% (N=343) of those not reporting symptoms were also treated. Of those reporting UI who were not treated at enrollment, 156 (6%) reported BAM use at later visits. 449 women (3%) started BAM treatment after enrollment. Of those treated and reporting cognitive impairment, about 33% reported concomitant use of cognition enhancing drugs. Of those treated, 52% did not report BAM use at later annual interviews. Of those that discontinued and had subsequent visits, 63% also reported UI at follow-up. Higher anticholinergic load (OR=3.24, 95% CI: 2.43-4.32) and mild cognitive impairment (OR=1.29, 95% CI: 1.04-1.60) were significantly associated with BAM use. CONCLUSION: Although UI symptoms are prevalent among older women, treatment is not curative and discontinuation occurs at high rates. The prescribing practice of combining BAM with anticholinergic drugs and/or with cognition enhancing drugs raises questions about safety and effectiveness.

Supported by: Acknowledgement: The National Alzheimer's Coordinating Center database is funded by NIA Grant U01 AG016976

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#45 Abstract Title: **Core Binding Factor beta is essential for female fertility in mice**

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Abstract: Core binding factor (CBF) is a small family of heterodimeric transcription factors comprised of a non-DNA binding subunit (CBFβ) and a DNA-binding subunit (one of three Runx proteins; Runx1, Runx2, and Runx3). CBFβ enhances DNA binding and stability of RUNX proteins. We previously demonstrated the spatiotemporally regulated expression of Runx1 and Runx2 in rat and human periovulatory ovaries. Our In vitro studies further demonstrated that RUNX1 and RUNX2 regulate the expression of several key genes in luteinizing granulosa cells, suggesting the role of CBFs in normal ovarian function. Mice deficient in Runx1, Runx2, and CBFβ die in the uterus or at birth, posing a challenge in demonstrating the physiological importance of CBFs in vivo. To determine the functional significance of CBFs in the ovary, we generated ovarian cell specific CBFβ knockout mice (CBFβ flox*Cyp19 cre). These knockout mice were infertile. The analysis of knockout mouse ovary showed negligible expression of CBFβ, Runx1, and Runx2 in corpus lutea (CL), whereas the expression of CBFβ, RUNX1, and RUNX2 was strong in the CL of wildtype mice. The levels of progesterone were very low in knockout mice compared to that of wild type mice. Histological analyses revealed abundant lipid droplet accumulation in all of the CLs of the knockout mouse ovary, whereas no visible lipid droplets in the CL of wildtype mice. Further analysis of proteins involved in steroidogenesis indicated that StAR expression was drastically reduced, but Cyp11a1 and 3βHSD expression were slightly higher in the CL of knockout mice compared to that of wildtype mice. In conclusion, this study provides the first evidence that CBFs are highly expressed in the CL and play a critical role in progesterone production by regulating the expression of steroidogenic enzymes. The infertility of ovarian cell specific CBFβ knockout mice is likely due to an inability to produce sufficient progesterone, a critical hormone for luteal function and establishment and maintenance of pregnancy.

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Thursday, March 27, 2014 **Lexington Convention Center**

#46 Abstract Title: **MiRNA Regulation of Endometriosis-associated Pain**

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Abstract: Chronic pain is one of the major symptoms associated with endometriosis. The etiology of this pain is still unknown. One of the recent theories is a role for epigenetics (including microRNAs) in pain. The objective of this study was to determine the regulatory role of microRNAs in pain in endometriosis. PCR arrays were used to measure miRNA and gene expression in peritoneal or ovarian endometriotic tissues obtained from IRB-approved and consented patients with +endometriosis/+pain, +endometriosis/-pain, and -endometriosis/-pain. Ingenuity pathway analysis and Targetscan were used for bioinformatics analysis of the differentially expressed microRNAs and target genes. MicroRNAs were isolated from samples and used for whole-genome human micronome PCR array. The tissue RNA was used for determining the target nociceptive genes by the Human pain: Nociceptive and Inflammatory array. A statistical and bioinformatics approach of the whole-genome micronome array determined microRNAs that were differentially expressed between patients who had pain versus controls who did not have pain. MicroRNAs such as let-7g, miR-29a, and miR-148a that target DNA methylases, opioid receptors, interleukin-6 receptor, prostaglandin receptor 4, etc. were upregulated, whereas other miRNAs that target opioid receptors and other inflammatory genes were downregulated in patients with pain compared to controls. Additionally, a human pain array revealed differential expression of genes involved in nociceptive pathways such as interleukins, prostaglandin receptors, voltage-gated sodium channels and opioid receptors in patients with pain compared to controls. Our studies suggest a regulatory role for microRNAs in pain associated with endometriosis. Validation of these target genes and their association with pain in endometriosis will identify potential targets for therapy.

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Thursday, March 27, 2014 **Lexington Convention Center**

#47 Abstract Title: **Breeding-induced endometritis: a transcriptomic approach**

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Abstract: While a transient endometritis after breeding is a physiological event, persistent breeding-induced endometritis (PBIE) affects fertility. Several studies have demonstrated that mares susceptible to PBIE had an alteration in endometrial mRNA expression of selected genes after breeding, compared to resistant mares. In order to develop targeted treatments for PBIE, a more global approach is necessary to thoroughly understand the normal inflammatory response to spermatozoa. Therefore, the objective of this study was to use RNA sequencing to investigate the inflammatory response to spermatozoa in healthy mares. Three mares resistant to PBIE were used for this study. Over two cycles, each mare had an endometrial biopsy taken 1) prior to breeding (0 hours), or 2) 6 hours after breeding with freeze-killed spermatozoa in semen extender. Total RNA was extracted and sequenced on an Illumina Genome Analyzer II. The mean expression of transcripts at 0 and 6 hours were compared, and significance was set to $p<0.05$. Approximately 300 genes were differentially expressed after breeding, with 95% of these genes being upregulated. The majority of the differentially expressed genes were involved in the inflammatory response, cellular movement/immune cell trafficking, and cell signaling. The most highly differentially expressed genes included CXCL10, IL1RN, and TIMP1, which are part of the immune response and tissue remolding. The results from this study can be used to identify specific pathways associated with normal breeding-induced endometritis, and this information can serve as a reference to study PBIE.

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Thursday, March 27, 2014 **Lexington Convention Center**

#48 Abstract Title:	**Epstein-Barr Virus and Cytomegalovirus: Relationships with Periodontal Disease Progression**
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Abstract: OBJECTIVES: Select human herpesviruses (HHVs) have been reported to play a role in periodontal disease progression by modulating inflammation or the local immune response against periodontopathogens. We tested the hypothesis that Epstein-Barr virus (EBV) and/or cytomegalovirus (CMV) is associated with the progression of periodontal disease in a longitudinal study design. METHODS: Eighty subjects (27F, 22-69 years old) diagnosed with chronic generalized periodontitis were randomly assigned to one of four treatment modalities: oral hygiene instructions and placebo (OHI+PL), OHI and n-3 PUFA (OHI+PUFA), scaling and root planning and placebo (SRP+PL), and SRP+PUFA. Each subject was followed for 6 months. Subgingival plaque samples were obtained from 3 healthy and 3 diseased sites from all patients at week 0, 16 and 28. In addition, periodontal sites that developed ≥2mm rapid attachment loss (RAL) compared to baseline were sampled for subgingival plaque at week 16 and 28. Plaque samples were assayed for P. gingivalis (Pg), T. forsythia (Tf), T. denticola (Td), CMV and EBV DNA using qPCR. RESULTS: RAL was observed at 97 sites in 30 of 80 subjects. Development of RAL was independent of treatment group ($p>0.05$). EBV was significantly more prevalent at disease sites than healthy sites ($p<0.001$), however EBV was not more prevalent at RAL sites than non-progressing disease sites ($p>0.05$). Also, EBV copy numbers were not significantly different at non-progressing disease sites compared to RAL sites. CMV was infrequently detected at disease sites, RAL sites and healthy periodontal sites. Additionally, the detection of EBV in subgingival plaque was related to the amount of Td in disease sites and the amount of Tf in healthy sites. CONCLUSION: In this study population with chronic generalized periodontal disease, EBV and CMV were not found to be associated with ongoing periodontal disease progression.

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Thursday, March 27, 2014 **Lexington Convention Center**

#49 Abstract Title:	**Association Analysis of Single Nucleotide Polymorphisms (SNPs) within or near the ActivinβA (INHBA), ActivinβB (INHBB) and/or Activin Receptor, Type IIA (ACVR2A) Genes and Naturally Missing Teeth (NMT)**
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Abstract: Objectives. The purpose of this study was to investigate potential genetic associations between various single nucleotide polymorphisms (SNPs) within or near the ActivinβA (INHBA), Activin□B (INHBB) and/or Activin Type IIA Receptor (ACVR2A) genes and Naturally Missing Teeth (NMT). Methods. Ethics approval was granted by the UK-Internal Review Board. Twenty-five unrelated Caucasians diagnosed with hypodontia and 68 unrelated Caucasian controls were consented from the faculty and graduate orthodontic and pediatric dentistry clinics. Hypodontia was defined as having 1 to 5 naturally missing (agenic) teeth in the adult dentition, excluding 3rd molars. Peg-shaped teeth were also noted. DNA was isolated from subject saliva and was genotyped on a Roche LightCycler480 for SNPs within or near the INHBA (rs2877098), INHBB (rs17625845) and ACVR2A (rs1364658) genes. Chi squared analysis was utilized to access Hardy-Weinberg Equilibrium (HWE) and to determine potential marker association(s) with hypodontia; significance at $p<0.05$. Results. Hypodontia occurred more frequently in females than males. The average ages for the hypodontia and control cases were 16.8+5.8 and 14.5+4.6 years, respectively. Maxillary-lateral-incisors were the most frequently affected by agenesis and/or peg formation, followed by mandibular-2nd-premolars and maxillary-2nd-premolars. All Control genotyping maintained HWE. There was no significance association identified between the markers tested and hypodontia (p-values 0.085 to 0.451). Conclusion. While the SNPs tested in this student's project were not associated with hypodontia, additional data gathered in our laboratory has identified a novel association of SNP rs7576183 near the Activin□B gene and hypodontia , particularly hypodontia of the upper arch.

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Thursday, March 27, 2014 **Lexington Convention Center**

#50 Abstract Title: **Evaluation of Insulin-Like Growth Factor-1 (IGF1) Single Nucleotide Polymorphisms (SNPs) in Sagittal Jaw Growth During Puberty**

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Abstract: Objective: To determine whether specific genotypes for three single nucleotide polymorphisms (SNPs) located near or within the Insulin-like Growth Factor 1 (IGF1) gene (rs10735380, rs1520220 and rs2946834) are associated with Caucasian sagittal jaw growth during puberty. Methods: IRB approval was obtained from Indiana University and the University of Kentucky. The study population consisted of 145 Caucasian subjects from Northern Indiana (77-females; 68-males) who began orthodontic treatment at cervical vertebrae maturation stages (CVMS) 2 or 3 and progressed to either CVMS4 or CVMS5 by the end of treatment. Buccal cells were harvested from the inner cheek of all participants using 2 soft-nylon brushes. DNA was isolated by standard methodology and IGF1 SNP genotypes were determined using Taqman® methodology on a Roche LightCycler480. Maxillary and mandibular jaw size (CO-POG and CO-ANS, respectively) were measured in pre- and post-treatment lateral-cephalometric radiographs using Dolphin software. Pre-orthodontic measurements and the average annualized change in maxillary and mandibular sagittal lengths were compared among genotypes for each SNP by ANOVA ($p \leq 0.05$). Results: All SNPs maintained HWE in males and females. When all subjects starting in CVMS2 and CVMS3 were analyzed together, there was no significant genotype-specific SNP association with annualized mandibular and/or maxillary growth in males and females. When focusing only on patients starting in CVMS3, SNP rs2946834 was significantly associated with annualized mandibular growth (CO-POG) in males only (n=36; p=0.007). Conclusions: While this study is ongoing, the initial data suggest that IGF1 SNP rs2946834 is associated with variation in sagittal jaw growth in Caucasian males.

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Thursday, March 27, 2014 **Lexington Convention Center**

#51 Abstract Title: **Post-Operative Care of Pediatric Patients after Dental Treatment under General Anesthesia**

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Abstract: Purpose: The aim of this study was to determine if variables including age, gender, ASA status, ethnicity, cost of treatment, type of dental insurance, and distance traveled for treatment are associated with returning for scheduled post-operative care after receiving dental treatment under general anesthesia. Methods: Information from the dental records of 798 pediatric patients treated at the University of Kentucky from June 2009 to June 2013 was recorded. Chi-square tests and binary logistic regressions were used to investigate associations between returning for post-operative care and age, gender, ASA status, ethnicity, cost of treatment, type of dental insurance, and distance traveled for treatment. Results: Fifty-seven percent of patients returned for post-operative care. When only ethnicity and post-operative care were taken into consideration, non-Caucasians were significantly more likely to return for post-operative care compared to Caucasians. When only distance traveled for treatment and post-operative care were taken into consideration, patients traveling shorter distances for treatment were significantly more likely to return for post-operative care compared to patients traveling greater distances. In a multivariate analysis, children traveling over 50.1 miles for treatment had lower odds of returning for post-operative care than those traveling less than 50 miles. Conclusions: Distance traveled for treatment has a significant impact on whether pediatric patients return for post-operative care after dental treatment under general anesthesia. Further investigation of factors influencing dental health behaviors of the pediatric population is needed.

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Thursday, March 27, 2014 **Lexington Convention Center**

#52 Abstract Title: **Zoledronic Acid Suppresses Trabecular Bone Remodeling in Rice Rats**

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Abstract: Objectives: The goal of this study was to examine the effect of zoledronic acid(ZOL) on trabecular bone remodeling by histomorphometric quantification of tibia sites in rice rats. Our long term goal is to examine bone turnover in the jaw and to study osteonecrosis. Methods: Rice rats(Oryzomys palustris) were either given i.v. saline(n=9) or ZOL(n=7), 2 doses (0.4mg/kg)/week for 12weeks via the tail vein. A pair of alizarin labels (20mg/kg) was administered i.p. 1week apart prior to drug administration. A pair of calcein labels(20mg/kg) was administered 1week apart prior to sacrifice. Specimens were fixed in formalin and embedded in plastic. Undecalcified sections, ~5microns thick, from the tibia were analyzed using Bioquant Osteo software(Nashville, TN). Mineral apposition rate(MAR, microns/day), mineralizing surface(MS/BS, %), and bone formation rate(BFR/BS, microns/day) were quantified in the proximal tibial metaphyses. TRAP stained sections were examined for osteoclast number/BS(Oc#/BS). All data was analyzed using the two-sample t-test except MS/BS and BFR/BS for the calcein labels and Oc#/BS, which were analyzed using the Wilcoxon rank-sum exact test($p<0.05$). Results: The mean(SD) BFR/BS(microns/day) for calcein in the control [0.282(0.087)] and experimental [0.048(0.051)] groups were significantly different($p<0.001$); there was a reduction of 83% in trabecular bone remodeling of the tibia. The mean(SD) for Oc#/BS(#/mm) in the control [0.904(1.502)] and the experimental [0.195(0.38)] groups were not significantly different($p>0.05$); however, there was high variability between animals in Oc#. Conclusion: High doses of ZOL have a dramatic effect on the BFR of trabecular bone surfaces in a rice rat model delivered via i.v. tail vein injections.

Supported by: Funding from the UK College of Dentistry

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Thursday, March 27, 2014 **Lexington Convention Center**

#53 Abstract Title: **Utility of in-vivo µCT in traditional histomorphometric bone analyses**

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Abstract: Objective: The aim of this project was to develop methods to allow for rapid identification of bone sections of interest from 3D image reconstructions. The resolution of current in-vivo µCT has not eliminated the need to perform histomorphometric analyses. However, the usefulness of µCT reconstructions to optimize histomorphometric studies has not been evaluated. Methods: In vivo µCT scans (Siemens Inveon Preclinical microCT, Knoxville, TN) were obtained at three time points during an 18-week study to examine the effects of a high-dose bisphosphonate on bone healing subsequent to dental extractions in a rice rat model. After harvest and fixation, MMA embedded undecalcified sections of the jaws were obtained. The µCT scans were imported into a 3D imaging software. The exact location of the 2D histological sections was determined visually within the 3D reconstructions. Results: The 3D imaging of the jaws allowed for precise location of the histological sections, which optimized the selection of the specimens to be further examined. In addition, the 3D images allowed us to focus on unique features, such as healing at extraction sites and bone adaptation subsequent to dental extractions. Another novel application that emerged during this study is the ability to generate 3D superimposition of bone structures from different time points. Discussion and Conclusion: Applications of 3D imaging are expanding to now include supplementation of histological analyses. While cellular details still must be obtained from traditional histological sections, understanding bone adaptation in 3D will overcome one of the most critical limitations of analyzing 2D bone sections.

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Thursday, March 27, 2014 **Lexington Convention Center**

#54 Abstract Title: **Association Analysis of Single Nucleotide Polymorphisms (SNPs) Within or Near the Vitamin D Receptor (VDR) Gene and Human Hypodontia**

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Abstract: Objective: This case-control study was designed to investigate whether Single Nucleotide Polymorphisms (SNPs) within or near the Vitamin D Receptor (VDR) gene are associated with human hypodontia. Method: This study protocol was approved by the UK IRB. Ninety-three unrelated, Caucasian Orthodontic patients have been recruited and classified into two groups: 25 unrelated patients with hypodontia and 68 unrelated controls. Hypodontia was defined as having 1-to-5 non-3rd molar teeth never form in the adult dentition. The number of partially formed teeth (peg-shaped) were also documented. DNA was isolated from patient saliva and SNPs within or near the Vitamin D receptor gene (rs4516035, rs1989969, rs2248098, and rs7975232) were genotyped using Taqman®-methodology on the Roche LightCycler480. A Chi-square analysis was used to access Hardy-Weinberg equilibrium (HWE) in the control population and to test for association of each SNP with hypodontia (significance at $p<0.05$). Results: In our clinics, more females exhibited hypodontia than males (4:1). The average ages+stdev for the hypodontia and control cases were 16.8+5.8 and 14.5+4.6 years, respectively. Maxillary-lateral-incisors were most frequently affected by agenesis and/or peg formation, followed by mandibular-2nd-premolars and maxillary-2nd-premolars. All Control genotyping maintained HWE. No significance associations were identified for the four VDR SNPs tested with hypodontia (p-values ranged from 0.217 to 0.996). Conclusion: The genetic markers tested in this study were not associated with hypodontia. While these data do not completely rule out a potential role for VDR in human hypodontia, they are suggestive that variations in the VDR are most likely not responsible for the phenotype.

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Thursday, March 27, 2014 **Lexington Convention Center**

#55 Abstract Title:	**Hemifacial Spasm, Headache, and Tinnitus: A Case Report of Multilevel Neurovascular Compression**
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Abstract: Introduction: Hemifacial spasm (HFS) is a rare condition characterized by unilateral, involuntary, and paroxysmal contractions of the musculature innervated by the facial nerve. Advanced imaging on a 64-year-old female patient with HFS, ipsilateral headache and tinnitus revealed unilateral neurovascular compression of several cranial nerves as a potential etiology for her syndrome. Methods: The patient presented with a 2.5-year history of persistent left-sided facial spasms, paroxysmal facial pain, hyperacusis, and tinnitus. The pain and facial spasms were a source of considerable distress. The patient was unable to tolerate oxcarbazepine and carbamazepine due to clinically significant hyponatremia and altered red blood cell count. Likewise, she was unable to tolerate pregabalin and was unwilling to try onabotulinum toxin A. Previous screening with routine MRIof the head was normal. Based on the clinical presentation, the possibility of a multilevel neurovascular compression syndrome was considered. Results: 3D FIESTA MR imaging through the posterior cranial fossa revealed left-sided neurovascular contact involving cranial nerves 5, 7, 8, and several lower cranial nerves near the jugular foramen. Conclusions: This case is unique in that previous standard MRI imaging was negative while high resolution FIESTA imaging sensitive for detection of neurovascular contact demonstrated multiple sites of compression. Demyelination occurring in areas of neurovascular compression is thought to predispose to hyperactive neuronal activity. Her tinnitus was likely associated with vestibulocochlear nerve compression. In patients who are medication-refractory surgical interventions are often effective for relief from neurovascular compression syndromes.

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Thursday, March 27, 2014 **Lexington Convention Center**

#56 Abstract Title: **Centrally-maintained Conditions are Distinguished from Temporomandibular Disorder Conditions by Self-reported Satisfaction With Life**

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Abstract: Aims of Investigation: To identify psychological similarities between centrally-maintained conditions: centrally mediated myalgia (CMM), fibromyalgia (FM) and continuous dento-alveolar pain (CDAP) patients and compare them to temporomandibular disorder (TMD) patients. Methods: Clinical records from 45 patients with CDAP, 27 with CMM, 43 with FM and 264 with TMD (capsulitis, myalgia, tendonitis and internal derangements) were evaluated. Psychological assessment tools included: Multidimensional Pain Inventory (MPI), Chronic Pain Acceptance Questionnaire (CPAQ), Post-Traumatic Stress Disorder-Checklist-Civilian Version (PCL-C), Satisfaction with Life Scale (SWLS), and Chronic Pain Graded Scale (CPGS). Initially, data from CCM, CDAP and FM groups were analyzed with one way ANOVA to determine similarity between groups. Next, contrast coding was used to compare the previous results with a TMD group to obtain variables that distinguished them. Results: Results revealed no significant differences on gender between groups. Regarding age, those in the TMD (M= 42.64 years) and CMM (M=42.96) groups were significantly younger than those in the CDAP (M= 54.89 years) and FM (M= 51.02 years) groups. Chronic pain acceptance, punishing responses, posttraumatic-stress, disability score, and satisfaction with life were similar across centrally-maintained conditions and different from TMD. After testing all variables, group classification (central vs. TMD) effects were largest on satisfaction with life, accounting for 5% of variance in SWLS after controlling for average pain intensity (R^2 total = .09, $F(2,351) = 18.90$, $p < .001$). Conclusion: Self-reported satisfaction with life distinguishes CCM, CDAP and FM patients from TMD patients.

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Thursday, March 27, 2014 **Lexington Convention Center**

#57 Abstract Title:	**Histopathological analysis of infraorbital nerve in a pre-clinical model of trigeminal nerve injury**
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Abstract: Injury to the trigeminal nerve as a result of sinus surgery, oral surgery, stroke or facial trauma may produce neuropathic facial pain. Traumatic peripheral nerve injury, proliferation of scar tissue from the epineurium can result in impediment to the regenerating axons that need to traverse the injury site resulting in dysfunction and pain. Pain management is currently the most common treatment for these nerve injuries. We sought to classify histological and inflammatory changes induced by a chronic constriction injury to the infraorbital nerve (ION) in rat, to determine if the resulting nerve damage warrants neuroprotective strategies. IONs were examined using bright field microscopy for H&E, cresyl violet histology, and CGRP-like immunoreactivity 8 weeks after ION-CCI, facial incision injury (sham injury) and were compared to naïve rats. Nerve tissue was examined in the cross sectional and longitudinal plane. Gross histopathologic changes in connective tissues and nerve fibers were evaluated. ION-CCI resulted in 1) epineurium and endoneurium fibrosis, 2) wallerian degeneration (presence of axonal digestion chambers), 3) axonal proliferation of fibroblast and 4) infiltration of macrophages. Taken together, ION-CCI meets the Seddon's nerve injury classification of neurotemesis: axonal interruption and connective tissue disruption with conduction failure being likely. These findings highlight the importance of an early diagnosis but also an appropriate pain management and neuroprotective protocol. This can be achieved through, among other well established protocols, neuroprotective/anticonvulsant medications such as topiramate and lamotrigine.

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Thursday, March 27, 2014 **Lexington Convention Center**

#58 Abstract Title: **Ameloblastomas: Diagnosis, treatment, and long term management**

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Abstract: Ameloblastomas are locally aggressive and potentially disfiguring oral cavity tumors. They typically present in the 3rd to 7th decades of life, with the posterior mandible representing the most commonly found site(1). The ideal management of an ameloblastoma should minimize recurrence, restore function, and appearance and present minimal donor site morbidity. Conservative management is associated with minimal morbidity but high recurrence rates. By contrast, segmental mandibulectomy with appropriate margins have much lower recurrence rates but presents the challenge of difficult reconstruction. In this presentation, I will present a solid, multicystic ameloblastoma in which we performed a segmental resection of the mandible with reconstruction via a fibula free tissue transfer completed by the University of Kentucky division of oral and maxillofacial surgery. I will go over the diagnosis, treatment planning, surgical, and post-surgical phases of care and discuss the pros and cons our treatment.

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Thursday, March 27, 2014 **Lexington Convention Center**

#59 Abstract Title:	**Postsurgical Osteomyelitis Following Bilateral Sagittal Split Osteotomy: Case Report and Perioperative Protocol Development**
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Abstract: Objectives: The purpose of this report is to compare two patients diagnosed with osteomyelitis following bilateral sagittal split osteotomy surgery. A review is completed to outline consistencies between the cases and to discuss the implications of perioperative protocol development. Study Design: A second case of osteomyelitis following bilateral sagittal split osteotomy is reviewed and compared to a previous case. A logical preoperative and postoperative protocol, including improved investigation of reported reactions to medications and subsequent administration of prophylactic antibiotics, is developed. Results: Consistencies were appreciated between the two cases: a reported penicillin allergy, use of preoperative and postoperative clindamycin monotherapy, and positive cultures for Eikenella corrodens. Conclusion: While the postsurgical incidence is small, the consequences for the individual patient are severe. An in depth review of reactions to medications is warranted and appropriate antibiotic prophylactic coverage is necessary.

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Thursday, March 27, 2014 **Lexington Convention Center**

#60 Abstract Title: **IL-1-Alpha/IL-1-RA Polymorphisms are Not Associated with External-Apical-Root-Resorption during Orthodontics**

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Abstract: Objective: The aim of this study was to investigate whether polymorphisms within the Interleukin-1-Alpha (IL-1A, rs1800587) and/or Interleukin-1-Receptor-Antagonist (IL1RA, rs419598) gene(s) were associated with External-Apical-Root-Resorption (EARR) of the maxillary incisors in patients undergoing orthodontic treatment. The null-hypothesis stated that variation in these polymorphisms would not be associated with EARR. Method: In this case-control study, 457 Caucasian orthodontic patients from Northern Indiana were consented and provided buccal swab DNA for genetic analysis. Patient occlusal and panoramic radiographs from pre- and post- orthodontic treatment were examined for the presence of EARR of the four maxillary-incisor roots by three investigators. Subjects were considered to be “affected” when at least two-of-three investigators agreed that moderate or severe EARR was present on at least one of the subject's maxillary incisors. Seventy-one patients with moderate to severe EARR were identified. Each EARR-affected individual was then age and gender matched to a control subject (41 females and 30 males in each group). Taqman®-based genotyping was utilized for the allelic discrimination of rs1800587 and rs419598 on the Roche LightCycler480®. Chi-square analyses were used to assess Hardy-Weinberg Equilibrium (HWE) in the controls and to test for association of markers with EARR. Result: The average age at start of treatment for the case and control groups was 15.9 years. The average length of treatment for the case and control groups was 2.5 and 2.1 years, respectively. All control genotypes maintained HWE. There was no significant difference ($p=0.4$) for either SNP examined between the case and control groups. There was a significant ($p<0.0001$) difference in the length of treatment between the case and controls groups by Student T-test. Conclusion: Based on the available data of the IL-1A and IL1RA polymorphisms, the null-hypothesis could not be rejected. However, the case group had a significantly longer average treatment time than the control group. This project was supported in part by the National Institutes of Health Center for Oral/Systemic Biomedical Research Excellence (COBRE) Award NIH/NCRR P20RR020145, The University of Kentucky E. Preston Hicks Endowed Chair and the Southern Association of Orthodontist.

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Thursday, March 27, 2014 **Lexington Convention Center**

#61 Abstract Title: **Linkage Analysis of Class III Phenotype and Human Chromosome 1**

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Abstract: Objective: Genetic markers were genotyped spanning the 1p22.1-22.2 region, within the Erythrocyte Membrane Protein Band 4.1 (EPB4.1) gene at 1p36 and within the Matrillin-1 (MATN1)gene to examine their potential genetic linkage to the Class III phenotype in two South American family-based cohorts. All three tested loci have previously been implicated in Class III dentofacial deformities. Method: Forty-one families (1,306 individuals) from Brazil and Colombia participated in this study after providing formal informed consent. DNA was isolated from blood, buccal swabs or saliva of 247 of these individuals, 160 of whom were affected by Class III. In subjects providing DNA, the Class III phenotype was defined using Cephalometric measurements for ANB, SNA, SNB; an edge to edge overbite and/or anterior crossbite. Class III was determined for individuals in the pedigrees not providing DNA using a combination of cephalometrics, visual examination, models and/or photographs. Nine Single Nucleotide Polymorphisms (SNPs) were analyzed using a Taqman®-based genotyping on a Roche LightCycler480®. Results: Statistical analysis of genetic markers is currently underway. We anticipate the results should provide information regarding the loci linked to the Class III phenotype or eliminate potential areas of linkage from consideration. Conclusions: If positive linkage is discovered at any of the studied loci, it will indicate a common genetic factor between Asian and South American peoples.

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Thursday, March 27, 2014 **Lexington Convention Center**

#62 Abstract Title: **Linkage Analysis of Human Chromosome 12 with Class-III Dentofacial Deformities**

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Abstract: Objective: A total of thirteen genetic markers were genotyped within the Dual-specificity-phosphatase-6 (DUSP6) gene at 12q21.33, near the Myosin 1H (MYO1H) gene at 12q24.11, or spanning the genomic region from 12q13.13 to 12q23 to study potential linkage to the Class III phenotype in two unique South American family-based cohorts. Methods: After obtaining proper informed consent in the country of origin: family pedigree summaries, facial phenotype information and DNA (from blood, buccal swabs or saliva) were collected from individuals within 41 South American families with a high prevalence of Class III dentofacial deformities. Twenty-three of the families in this study were from Bogotá, Columbia and 18 families were from Brasilia, Brazil. Cephalometric values for ANB, SNA, and SNB; an edge to edge overbite and/or anterior crossbite were used to define the Class III phenotype for all individuals providing DNA. The dentofacial phenotypes of relatives described within the pedigrees who did not provide DNA were determined using a combination of Cephalometric values, visual examination, dental models and/or facial photographs. Thirteen Single Nucleotide Polymorphisms (SNPs) were genotyped using Taqman®-based methodology on the Roche LightCycler480® and DNA obtained from 247 subjects within this cohort, including 160 Class-III-affected individuals. Results: Linkage analysis of these genetic markers is currently underway. Once completed, the results should provide information regarding the loci linked to the Class III phenotype or eliminate potential areas of linkage from consideration. Conclusions: If positive linkage is discovered at any of the studied loci, future experiments will utilize DNA sequencing to identify causal variations leading to the formation of the Class III phenotype in these South American families.

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Thursday, March 27, 2014 **Lexington Convention Center**

#63 Abstract Title: **Update on Skeletal Anchorage in Orthodontics**

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Abstract: One of the major challenges in orthodontics is the preservation of anchorage. Traditional orthodontic appliances are attached to the teeth, and the orthodontist uses the appliances to exert force on teeth he or she would like to move using the anchorage of other teeth that they do not wish to move. Occasionally, the desired tooth movement results in undesired movement of other teeth in the dental arch. Traditionally, one way to circumvent the undesired tooth movement was the use of extra oral anchorage, such as a head gear. While this is an effective means of anchorage preservation, patient compliance has always been an issue. Dental implants now provide orthodontists with a solution to the anchorage issue. Skeletal anchorage is now a routine part of modern orthodontic treatment planning. Skeletal anchorage can be accomplished through the use of osseointegrated implants, surgically placed bone plates, or temporary anchorage devices (TADs). The goal of this poster is to present the indications, effectiveness, and complications for each of these types of skeletal anchorage.

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Thursday, March 27, 2014 **Lexington Convention Center**

#64 Abstract Title:	**Orthodontists' and Parents' Attitudes on Addressing Obesity in Orthodontic Practice**
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Abstract: Objectives: Current research shows that one third of American children and adolescents are either overweight or obese, a demographic that includes many orthodontic patients. Addressing healthy weight issues will involve efforts by a broad range of healthcare providers and acceptance of these messages by caregivers. Objectives of this biphasic study were to 1) determine attitudes and opinions of orthodontists about addressing healthy weight\obesity in their practices, and 2) determine attitudes of orthodontic patient caregivers about receiving healthy-weight messages in the orthodontic office. Methods: Phase 1: A 113-item validated questionnaire on attitudes on addressing obesity, previously administered to general and pediatric dentists by Curran et al, was sent via email using REDCap to members of the American Association of Orthodontists . Phase 2: Based on results of Phase 1, a second survey was conducted among the caregivers of pediatric orthodontic patients at the University of Kentucky College of Dentistry using an original questionnaire. Results: Phase 1: Responses of 408 orthodontists were analyzed. Fewer orthodontists (34%) expressed interest in addressing obesity when compared to pediatric dentists (53%) and general dentists (48%). Orthodontists were significantly more likely to report fear of offending the parents (65%) as a barrier than pediatric (57%) and general dentists (56 %) (p=0.0001). Lack of trained personnel was reported as another major barrier (52%) .Phase 2: Three-hundred seventy parents of orthodontic patients were neither strongly in favor of nor strongly opposed to discussion about obesity in the orthodontic office. Conclusions: Fewer orthodontists expressed interest in addressing obesity than their pediatric and general dentist colleagues. Fear of offending patients and parents, and lack of training are major barriers. However, some parents of orthodontic patients appear to be open to discussions in the orthodontic office. Research on education for orthodontists on initiating discussions with caregivers in a nonthreatening, nonjudgmental manner is needed.

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Thursday, March 27, 2014 **Lexington Convention Center**

#65 Abstract Title: **Analysis of Pain Perception and COMT Haplotype Following Orthodontic Separator Placement.**

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Abstract: Objectives: To determine: (1) whether there is a variation in average pain perception at different time points over one week after separator placement, and (2) if specific catechol-O-methyltransferase (COMT) haplotypes correspond with pain perception. Methods: Sixty six subjects were recruited, separators placed and saliva collected for determination of COMT genetic haplotypes. Pain perception was indicated by Visual Analogue Scale (VAS) at 1, 4, 24, 72 and 168 hrs after separator placement. Eighteen subjects were excluded for either missing VAS Forms or genotyping issues. Hence COMT haplotypes previously associated with high or lower pain sensitivity were determined in 48 subjects (25 males, 23 females) at 1, 4, 24, 72 and 168 hours VAS scores. Statistical analysis was by Shapiro-Wilk, and Kruskal-Wallis tests, significance at $p<.05$. Results: The average VAS scores of the time points were not normally distributed ($p= 0.000004$). There is a significant difference in the VAS median values of the five haplotype pain susceptibility combinations ($p=0.04$), with the two highest combinations including the predicted high pain haplotype. Conclusions: There is a trend for individuals with one predicted high pain haplotype to have a higher VAS score secondary to orthodontic separator placement. However, there is marked variations with some individuals having a predicted high pain sensitivity but low pain perception. COMT central block haplotypes have accounted for 11% of pain perception in the literature. Analysis of pain perception, and COMT haplotype and other genetic markers could develop into a model for studying orthodontic pain, as well as pain in general.

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Thursday, March 27, 2014 **Lexington Convention Center**

#66 Abstract Title: **Expression Analysis of Neuropeptides in Periodontal Disease**

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Abstract: Objective: Neuropeptides (NPs) are pivotal regulators (i.e., anti- and pro-inflammatory) of the immunoinflammatory response. Although variation in the levels of a limited number of NPs has been associated with periodontal lesions; the role of NPs in periodontal disease remains unknown. We aimed to determine changes in the gene expression of a group of NPs and their receptors (NPRs) associated with initiation, progression and resolution of periodontitis. Methods: The ligature-induced periodontitis model was used in rhesus monkeys (n=18). Gingival tissues samples were taken at baseline pre-ligatures, 2 weeks and 1 month (Initiation), and 3 months (Progression) post-ligation. Ligatures were removed and samples taken 2 months later (Resolution). Total RNA was isolated from tissues and the Rhesus Gene Chip 1.0 ST (Affymetrix) used for NPs/NPRs gene expression analysis. Results: There were not significant changes in the expression of pro-inflammatory NPs/NPRs associated with periodontitis. However, significant increase in the expression of anti-inflammatory NPs (ADM, GAL) and receptors (CALCRL, and RAMP3) was observed during initiation and progression of disease. VIPR1 expression was reduced during the course of the disease. Moreover, a subset of anti-inflammatory NPs/NPRs (i.e., ADM, GAL, CALCRL, RAMP2/RAMP3), exhibited a significant positive correlation with both the molecular (IL-1B and RANKL) and clinical (BOP and PD) measures of inflammation and tissue destruction. In contrast, TAC1 and VIPR1 expression correlated negatively with the same disease-related measures. Conclusion: Up-regulation of various anti-inflammatory NPs and their receptors occurs during the course of periodontitis and these changes correlate with molecular and clinical measures of disease. These results suggest that the net result expression of NPs/NPRs during the initiation and progression of periodontitis could be enhancing a tolerogenic environment, which may delay the resolution of infection and inflammation as suggested in other inflammatory diseases.

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Thursday, March 27, 2014 **Lexington Convention Center**

#67 Abstract Title: **Autophagy Pathway Gene Expression Profiles During Progressing Periodontitis**

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Abstract: Objective: Autophagy is a physiologic mechanism by which cells process damaged organelles and maintains tissue homeostasis. Deficient autophagic responses increase inflammation and susceptibility to infection. At sites of periodontitis, the subgingival microbiota and the resulting host's inflammatory response, subject cells to stress that damages organelles. Therefore, we hypothesize that autophagy-related genes will be differentially expressed during the course of periodontitis, with a net gene expression suggesting an impaired gingival autophagic response associated with disease. Methods: The ligature-induced periodontitis model was used in rhesus monkeys (n=18). Gingival tissues samples were taken at baseline pre-ligatures, 2 weeks and 1 month (Initiation), and 3 months (Progression) post-ligation. Ligatures were removed and samples taken 2 months later (Resolution). Total RNA was isolated from tissues and the Rhesus Gene Chip 1.0 ST (Affymetrix) used for gene expression analysis of autophagy-related genes. Results: There was a significant ($p \leq 0.05$) increase in the expression of genes (PIK3CG, AKT1, and FLIP/CFLAR) that are negative regulators of autophagy during initiation and progression of periodontitis. Although increased expression of downstream positive regulators of autophagy (SHIP2, ULK2, and ATG8) was observed during initiation/progression of periodontitis, another subset of positive regulators of autophagy (AMPK, ATG14 and ATG10) was significantly down-regulated during the same phases of disease. Most of these changes tended to return to BL levels during resolution of disease. Conclusion: Significant variation in the gingival expression of autophagy-related genes occurs during initiation, progression and resolution of periodontal disease. The gingival net gene expression profile suggests that autophagy could be impaired/blocked during the initiation and progression of periodontal disease. A reduced autophagic response in gingival tissues potentially orchestrated by oral pathogens could increase the risk for persistent infection and inflammation in periodontal disease.

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Thursday, March 27, 2014 **Lexington Convention Center**

#68 Abstract Title: **Effect of Bisphosphonate and age on Implant Success Using Patient Reported Outcomes**

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Abstract: Purpose: There is inconsistency in literature with regards to certain factors that can significantly increase the risk of implant failure. The purpose of this study is to report an association between variables such as patient age, smoking status, presence diabetes, presence of osteoporosis, use of bisphosphonate on implant success and survival. Materials and methods: A retrospective analysis of implants placed in the implant training program at University of Kentucky College of Dentistry during the period January 2000 through 2006 with regard to identify the influence of potential risk factors that affect implant success versus implant failure using Implant Quality Assurance Program (IQAP). Patient satisfaction with the appearance, function, and surgical experience, in addition to lack of pain and mobility associated with the implant(s) were the benchmarks for successful implant. A formal survey was implemented by a trained clinician and the data was collected either chairside at a scheduled maintenance appointment, or via telephone. Both patient level and implant level responses were analyzed. Results: From the total of 415 patients (963 implants) interviewed, the implant(s) survival rate was 97%, while 88% of the implant(s) were successful. Increasing age was associated with increased risk of implant failure, while bisphosphonate use was associated with reduced risk of implant failure. Conclusion: Our data suggest a possible association between aging and bisphosphonate use and implant success.

Supported by: NA

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Thursday, March 27, 2014 **Lexington Convention Center**

#69 Abstract Title: **Immediate Loading of Unsplinted Implant Retained Mandibular Overdenture: A Randomized Controlled Clinical Study**

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Abstract: Introduction: When a fixed prosthesis anchored to implants is not indicated, implant-retained overdentures may be considered as possible alternative treatment. The early loading protocol showed equivalent survival rates (98% and 97% for delayed and early loading, respectively). However, there is a lack of comparative studies on immediately loaded of unsplinted implants retained mandibular overdentures. Purpose: This study aimed to evaluate the implant success rate and peri-implant tissue response of immediately loaded mandibular overdentures using two unsplinted implants compared with delayed implant protocol. Materials and Methods: Twenty completely edentulous patients will be selected. 10 patients will receive 20 implants and immediately loaded in test group and 10 patients will receive 20 implants and conventionally loaded in the control group. All participants will receive new complete dentures prior to implant placement. Two implants will be placed at the mandibular canine positions. Locator™ abutments will be torqued and primary closure will be achieved. Attachments will be picked up intra-orally and light retention inserts will be placed. Data Collection: The following parameters will be recorded; implant success rates, marginal bone level changes (MBL), Osstell® values: (Resonance Frequency Analysis), modified plaque index, surgical and prosthetic complications. MBL changes will be recorded for both the mesial and distal sites for each implant from the RL. The junction between the implant platform and the adjacent bone will be used as the reference line (RL).Recorded data will be statistically analyzed using the Paired Samples t-Test and the Wilcoxon Signed-Ranks. The level of significance will be $\alpha = 0.05$.

Supported by: The project described is an independent project.without funding.

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Thursday, March 27, 2014 **Lexington Convention Center**

#70 Abstract Title: **Characterization of cortical pERK expression after trigeminal inflammatory compression (TIC) of the infraorbital nerve**

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Abstract: A trigeminal inflammatory compression model (TIC) of neuropathic pain was recently established, resulting in mechanical and cold sensitivity which was attenuated with microglial inhibitors. Noxious stimulation induced phosphorylation of ERK (pERK) is often used as an activation biomarker in the trigeminal ganglion and nucleus caudalis. Since clinical orofacial neuropathic pain (ONP) patients are at high risk for developing affective mood disorders, and to the extent that ONP might involve ERK-phosphorylation in affective brain regions, we sought to determine the effects of TIC injury on non-evoked pERK immunoreactivity (IR) in the forebrain of mice 1 and 3 weeks after injury. Forebrains from TIC mice demonstrated non-evoked pERK-IR in medial pre-frontal cortex (mPFC), primary motor cortex (M1), somatosensory cortex-jaw (SIJ) and anterior insula (AI) 1 and 3 weeks after injury. One week post injury, increased pERK-IR was observed ipsilateral to injury in AI, while MI and SIJ showed increased pERK-IR contralateral to injury. Contralateral vs ipsilateral differences were less striking for each cortical region 3 weeks after injury but significantly more intense than 1 week post injury. Three week TIC-injury resulted in greater mPFC pERK-IR than after one week. Entire forebrain cortex was also quantitated for pERK using an Aperio ImageScope and demonstrated greater IR-intensity 3 weeks post injury. These results demonstrate that TIC injury results in a temporal and region specific cortical profile of pERK immunopositive microglia. Cortical ERK phosphorylation may contribute to the pathogenesis of cognitive affective disorders as a result of ONP.

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UK College of Dentistry Research Day
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Thursday, March 27, 2014 **Lexington Convention Center**

#71 Abstract Title: **Digital complete denture, a simple technology for everyday clinical practice.**

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Abstract: Computer Aided Design – Computer Aided Manufacturing (CAD/CAM) technology has made significant improvement in modern dentistry. CAD/CAM applications in dentistry include fabrication of inlays, onlays, crowns, fixed partial dentures, and implant abutments/prostheses. Recently, computer-aided technology is a new method commercially available for fabricating complete dentures. This system facilitates impressions, interocclusal records, and tooth selection to be completed in one appointment. The dentures are then fabricated using CAD/CAM technology and placed in the second appointment. 2 commercial manufacturers in the United States are currently fabricating complete dentures with computer-aided design and computer-aided manufacturing (CAD/CAM) technology for clinicians world-wide. These manufacturers have definitive protocols and offer exclusive dental materials, techniques, and laboratory support. CAD/CAM technology allows the clinician to design complete dentures and create natural looking superstructures. The CAD/CAM technique provides precise fit, reduces number of visits and the cost of the procedure, and eliminates dimensional inaccuracies due to conventional processing techniques. The aim of this presentation is to describe a simple technique for complete denture procedure using CAD/CAM technology.

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Thursday, March 27, 2014 **Lexington Convention Center**

#72 Abstract Title: **Cytokines gene expression during initiation, progression and resolution of Periodontitis**

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Abstract: Objective: Although clinical and animal studies (i.e., mice) support that cytokines are involved in the pathogenesis of periodontal disease, it remains unclear what type of cytokine response(s): (i) are related with initiation, progression and resolution of periodontitis, and (ii) could be related to tissue protection or destruction. We sought to evaluate the expression of 19 T-cell helper (Th) cytokine genes during initiation, progression, and resolution of periodontitis, and their potential correlation with soft (i.e., MMP2 and MMP9) and bone (i.e., RANKL and CTSK) tissue destruction genes (TDGs). Methods: The ligature-induced periodontitis model was used in rhesus monkeys (n=18). Gingival tissues samples were taken at baseline pre-ligatures, 2 weeks and 1 month (Initiation), and 3 months (Progression) post-ligation. Ligatures were removed and samples taken 2 months later (Resolution). Total RNA was isolated from tissues and the Rhesus Gene Chip 1.0 ST (Affymetrix) used for cytokines gene expression analysis. The expression of a selected group of cytokines with significant changes during the course of disease was validated by qPCR. Results: Initiation/Progression of periodontitis was characterized by significant over-expression of Th17 cytokine genes (IL-1β, IL-6, and IL-21) and under-expression of Th1/Th2 cytokine genes (IL-18 and IL-25). Increased IL-2 and decreased IL-10 levels were seen during disease resolution. Several Th17/Treg cytokine genes positively correlated with TDGs, whereas most Th1/Th2 cytokine genes exhibited a negative correlation. Conclusion: Initiation, progression and resolution of periodontitis involve over- or under-expression of cytokines genes related to more than one T-helper subset. Therefore, associating an individual T-helper response subset/gene pattern to a given phase of the disease or to protective/destructive responses is complex. The increasing variety of cytokine functions and their potential interactions (cytokines networks) highlight the need for using systems approaches, rather than focusing on single mediators for a better understanding of the nature of immune responses in periodontitis.

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Thursday, March 27, 2014 **Lexington Convention Center**

#73 Abstract Title: **Gingival Expression of Microbial Sensing Molecules with Aging and Periodontitis**

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Abstract: OBJECTIVE: Both immune and non-immune mucosal cells are decorated with an array of cell membrane and intracellular bacterial sensing Pattern Recognition Receptors (PRRs), which regulate inflammatory responses to the microbiota. We sought to determine variations in PRRs expression related to aging and periodontitis. METHODS: Macaca mulatta (3-24 years, n=34) were evaluated for Bleeding on Probing (BOP) and Pocket Depth (PD). Gingival tissues were obtained, RNA isolated, and microarray analysis conducted for expression of 35 microbial sensing PRRs. An additional group of adult/aged animals (7-22 years, n=18) was subjected to a 5 month longitudinal study examining the initiation/progression/resolution of periodontitis. RESULTS: Surface PRRs, including CD14, CD209, and CLEC4E, and intracellular receptors NAIP and ZBP1/DAI significantly increased their expression with age in healthy gingival tissues. CD14, CLEC4E, TLR2, and NAIP expression levels were also increased in periodontitis tissues compared to healthy tissues from the same age groups. Of the 35 PRRs evaluated, 15 demonstrated significant differences from baseline during the longitudinal study. Interestingly, TLR-1,-2,-4,-6,-8,-9, and CD14 all demonstrated a similar pattern with significant increases during initiation/progression of the disease; however, TLR-1 levels dropped to baseline by 1 month. All these PRR expression levels decreased to baseline levels with resolution of the disease. Whereas, multiple PRRs were positively correlated with increasing BOP with periodontitis, including CLEC isoforms and TLRs, very few correlated with mean PD in the established periodontitis animals. Of particular interest was the substantial numbers of these gene expression levels that were significantly correlated with BOP (15/35) and PD (12/35) during the resolution phase of the disease. CONCLUSIONS: These results show oral mucosal changes in PRRs with aging and periodontitis. Of interest in the biology of this disease, is that differential expression in established lesions appeared different than those changes occurring early in disease initiation and progression.

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Thursday, March 27, 2014 **Lexington Convention Center**

#74 Abstract Title: **Porphyromonas gingivalis Evades the Immune System by Modifying M1 Macrophage Functions**

Author(s): C. Brad Huang, COHR, U of Kentucky
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Abstract: Objectives: Macrophages are crucial immune cells in innate and adaptive immunity for combating pathogens. They polarize in functional development into M1 macrophages involved in inflammation and with bactericidal capabilities, and M2 macrophages playing major role in wound healing and tissue repair. P gingivalis (Pg), is considered an important pathogen in chronic inflammatory periodontitis and is now thought to have a primary role in altering the microbial environment and ecology at sites of disease. Related to this concept, we hypothesized that Pg might be able to manipulate the M1 macrophage functions. Methods: Using a THP-1 cells, treated with LPS+INFγ to induce a classic M1 macrophage, we evaluated the impact of live Pg on the resulting cellular functions. Results: Pg had a significant effect resulting in what appeared to be “functionally atypical” M1 macrophages with elevated levels of inflammatory cytokines (↑IL-1ß, IL-6, TNF□), but with a significantly reduced chemokine profile (↓CCL5, CXCL4). Pg appeared to primarily alter the Jak-STAT pathway of IFN□ signaling (chemokines), while enhancing the TLR/NF-□B pathway (inflammatory cytokines). Pg reduced the gene expression of the key transcriptional factor STAT1, leading to decreased protein levels and phophorylated STAT1 for nuclear translocation. Pg also increased the expression of SOCS1, a strong STAT1 inhibitor. Conclusions: This Pg-induced atypical M1 macrophage could result in increased local inflammation, but with reduced ability in bacterial clearance and communicating with the adaptive immune system. Thus, an approach that Pg could use to modify the local microbial and host environment is a molecular strategy to evade the immune system and enrich the local inflammatory environment for their survival, with periodontitis as collateral damage from this process.

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Thursday, March 27, 2014 **Lexington Convention Center**

#75 Abstract Title: **Identification of novel biomarkers for Crohn's disease by screening mucosal biopsies from colon, ileum and gingiva for expression of inflammation-associated genes**

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Abstract: Inflammatory bowel diseases, including Crohn's disease (CD) and ulcerative colitis, are idiopathic chronic and relapsing diseases of the gastrointestinal (GI) tract, originating from an exacerbated immune response to the gut microbiota in genetically predisposed individuals. CD is characterized by patchy transmural granulomatous inflammation affecting any part of the GI tract, from the mouth to the anal-rectum, but primarily localized to the ileum and/or colon. Up to 20% of CD patients can develop oral lesions. Genetic, environmental, immunological and microbial factors contribute to the complex etiology of IBD. Given the heterogeneity of IBD, it is important to identify novel molecular biomarkers for CD that will improve diagnosis and enable personalized therapy. The NanoString nCounter RNA hybridization system was used to screen for expression of 179 inflammation-associated genes in biopsies of non-inflamed mucosa from the colon, ileum and gingiva, obtained from 35 CD patients and 38 healthy controls. Using variable mapping and principal component analysis, we identified 15 biomarkers, specific for colon (STAT1, MYD88, IL-18, IL-12, IL-6R), ileum (NOS2, C2, CXCL3, TRAF2, MAP3K1) or gingiva (CD40LG, CD4, IL10R, HLA-DRA, HSP27), which significantly discriminated between CD patients and healthy individuals. Our findings suggest that inflammation at different sites in the alimentary canal is characterized by unique patterns of gene expression. Ongoing studies to define links between biomarker expression and clinical disease may enhance personalized diagnosis and treatment of CD patients.

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Thursday, March 27, 2014 **Lexington Convention Center**

#76 Abstract Title: **Participation of Kentucky General Dentists in Medicaid/KCHIP, ARC Region, 2011 and 2012**

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Abstract: Introduction: In 2011, Kentucky's Medicaid program implemented state-wide managed care. In planning for an Appalachian Rural Dental Education Project, a comprehensive dental needs assessment was conducted, including dentist participation. Improved understanding of general dentist participation in Medicaid at regional levels is an important access and policy matter. Objective: Determine baseline general dentist participation rates for the ARC region (2011) and changes for 2012. Methods: Total numbers of dentist by county were obtained from dental licensure records. Medicaid participation and participation level were determined using actual paid dental claims for the ARC region that were aggregated for each individual dentist, combining all payments for different practice locations and Medicaid numbers. National Provider Identifier (NPI) numbers were used to insure each dentist was only counted once. Findings: In 2012, 723 of 2063 (37%) general dentists in Kentucky participated in Medicaid. The Central Kentucky participation rate was 28 %. Across the 54 county ARC region, participation was much higher (63%). For ARC sub-regions, general dentist participation varied from 54% (North East and I-75), 69% (Big Sandy), 83% (Lake Cumberland) and 90% (Kentucky River). In 2011, 46 general dentist's participated who did not participate in 2012. Only 14 new general dentists participated, resulting in a net decline of 32 participating dentists in the ARC region. Conclusions: The participation of general dentist across the ARC region is much higher than the rates for Kentucky or Central Kentucky. In 2012, a significant decrease occurred. This trend has important health policy implications and should be closely monitored.

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Thursday, March 27, 2014 **Lexington Convention Center**

#77 Abstract Title: **Perceptions of Oral Health among Students at Morehead State University: Findings from a Focus Group Investigation**

Author(s): A. Scott, U of Kentucky
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Abstract: Poor oral health creates major societal health expenses in Appalachia Kentucky that far exceed the direct costs of dental services. To improve oral health in the region, however, we must first accurately understand local perceptions and behaviors related to oral health. We conducted seven focus groups of 7-11 students each at Morehead State University, which yielded a total sample of 67 students (male=30, female = 37). The average age of participants was 20.0 years old (SD = 3.3 years, range = 18-40 years). Most of the participants (n = 58, 86.6%) were White, and the remaining participants (n = 9, 13.4%) reported a different ethnic background. The participants represented 24 counties in Kentucky. We used inductive thematic analysis to better understand the lexicon, knowledge, interests, needs, attitudes, beliefs and behaviors regarding the oral health of students from Appalachia Kentucky. We discovered two clusters of oral health behavior: Some participants reported that they did not consistently brush their teeth or visit the dentist, whereas other participants reported that they were “obsessive” about brushing their teeth because they were worried about falling into the stereotype of being from Appalachia and having poor oral health. Participants identified more barriers to receiving dental care (including mistrust of providers and lack of convenient access on campus) than benefits (which included being more physically attractive and feeling healthy). These results provide valuable insight message design and dissemination strategies for targeting oral health improvement among college students in the region.

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Thursday, March 27, 2014 **Lexington Convention Center**

#78 Abstract Title: **Dental Utilization, Medicaid and KCHIP Patients in Kentucky's ARC Region, By Age Group, 2011 and 2012**

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Abstract: Introduction: In 2011, Kentucky's Medicaid program moved to a state-wide managed care model. In planning for an Appalachian Rural Dental Education Project, a comprehensive dental needs assessment was conducted, including Medicaid dental claims for 2011 and 2012. Understanding existing dental utilization rates and changes in utilization overtime are important to assess the outcomes of managed care. Objective: Determine baseline dental utilization for the ARC region and changes after one year of managed care. Method: Retrospective Medicaid dental claims for Kentucky were analyzed by age group and region of Kentucky to determine unique Medicaid and KCHIP enrollees who received one or more dental services each calendar year. Age specific annual enrollment and utilization totals were used to determine utilization rates for age groups across the life span. Findings: Baseline utilization (2011) for all enrollees was 35%. Rates varied widely across age groups ranging from 35 % (15-20 age group) to 68% (0-4 age group) for children and 5% (71 + age group) to 32% (21-30 age group) for adults. A major decrease in utilization were found after one year of Medicaid managed care, particularly among younger children. Conclusion: Dental diseases involve chronic infections that can progress to serious pain, quality of life and general health complications. These utilization findings raise serious access concerns. As the ACA and Medicaid managed care models are implemented in Kentucky, the patient and population outcomes and the costs of dental services for both children and adults will emerge as a significant state policy considerations.

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Thursday, March 27, 2014 **Lexington Convention Center**

#79 Abstract Title: **Oral Health Practices, Literacy, and Relevant Belief Systems among Young Adults in Appalachian Kentucky**

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Abstract: Improving oral health literacy and understanding relevant belief systems about oral health practices are foundational elements for long-term improvement to community oral health in Eastern Kentucky. Under the foundation of the Appalachian Regional Dental Enhancement Program, researchers at the University of Kentucky have partnered with Morehead State University (MSU) to develop a university oral health literacy and promotion campaign. To inform the development of the campaign that will be launched in the fall of 2014, we conducted an online survey among a representative stratified sample of undergraduate students from MSU during the spring 2013 semester. In total, 603 students (male = 170, female = 433) participated. We found interesting descriptive results about oral health practices. For instance, only 10% of students utilized a local dentist in Morehead at their last dental visit, 29% of students do not or do not know whether they have dental insurance, 24% of students believe they have current active dental decay, 35% of students have not had a dental cleaning in the last year, 43% of students brush less than twice per day, and 78% of student floss less than once per day. We are currently analyzing data to determine the students' oral health literacy and relevant beliefs about oral health. In addition, we are content analyzing open-ended suggestions concerning how to disseminate oral health information and improve oral health behavior among students at MSU. These results will provide valuable insight into the design of campaign messages and best practices for campaign implementation among a targeted student population to improve oral health among future leaders of Appalachian Kentucky.

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Thursday, March 27, 2014 **Lexington Convention Center**

#80 Abstract Title: **Mandibular symphyseal morphometry from CBCT images**

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Abstract: Objective: The objective of this study was to use Cone-Beam Computerized Tomography (CBCT) to measure the morphometrics of bone in the symphysis of the mandible. Methods: Deidentified CBCT data was obtained. The images were taken as part of routine radiographic acquisition using a Newtom 3G (Verona, Italy). The DICOM image files were imported into a Bioquant Osteo software. Images from 10 male and 10 female patients, with age ranging from 18-73 yr. were analyzed. The Region of Interest (ROI) for symphyseal morphometry was defined based on typical surgical techniques of bone harvest. The following outcome variables were measured: Bone Volume (BV) (sq. mm), Tissue Volume (TV) (sq. mm), Cortical Bone Volume/Total Bone Volume (BV/TV) (%) and Buccal Cortical Bone Thickness (mm). A two sample t test was used to analyze the data. Results: The mean (SD) of the BV/TV (%) of the male and female groups were 53.3 (7.1) and 51.5 (6.9) respectively (p=0.62). However, there was a trend for the BV to be larger in the males and the TV was significant larger in the males (p=0.012). The mean (SD) of the cortical bone thickness (mm) of the male and female groups were 2.36 (0.27) and 2.09 (0.40) which was not significant (p=0.1). Conclusion: Autogenous bone grafts obtained from the chin can be expected to have an average thickness above 2 mm with approximately 50% of the harvested graft being cortical bone. In general, the tissue volume obtained from males is great than in females.

Supported by: none

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Thursday, March 27, 2014 **Lexington Convention Center**

#81 Abstract Title: **Comparison of Condylar Morphometry from CBCT Images**

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Abstract: Objectives – The purpose of this study was to evaluate intra and inter patient variability in mandibular condylar morphometry from 3D images. Methods – Deidentified CBCT data was obtained. The images were taken as part o routine radiographic acquisition using a Newtom 3G. To study the mandibular condylar bone and tissue volume BioQuant imaging software (Nashville, TN) was used to analyze data from the CBCT of 9 patients with an age range of 18---58 yrs (7 females and 2 males). Identical regions of interests were defined on both condyles and were consistently used for each patient. Morphometry measurements in the axial, frontal, and sagittal planes was obtained. The following variables were examined: bone volume (BV, mm2), tissue volume (TV, mm2) and bone surface (BS mm). Results: The mean (SD) for BV/TV (%) in axial, frontal, and sagittal planes were a follows: 60.58 (6.49), 46.62 (6.54), and 55.13 (7.41) and were not significantly different ($p > 0.05$). The mean (SD) for percentage (%) difference in TV between t left and right condyle in axial, frontal, and sagittal planes were as follows: 13.52 (10.36), 10.13 (11.70), and 10.52 (7.48) and were not significantly different ($p > 0.05$). Conclusions: The left and right condyle patient comparisons shows some asymmetry however, it was not significantly different. Our normative data also helps to serve as standard that will aid in understanding bone loss as a result of pathologic conditions that can occur in the condylar structures.

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Thursday, March 27, 2014 **Lexington Convention Center**

#82 Abstract Title: **Year One Outcomes Following Implementation of Managed Care Organization Model for Dental Services in Kentucky**

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Abstract: Introduction: A statewide Medicaid managed care system was implemented in 2011 for health services in Kentucky. Objective: Document specific year one dental outcomes from implementation of the statewide Medicaid managed care system. Methods: Medicaid dental claims were used to compare dentist participation pre (2011) and post (2012) implementation and dental utilization (defined as patients who received at least one dental service). Using the Kentucky Medicaid database, Medicaid expenditures for dental services were compared for 2011 and 2012. Findings: There was a decrease in the percentage of dentists who were paid Medicaid dental claims in 2012 (38.39%) compared to 2011 (43.32%). Dental utilization decreased with 34,813 fewer enrollees receiving dental services in 2012 (-9.9%) and nearly $38 million less in dental claims paid compared to 2011. Conclusions: Year one of Medicaid managed care in Kentucky demonstrated significant declines in dentist participation, dental utilization, and dental expenditures.

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Thursday, March 27, 2014 **Lexington Convention Center**

#83 Abstract Title: **Bilayered Calcium Sulfate/Calcium Phosphate Composite Bone Graft Substitutes**

Author(s):
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Abstract: Introduction: Alloplastic bone graft materials are being developed as an alternative to autologous bone that can be utilized in near infinite amounts without the occurrence of a second surgery or donor site morbidity. With the potential for release of bioactive agents and customizable erosion timing, combined with the structural functionality to prevent infiltration of soft tissue, these synthetic composites may offer a suitable substitute to the current gold standard. Methods: Dicalcium phosphate dihydrate (DCPD) and calcium sulfate hemihydrate (CS) were separately incorporated into cylindrical molds comprising concentric core and shell layers. Single-layered samples were made for comparison. Physical, chemical, and mechanical properties were characterized by microcomputed tomography, destructive mass loss measurement, and compression testing. Results: The single layer DCPD samples had a significantly ($p<0.05$) higher ultimate compressive strength (UCS) than did the DCPD-core/CS-shell samples, but UCS for the other samples was similar. The single layer DCPD and DCPD-shell/CS-core samples experienced the least mass loss (19.9% and 27.3%, respectively) during incubation for 60 days, while the single layer CS and CS-core/shell were entirely eroded by day 32. DCPD-core/CS-shell samples demonstrated an initial mass loss rate similar to the CS samples until day 16, and then exhibited a rate similar to the single layer DCPD samples. Conclusion: The combination of DCPD with CS in a layered system provides adequate compressive strength comparable to CS alone. The layered implant has potential for customizable erosion timing and drug release that could be useful as a bone graft substitute.

Supported by: The project described was supported by the UKCD Student Research Fellowship

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Thursday, March 27, 2014 **Lexington Convention Center**

#84 Abstract Title: **Effect of Recombinant Human Bone Morphogenetic Protein on Alveolar Bone Grafting in Cleft Lip and Palate Patients**

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Abstract: Objectives: Orofacial clefting of the lip and palate are the most prevalent craniofacial birth defects in the United States. This study hypothesized that the number of surgical procedures needed to repair the alveolar cleft would be decreased by augmenting the iliac crest bone graft (ICBG) with recombinant human bone morphogenetic protein (rhBMP-2). Methods: A retrospective chart review was executed to evaluate cleft repair surgeries performed by two participating surgeons from April 2006 to August 2013. Patients were identified from the EHR focusing on CPT code 42210. A total of 70 patients met the criteria. These data were analyzed using Student t-test, Fisher's Exact test, and logistic regression. Results: Of the 70 patients, 45 received ICBG and 25 received ICBG with rhBMP-2. 15/45 (33%) of patients treated with an ICBG required an additional operation compared to only 4/25 (16%) for those treated with ICBG and rhBMP-2 (p=0.12). 27% of patients required a second operation, that was deemed necessary for orthodontic treatment (mean age 11.38 years), due to inadequate bone support in the cleft site. Overall, patients with a right unilateral cleft who were treated with rhBMP-2 had the lowest probability of having a second surgery. Conclusions: This study supports the potential for rhBMP-2 reducing the need for secondary bone grafting surgery for cleft repair. This quality analysis currently indicates that 73% of cleft lip and palate patient's treated at UKCD are successfully treated with one surgery. These data suggest that the percentage could continue to improve with the use of rhBMP-2 during alveolar cleft augmentation surgeries.

Supported by: University of Kentucky College of Dentistry Student Research Fellowship Scholarship

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Thursday, March 27, 2014 **Lexington Convention Center**

#85 Abstract Title: **Bone Grafting in Preparation for Implant Placement: A Clinic View**

Author(s): Nathan Krauss, Div of Oral & Maxillofacial Surgery, U of Kentucky
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Abstract: Objective- The purpose of this poster is to show a brief overview of different bone grafting techniques employed by our residents here at UK to prepare a site for implant placement. The aim is to educate both practicing dentists and the dental students about the scope of osseous preprosthetic surgery that is available in preparation for implant rehabilitation of complete and partial edentulism. Methods- The cases shown here are cases that were managed by our OMFS residents in the 5th floor clinic, the VA clinic, or in one of the operating rooms here on campus. Consent for photo-documentation was acquired. Results – Several successful cases have been selected to display. Conclusions- One of the most challenging aspects to implant planning is the restoration of horizontal and vertical osseous defects. However, if the dentist and surgeon are familiar with different bone grafting techniques, this hurdle can be overcome.

Supported by: This is a clinical overview, coming from cases performed by residents in the various clinic and OR settings at UK Chandler, the VA hospital, Good Samaritan Hospital, and the UK COD.

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Thursday, March 27, 2014 **Lexington Convention Center**

#86 Abstract Title: **Oral Sedation Effectiveness at a Pediatric Dentistry Residency Clinic**

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Abstract: Purpose: The purpose of this study was to evaluate effectiveness of oral sedation regimens at the University of Kentucky pediatric dentistry residency clinic. Methods: A retrospective study of oral sedations performed from April 2006 to June 2013 was conducted. Outcome variable was effectiveness. Covariates included age, gender, indication, pre-sedation cooperation, sedation behavior, and sedation level. Results: A total of 290 sedation records were reviewed. The average patient age was 5.79 years. Sedation was ineffective in 15.5% (n=45), effective in 49.6% (n=144) and very effective in 34.8% (n=101) of the cases. The most common indication for sedation procedure was “to protect patient’s developing psyche” (46.2%). The most common pre-sedation cooperative level was “cooperates freely” (49%). Choice of medication was based on the extent and anticipated duration of treatment. Most common and most effective sedation regimen was hydroxyzine + chloral hydrate + meperidine (24%) (P=.05 Fisher’s exact test). For the purpose of calculating odds ratio, effective and very effective values were combined into effective. Effectiveness of sedation was significantly higher when sedation level was moderate compared to mild (OR=4.8, CI 1.18-19.6, P=.0013). The adjusted odds ratios revealed that the sedation effectiveness was higher in girls than boys. Older children (average 6 years old) were 61% more likely to have an effective sedation than young children (average 4.3 years old) (OR=1.61, CI 1.1-2.2, P<.0001). Conclusions: This study found a statistical correlation between gender and age of children and the effectiveness. The most common sedation protocols involved three drug combinations.

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Thursday, March 27, 2014 **Lexington Convention Center**

#87 Abstract Title: **Comorbidities of Children Treated Under General Anesthesia for Oral Disease**

Author(s): D.J. Patel, Dept of Pediatric Dentistry, U of Kentucky
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Abstract: Purpose: The purpose of this study was to describe and analyze the characteristics of the children receiving oral rehabilitative care under general anesthesia with a specific focus on associated comorbidities. Methods: Dental charts (n=542) of children who received care under general anesthesia were analyzed to determine the demographic characteristics of the children as well as the number and type of comorbidities associated with the primary diagnosis of dental disease. Results: The majority of the children treated in the operating room were less than 6 years, 61.4%; 27.9% were 6 to 12 years and only 10.7% were more than 13 years. Males constituted 58.4% of the children; females, 41.6%. The population was 73.2% Caucasian; 7.8% African-American, 11.8% Hispanic, with 7.2% categorized as other. Medicaid was the primary insurance carrier (90.8%). No associated comorbidities were identified in 43.6% of the children; 37.4% had two or fewer, and 19.0% had more than two. The most common comorbidities were developmental delay (9.68%), asthma (8.67%), heart murmur (5.06%); ADHD (4.34%); speech disorders (4.62%); seizure disorder (4.05%); autism (3.76%); GERD (3.76%); cerebral palsy (3.47%); Down syndrome (3.32%). 92.4% of the patients were treated in the Center for Advanced Surgery, with 7.6% being treated in the major operating room suite. Conclusions: The results of this study provide data previously unavailable, data which can improve understanding of the population of children being treated under general anesthesia, and inform policy in the utilization of general anesthesia for care at the University of Kentucky.

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Thursday, March 27, 2014 **Lexington Convention Center**

#88 Abstract Title: **Dosimetry of two direct digital imaging devices using a pediatric phantom.**

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Abstract: Purpose: The purpose of this study is to provide effective dose measurements for two direct digital imaging devices, the Planmeca intra and the Gendex panoramic unit using a pediatric phantom. Methods: Thermoluminescent dosemeters (TLDs) were placed at 24 sites throughout the layers of the head and neck of a tissue-equivalent human phantom simulating the anatomy of a 10 year old child. Two bitewings (one for each side) and a panoramic film were simulated. Ten exposures for the panoramic unit and 200 exposures for the bitewing technique were used to ensure a reliable measure of radiation from the dosemeters. Radiation weighted doses to individual organs were summed using 2007 ICRP tissue weighting factors to calculate whole-body effective dose. Results: The overall effective dose for two bitewings was 7uSv. The highest effective doses were recorded in the dosemeters located at the salivary and thyroid glands. The overall effective dose for the panoramic film was 9.1uSv. The highest effective doses were recorded at the thyroid and salivary glands. A panoramic film and two bitewings recorded a combined effective dose of 4.7 uSv to the thyroid gland.

Supported by: Residency Program

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Thursday, March 27, 2014 **Lexington Convention Center**

#89 Abstract Title:	**Antenatal and Intrapartum Risk Factors for Use of Medicaid Dental Services**
Author(s):	R.C. Kilty, Dept of Dentistry, U of Kentucky J. F. Yepes, Dept of Dentistry, U of Kentucky

Abstract: A retrospective cohort study was completed subsequent to approval by University of Kentucky Institutional Review Board. Medicaid-enrolled children born in the Commonwealth of Kentucky in 2000, were monitored longitudinally until in 2010. The study was based on the following Kentucky databases: 1) Composite birth records (from Vital Health Statistics) from the 2000 calendar year; 2) Individual Medicaid eligibility files for all children born in 2000 and enrolled continuously in the Medicaid program from 2000 to 2010; and 3) Medicaid dental claims data covering 2000-2010. The study focused on claims filed through Medicaid for oral health services. Outcome variables were categorized according to type of dental visit (preventive or restorative). Antenatal and intrapartum risk factors were obtained from the composite birth records. Mode of delivery (vaginal vs. C-section), mother's race (Caucasian vs. African-American), and age at the first dental claim were the variables included in the analysis. The major outcome variables were the dental claims. Results: The analysis revealed that only 1.6% of children had a preventive dental visit before the age of 18 months. Children who had a preventive visit before the age of 3 years had fewer restorative claims. The adjusted analysis found Caucasian mothers had a higher odds ratio of having a dental claim than did African-American mothers. When race was analyzed separately, in African-American mothers, the odds of a restorative claim were higher in children delivered by C-section compared with vaginally delivered. Conclusions: This study found an association between children of Caucasian mothers and the likelihood of experiencing claims. A relationship was found between children born via C-section and the likelihood of use of Medicaid dental services.

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Thursday, March 27, 2014 **Lexington Convention Center**

#90 Abstract Title:	**Comparison of BioXclude and Mem Lok Membrane for Socket Bone Augmentation: A Prospective Randomized Controlled Clinical and Histological Study.**
Author(s):	S. Faraj, Resident, Periodontics Div M. Al Sabbagh, Periodontics Div D. Dawson, Periodontics Div A. Kutkut, Prosthodontics Div

Abstract: we aim to compare two resorbable membrane (allograft placental-BioXclude versus xenograft collagen- Mem Lok) in order to find out whether one of these membrane could provide better soft tissue healing and better bone quality before implants are placed. Both membranes are FDA approved and tested for human use. Their proposed use in this study is FDA approved. This research is IRB approved.

Supported by: Division of Periodontics - UK college of Dentistry Snoasis Medical - Denver, Colorado

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Thursday, March 27, 2014 **Lexington Convention Center**

#91 Abstract Title:	**Sox11 Regulates Expression of Neurogenic Factors Involved in Retinal Cell Fate Specification**

Author(s):
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Abstract: The SRY-Box transcription factor Sox11 is critical for normal vertebrate eye development. Previously, we have shown that reduced levels of sox11 in zebrafish result in in microphthalmia, coloboma, specific reduction in rod photoreceptor cells, and an up-regulation of the Hedgehog (Hh) pathway. The goal of this study was to investigate the mechanism of action of Sox11 during retinogenesis in zebrafish. Atonal-homologue 5 (ath5) is a proneural gene expressed as retinoblasts exit the cell cycle and start the process of differentiation. Shh derived from the ventral-midline region regulates the timing of ath5 expression in the zebrafish retina. Since Sox11 regulates Shh signaling, we hypothesized that ath5 expression would be altered in zebrafish with reduced levels of sox11. At 30 hpf, 80.0% of control retinas displayed expression of ath5 in the ventral patch, whereas only 50.0% of sox11 MO had ventral patch expression. At 48 hpf, ath5 was expressed in the ganglion cell layer in the control morphant. However, sox11 morphants retinas displayed a marked reduction in the spread of ath5 expression. Knockdown of sox11 resulted in elevated expression of shha in the hypothalamus, ventral midline as well as in the floorplate cells as compared to control MO. Pharmacological rescue of sox11 MO using cyclopamine significantly rescued the elevated shha expression as well as the abnormal eye morphology. Our results suggest that sox11 is required for the proper developmental timing of ath5 expression during retinal neurogenesis. It has been shown that ath5 positive cells contribute significantly to the photoreceptor cell lineage; therefore, our observation of delayed/reduced ath5 expression in sox11 morphants may underlie the delayed rod photoreceptor differentiation observed at 72 hpf. Additionally, we have shown that elevated levels of shha contribute towards the abnormal sox11 MO ocular phenotypes.

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Thursday, March 27, 2014 **Lexington Convention Center**

#92 Abstract Title: **The effects of muscle injury on synaptic transmission, axon conduction and muscle in relation to K+ in deep tissue injury**

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Abstract: Currently, the only accepted standard of treatment for deep tissue injuries (DTI) of skeletal muscle and skin is to treat them similarly to Stage III or IV pressure ulcers. However, primary skeletal muscle damage can produce secondary effects which can increase the spread of the damage zone. This can be caused by the additive effects of intracellular contents, particularly the ion K+, released from crushed muscle cells. It has been known since the 1930's that fluid from damaged skin tissue causes sensory neurons to stop responding. Also, it is well known that increasing the [K+] o in a saline 10 times higher than normal will result in cell (i.e., muscle) necrosis. However, consideration in the exposure time and effects of restoring normal [K+] o on the health of skeletal muscle and synaptic transmission has not been fully addressed. We are examining the effects of rapid rises of [K+]o over various periods of time before returning to normal levels on the health of the muscle and the effects on synaptic properties at neuromuscular junctions. With prolonged exposure to 40mM as compared to 20mM results in longer time to recover synaptic transmission and muscle membrane potential. The muscle membrane potential changed from -70 to -30mV for 20mM and to -20mV for 40mM.The time to return to a normal potential is inversely related to [K+] o and duration of exposure. The synaptic responses return slower than recovery of skeletal muscle potential. At present we are conducting further investigations on the crayfish opener muscle and Drosophila larval body wall muscles as models for effects on synaptic transmission with muscle injury. It appears the axon becomes blocked in conduction with raised [K+] o which is likely due to the inactivation of the NaV channels. Thus, a nerve close to a site of injury may not necessarily be physically injured but conduction of electrical signals may be hampered, due to a localized raised [K+] o . The goal of these studies is to use these findings to help establish rodent models and development of experimental paradigms which may lead to better treatment and assessment of DTIs in urgent care centers for humans.

Supported by: personal funds

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#93 Abstract Title:	**Modulatory role of serotonergic system in locomotion neural circuitry and behavior in Drosophila melanogaster**

Author(s): E. A. AbdelJaber, Dept of Biology, U of Kentucky
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R. L. Cooper, Dept of Biology, U of Kentucky

Abstract: Serotonin (5-hydroxytryptamine, 5-HT) is an indispensable neurotransmitter and neuromodulator that plays essential roles in modulation of neural circuitry and behavior. In this study, we investigated the role of 5-HT system in locomotion behavior as well as sensory-motor circuit activity in the fruit fly, Drosophila melanogaster. We employed genetic approaches to manipulate either 5-HT neurons or various 5-HT receptors. 5-HT actions are mediated by 5-HT receptors, which are dubbed G-protein coupled receptors (GPCR). Five 5-HT receptor subtype genes, 5-HT1Adro, 5-HT1Bdro, 5-HT2Adro, 5-HT2Bdro and 5-HT7dro reside in Drosophila genome. We have shown that a potent 5-HT2 agonist (R(-)-DOI) can modulate sensory-motor circuit function, and pharmacological blockage of serotonin transporter (SERT) by fluoxetine decreases the circuit activity. Using thermogenetic approach, the electrical activity in 5-HT neurons was increased in a spatial and temporal controlled manner by expressing temperature-sensitive cation channel (TrpA1). The results demonstrate that acute activation of 5-HT neurons decreases the locomotion behavior in both larvae and adult stages. Moreover, the synaptic transmission of serotonergic neurons was blocked by misexpressing dominant negative mutant shits using a specific Gal4 driver. Inhibition of the 5-HT neurons did not result in a noticeable effect in locomotion behavior. From these results we can draw a conclusion that 5-HT is essential for the modulation of locomotion behavior in Drosophila that might be mediated through activation of 5-HT2 receptors.

Supported by: Gertrude Flora Ribble Research Scholarship (E. A. AbdelJaber) Higher Committee for Education Development in Iraq (HCED) (Z. R. Majeed) Personal funds (R. L. Cooper)

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#94 Abstract Title:	The effects of GABA on sensory-motor circuit activity, behavior and development in Drosophila

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Abstract: Drosophila melanogaster is an excellent model system in studying various biological processes since it is easy to breed them, and they have a wealth of genetic tools. Key questions in understanding the function of the central nervous system (CNS) in physiologic and pathologic conditions can be addressed in this system quickly and cheaply to develop a foundation which can be followed up in mammalian systems. We addressed the role of GABA, a neurotransmitter in the CNS, which is also a common dietary supplement. We examined the effects of administering varying levels of GABA to the organisms through tests on neural circuitry, behaviors and development. The developmental time to pupation and to eclosion as well as behavioral tests were also investigated. The larval development has been shown to be slowed in a dose-dependent manner with feeding GABA. Locomotive behavior and mouth hook movements were reduced in the third instar larvae that were fed GABA. This study shows that GABA retarded larval development and altered behaviors. We are now addressing GABA directly on the larval CNS and assessing sensory-motor neural activity. This study has implications regarding dietary supplements and pharmacological agents used clinically that modify the GABAergic system in the CNS of humans. This multifaceted project is attempting to obtain an insight into the effects of GABA on several levels from the exogenous aspects, to the altering of neuronal activity for the treatment of diseases.

Supported by: Gertrude Flora Ribble Scholarship (N. Dabbain) Personal funds (R.L. Cooper)

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#95 Abstract Title: **Studying the role of serotonin in neural circuit modulation and behavior in Drosophila melanogaster**

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Abstract: The fruit fly, Drosophila melanogaster, uses the same neurotransmitters and neuromodulators as higher vertebrates to perform various physiological actions. The activity of the sensory-motor circuits is tuned by neuromodulators to prepare the organism to survive the ambient changes. 5-HT increases the activity of locomotion related neural circuitry in Drosophila. We are interested in characterizing 5-HT receptor subtypes that are involved in the modulation of neural circuitry and the role of 5-HT system in locomotion and feeding behaviors. The Drosophila genome harbors five 5-HT receptor subtypes. We used both pharmacological and genetic approaches to identify 5-HT receptors and manipulate 5-HT neurons to further understand the importance of 5-HT in the function of given neural circuits. The segmental nerves of dissected third instar larvae were stimulated at 40Hz, 10 pulses while the excitatory junction potential (EPSP) in muscle fibers were recorded. The evoked EPSPs in muscles 6 or 7 were counted before and after adding various pharmacological agents. 5-HT agonists (5-HT1A: 8-Hydroxy-DPAT hydrobromide; 5-HT1B: CP93129; 5-HT2: DOI; and 5-HT7: AS19) were employed. The UAS-GAL4 system was used to manipulate the activity of 5-HT neurons. Pharmacological data demonstrate that 5-HT2 and 5-HT7 receptors increase the activity of neural circuitry. Also, the results show that overexpression of serotonin transporter (SERT) decreases the climbing ability in adult flies. It has been concluded that 5-HT7 and 5-HT2 signaling pathways modulates the neural circuitry and decreasing 5-HT signaling by overexpression of SERT, which terminates 5-HT action by transporting it back into the terminals, diminishes the activity.

Supported by: Higher Committee for Education Development in Iraq (ZRM) Personal funds (RLC)

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#96 Abstract Title: **The Effects of Amphetamine and Food Restriction on Rat's Reward Choice**

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Abstract: This study determined if the neurotransmitter, dopamine, affected preference for a large versus small reward. Adult male rats were trained to choose between two levers providing either one or three food pellets. Prior to experimental trials, rats received an injection of saline or D-amphetamine, a drug that stimulates dopamine release. Amphetamine did not affect lever choice. In a second study, we found that allowing rats to eat before each trial decreased lever pressing but amphetamine still did not alter large reward preference. Elevating brain dopamine levels does not alter preference for large rewards regardless of motivational state.

Supported by: This research was supported by grants from the National Institute of General Medical Sciences (8P20GM103436) and National Institute of Mental Health (1R15MH094955).

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Thursday, March 27, 2014 **Lexington Convention Center**

#97 Abstract Title: **Drosophila dopamine receptor mutants exhibit locomotion abnormalities in response to light-touch stimuli**

Author(s): D. Potts, Dept of Biology, U of Kentucky
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R.L. Cooper, Dept of Biology, U of Kentucky

Abstract: Several homologies exist between the arthropod central complex and the vertebrate basal ganglia, particularly with regard to motor control and modulation. Both structures are innervated by dopaminergic fibers that modulate motor output through metabotrophic receptors. Dopamine (DA) depletion in this region has been shown to cause a variety of phenotypes related to locomotion and action selection. In this study we are investigating the role of DA in sensory-motor transformation. Third instar Drosophila larvae were administered light-touch stimuli along the first three anterior segments and their time before resuming normal crawling behavior was measured in two mutants, a type-1 dopamine receptor mutant (Dop1) and a type-2 dopamine receptor mutant (Dop2). The Dop2 receptor mutant showed longer intervals between the stimulus and resumption of crawling than the Dop1 mutant, and the Dop1 mutant a longer interval than the wild type line. We believe these phenotypes are caused by lack of DA modulation, mediated by the Dop1 and Dop2 receptor mutations, as they are reminiscent of known phenotypes derived from depletion of DA modulation. Yet, this shows that even mechanosensory inputs are subject to the lack of DA modulation when selecting a motor plan, and that these DA receptors, Dop2 more than Dop1, play a crucial role in modulation of this pathway from tactile stimulus to motor output. These findings help to elucidate the role of different types of DA receptors in the pathways they modulate, and due to the deep homology between the arthropod central complex and vertebrate basal ganglia may shed some light onto the intricacies of the analogous pathways in vertebrates.

Supported by: G. Ribble undergraduate funds Biology Dept. (DP) & personal funds (RLC)

Group: Undergraduate Student

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#98 Abstract Title: **A Novel System to Investigate Sensory Habituation**

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Abstract: Sensory habituation is a neuronal mechanism that enables animals to ignore unimportant stimuli in favor of novel or salient stimuli. Though this phenomenon appears to be a common way for neurons to process various forms of sensory input in different animals, it is not yet clear how habituation is scaled up to the neural circuit level. The tools for controlling neural activity and molecular pathways in specific subsets of neurons make Drosophila melanogaster a useful model for investigating habituation. Here we describe a novel system in which to investigate mechanosensory habituation, i.e., Drosophila larvae. Habituation curves, measured as the percentage of larvae responding to a light brush along the anterior segments, were generated over a range of inter-stimulus intervals (ISI) and spontaneous recovery times. On average, 93.7% of wild type larvae (Canton-S) responded to the initial stimulus, whereas only 36.7% responded to the 25th stimulus (5s ISI). The magnitude and rate of habituation were lower in response to 10s ISI. Two other pieces of data indicate this is truly habituation in the CNS, first is that the conditioning stimulations were delivered to the same side, and upon stimulating the contralateral side, response probabilities were still significantly less than controls. Second is that after delivering 25 conditioning stimulations, the response was dis-habituated by an abdominal tactile stimulus with greater force (25mN). Larvae did not habituate to this more noxious stimulus applied to either the head or tail regions. These data provide a foundation for further studies into the molecular mechanisms of habituation in specific types of sensory neurons and at different stages of development.

Supported by: G. Ribble undergraduate funds Dept of Biology (SB) & personal funds (RLC)

Group: Undergraduate Student

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#99 Abstract Title: **The Effects of Early-life Risperidone on Locomotor Responses to Amphetamine during Adulthood**

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Abstract: Antipsychotic prescriptions for pediatric populations increased tremendously over the past 20 years, particularly the use of atypical antipsychotic drugs such as risperidone. Although risperidone may have transient effects on adult brain functions, early exposure may permanently alter the developing brain, even long after cessation of treatment. Animal studies have demonstrated that early-life risperidone treatment changes forebrain dopamine, serotonin, and glutamate receptor densities. Thus early-life risperidone would be expected to alter behaviors related to dopamine, serotonin, or glutamate function during adulthood. The purpose of this study was to evaluate the effects of early-life administration of risperidone on locomotor responses to amphetamine - a drug that enhances forebrain dopamine release. Thirty-five rats received one of four doses of risperidone (vehicle, 0.3, 1.0, 3.0 mg/kg) from postnatal day 14 through 42. Locomotor activity was measured for 60 minutes on postnatal days 14, 46 and 47. The following two weeks, each rat was habituated to the locomotor chambers for 24 hours on two occasions. Subsequently, rats received each of the four doses of amphetamine (saline, 0.3, 1.0, 3.0 mg/kg), one dose per week randomly over four weeks, beginning on postnatal day 75. After amphetamine administration, locomotor activity was measured for 27 hours concurrent with two hours of stereotypy measurements. An analysis of variance for the 27-hour locomotor data revealed main effects for risperidone and amphetamine treatments, but no interaction between them. While early-life risperidone administration increases activity, as does acute amphetamine administration, it does not significantly enhance the locomotor-elevating effects of amphetamine during adulthood.

Supported by: National Institute of General Medical Sciences (8P20GM103436) and National Institute of Mental Health (1R15MH094955)

Group: Undergraduate Student

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#100 Abstract Title: **Effects of early risperidone use on the density of dopamine receptors in adult rats**

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Abstract: Risperidone is an antipsychotic drug used for psychiatric disorders in children. Pharmacologically, risperidone blocks brain dopamine receptors, and chronic antipsychotic administration during adulthood elevates dopamine receptor density. This study used rats to determine if long-term risperidone use during development increased the density of D2-type dopamine receptors later in adulthood. Rats were administered vehicle, risperidone 1.0 mg/kg, or risperidone 3.0 mg/kg daily from postnatal day 14 to 42. Early-life risperidone administration did not significantly change D2 receptor density during adulthood. Unlike adult brains, developing brains may be less prone to compensatory increases in dopamine receptors induced by chronic antipsychotic drug administration.

Supported by: National Institute of General Medical Sciences (8P20GM103436) and National Institute of Mental Health (1R15MH094955)

Group: Undergraduate Student

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Thursday, March 27, 2014 **Lexington Convention Center**

#101 Abstract Title: **Alternative Splicing of CD33 Associates with Alzheimer's Disease Associated Polymorphism, Revealing a New Therapeutic Target**

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Abstract: Recent genome-wide association studies have identified the single nucleotide polymorphism (SNP) rs3865444, located 372 base pairs upstream of CD33, as a modulator of Alzheimer's disease (AD) susceptibility. CD33 is a sialic-acid binding inhibitory receptor, postulated to have an immunosuppressive effect on microglia in brain, but the function of rs3865444 in AD has been unclear. Here, we illustrate the mechanism of rs3865444 action on CD33 splicing and expression in human brain. Our long-term goal is to develop therapies that mimic the effects of protective SNPs in order to combat AD onset. We begin by identifying CD33 isoforms expressed in human brain, finding a predominant form that lacks exon 2 (D2 CD33) and a form that retains intron 1 (R1 CD33). Using qPCR, we quantify total CD33, D2 CD33, and R1 CD33 from cDNA prepared from 30 AD and 30 non-AD brains. We find a significant association between exon 2 skipping and rs386544 genotype, indicating that the AD-protective allele of the SNP promotes skipping of exon 2 and production of non-functional CD33. We identify a co-inherited exon 2 SNP, rs12459419, as the functional SNP that modulates exon 2 splicing. We find that rs3865444 also associates with increased retention of intron 1, leading to production of a prematurely truncated CD33 protein. Thus, we conclude that the minor allele of rs3865444 functions to decrease AD risk by inhibiting CD33 function, thereby enabling microglial mobilization against amyloid. We propose that an antibody treatment that clears surface CD33 will be therapeutic against AD.

Supported by: NIH grant P01-AGO30128 and U of Kentucky Bucks for Brains Program

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Thursday, March 27, 2014 **Lexington Convention Center**

#102 Abstract Title: **Dependence of Volume of Distribution on Gel Strength for Convection Enhanced Delivery of Drugs to the Brain.**

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Abstract: Convection Enhanced Delivery (CED) is emerging as an effective clinical method for delivering therapeutic agents directly to the brain to treat neurological diseases, including Parkinson's disease. While this method has had varying success in clinical trials, standardized CED in vitro models are needed to develop CED techniques which improve the reliable distribution of therapeutic compounds. Many groups, including ours, have conducted model studies using agarose gel mimics, which simulate the isotropic, porous environment of grey matter structures, such as the putamen. However, the composition of the gels is not defined in the literature. To gain insight into the dependence of the infusion pressure required, and the volume of distribution of compounds as a function of varying agarose gel strength, we infused safranin O dye into 0.6% agarose gels of low, medium, and high tensile strengths. Our results show that the volume of distribution and the infusion back pressure is dependent on agarose gel strength, with the high tensile strength better approximating CED delivery in the porcine brain. This information will be useful for future standardized in vitro evaluations of CED procedures.

Supported by: University of Kentucky Office of Undergraduate Research Codman-Shurtleff Chris Ross, Engineering Resources Group Michael J. Fox Foundation/Kinetics Foundation University of Kentucky College of Medicine Startup Funds

Group: Undergraduate Student

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#103 Abstract Title: **The Depth of Destruction: variables in the cortical contusion model of TBI**

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Abstract: Traumatic brain injury (TBI) is a major health problem worldwide. It is important to have adequate animal models to develop rationale therapies for. One of the main rodent models used in TBI research is the controlled cortical contusion (CCC) model. With this model the severity of injury can be manipulated through changes in three different primary variables: i.e. depth of impact, velocity of impact, and duration (dwell) of impact. There is some disagreement on what value is important when modeling TBI. Using the PSI TBI 0310 impactor, we studied how altering different variables could affect the injury severity. Adult male Sprague-Dawley rats were anesthetized with isoflurane and subject to a TBI by varying the three primary variables. At seven days post injury the animals were killed by perfusion and the brains evaluated for possible injury using an image analysis system. The percent of cortical tissue sparing was evaluated using the uninjured hemisphere as an internal control. The depth of cortical impact was evaluated at 1.0,1.5, 1.7, 2.0, 2.3 and 2.5 mm. The velocity was evaluated at 2.5, 3.5, and 4.5 m/sec. The dwell time was evaluated at 50, 100, 200, and 500 msec. Different combinations of the variables were evaluated. The results showed that while depth of impact and velocity were more important than dwell time, the depth variable was a better predictor of injury severity than velocity. Velocity greater than 3.4-4.0 m/sec did not significantly alter severity of injury regardless of depth or dwell time. These results help to characterize the CCC model and give the neurotrauma researcher greater flexibility in designing experiments.

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Thursday, March 27, 2014 **Lexington Convention Center**

#104 Abstract Title: **Genetic Model of Retinitis Pigmentosa (RP)**

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Abstract: Retinitis Pigmentosa (RP) is an inherited group of eye diseases characterized by primary degeneration of rod photoreceptor cells (PRCs), followed by secondary loss of cone PRCs. Clinically, RP often presents with nyctalopia (night blindness), which may progress to total vision loss. RP affects 1 in 4000 people worldwide. Currently, there are no effective treatments and no cure for RP. RP causing mutations have been identified in more than 50 loci, with more than 3100 individual pathogenic mutations. Rhodopsin (RHO), which is often mutated in RP, is expressed only in rod PRCs. More than 160 mutations in RHO have been causatively linked to RP, and for many there is little or no information concerning the pathogenicity of the mutations. For most, no animal models exist. Using an inducible expression system, we are creating zebrafish models of RP, in which expression of human RHO is controlled through the addition of an exogenous ligand. Previously, our lab has shown that ligand treatment of injected embryos produces transient expression of RHO. Additionally, we have identified several transgenic zebrafish lines using PCR based genotyping, and are working to validate expression of the transgenes. These models will permit careful dissection of several human RHO mutations, which will allow us to determine the mechanisms by which degeneration occur. Additionally, because zebrafish are able to regenerate damaged or lost central nervous system neurons, this system will allow us to observe regeneration of PRCs after induction is quenched.

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#105 Abstract Title: **Delayed Administration of Perlecan Domain V Significantly Increases Neurogenesis and Functional Recovery after Experimental Ischemic Stroke**

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Abstract: Stroke remains a major cause of morbidity and death with limited therapeutic options. In our efforts to develop novel stroke therapies, we have focused on exploiting the brain's own neuroreparative potential with focus on perlecan, a prominent proteoglycan in the brain's extracellular matrix which is processed into the bioactive protein fragment domain V (DV) after stroke. DV is naturally neuroprotective and enhances angiogenesis (a key mechanism of neurorepair). In rodents, functional outcome can be significantly improved by administering DV 24 hours after experimental stroke. *In vitro* studies have shown that DV also increases neurogenesis. As neurogenesis is another key, but ultimately insufficient (few new neurons survive) component of neurorepair, we studied the potential of delayed DV administration, 7 days post-stroke, to increase neurogenesis and improve functional outcome in 3 month old C57/BL6 male mice. After two doses of DV, mice subjected to experimental stroke had significant functional improvement as measured by rotor rod (significantly increased latency, equal number for control and DV treated groups, n=6, experiment repeated, $p<0.05$) as compared to vehicle treated stroked controls. Brain immunohistochemistry 21 days after stroke demonstrated that DV treated mice had more cells that were positive for BrdU (cell division marker), doublecortin (immature neuronal marker) and NeuN (mature neuronal marker) in the infarct area. These results suggest that delayed DV treatment after experimental stroke increases neurogenesis, increases the number of new neurons that reach stroked brain regions and survive, and improves functional outcome. Importantly, we are unaware of any other **delayed** stroke treatment, other than or combined with physical/occupational/speech therapy that significantly improves functional outcome. Collectively, our data supports the promise of DV as a novel stroke therapy.

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Thursday, March 27, 2014 **Lexington Convention Center**

#106 **Abstract Title:**	**Early Detection of Motor Intent from the Electroencephalogram for Brain-Machine Interface Control**

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Abstract: Brain-machine interfaces (BMIs) decode brain signals into control commands for external devices. In doing so, they provide an alternate means of interaction with the environment for individuals with severe motor impairment resulting from neural injury or degenerative disorders. Apart from assistive functions, BMIs may also aid in rehabilitation by providing sensory feedback in response to user effort. In such applications, smooth BMI function relies on timely and accurate detection of attempted movement. The sensorimotor "mu" rhythm of the electroencephalogram (EEG) is commonly used for BMI control. This idling rhythm (seen at rest) is suppressed by actual/imagined movement. Here, we attempt early detection of cued hand movements from continuously recorded EEG. We measured EEG and grasping force in five healthy volunteers over three weekly sessions with IRB approval. Subjects responded to intermittent visual cues by squeezing a hand dynamometer. Their EEG was classified offline in 125 ms intervals based on EEG spectral features using a hidden Markov model into rest and movement-related states, estimated for each subject from a training session and tested on two subsequent sessions. Excluding one subject with poor signal quality, the onset of movement was detected with a mean sensitivity of 78% (64-86%) and specificity of 70% (59-77%); on average, true positive detections preceded movement by 31 ms (-191 to 278 ms). Hence, movement-related brain activity can be detected in close temporal correlation with effort, thus enabling timely sensory feedback to the user.

Supported by: The project described was supported by startup funds from the University of Kentucky College of Engineering.

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#107 Abstract Title: **Exploring the Effects of Developmental Alcohol Exposure in the Absence of Sensory Preexposure on Adolescent Drinking Habits in Rats.**

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Abstract: It is known that alcohol exposure during fetal development can have multiple negative long-term effects for exposed offspring, including increased risk for problem drinking and alcohol-related problems later in life. This increased risk has been linked to reduced sensitivity to the aversive chemosensory (smell and taste) properties of alcohol (ETOH) (Spear & Molina, 2005), which normally suppress drinking. The current study investigated the effects of fetal/neonatal ETOH exposure in the absence of exposure to the taste and smell of ETOH on adolescent drinking habits. On postnatal days (PND) 1-7, Sprague-Dawley rat pups were intubated with 6.0g/kg/day ETOH, an equivalent volume of milk or received no treatment. These intubations of ETOH produce the physiological effects of ETOH in the CNS but bypass taste/smell processing. From PND 45-60 (late adolescence), drinking behavior was assessed in a limited-access drinking paradigm. During each session, water-restricted subjects were allowed to drink from a bottle containing one of the following solutions ETOH (.05%, 3%, 6% and12%), sucrose (sweet) (.03, .01, .1, and 1M), and quinine HCl (bitter) (.001, .01, .1, and 1mM). The ETOH-exposed offspring did not show an increased preference for any of the ETOH doses, or to sweet or bitter controls. Females consumed more of the bitter solutions when corrected for bodyweight relative to males, but only in the non-treated control group. These results suggest that increases in adolescent or adult alcohol consumption after developmental exposure may be due to previous exposure to the taste/smell of ETOH rather than any CNS mediated change.

Supported by: Supported in part by pilot grant funding from the University of Kentucky and from NIAAA 017956 to SB.

Group: Undergraduate Student

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#108 Abstract Title:	**Adolescent Binge Alcohol Exposure Does Not Produce Persistent Decrease in Neurogenesis**

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Abstract: Excessive ethanol consumption characteristic of alcohol use disorders (AUDs) results in neurodegeneration that may underlie the downward spiral into addiction. Ethanol's effects on the hippocampus, specifically changes in adult neurogenesis, may contribute to AUDs and associated cognitive and behavioral impairments. The adolescent hippocampus is particularly vulnerable to ethanol, and ethanol-induced effects on adult hippocampal neurogenesis may contribute to hippocampal neurodegeneration and dysfunction observed in AUDs. Although alcohol intoxication initially inhibits adult neurogenesis, after 7 days of abstinence (T7) following a 4-day binge, there is an increase in hippocampal subgranular zone cell proliferation and adult neurogenesis. Furthermore, at 35 days post-ethanol exposure (T35), a 32% decrease in cell proliferation marker, Ki67, has been observed. Therefore, to investigate whether 4-day binge ethanol exposure has long-term effects on adult neurogenesis, adolescent rats were treated with ethanol (n=13) or isocaloric control (n=14) diet via intragastric gavage every 8 hours for 4 days. At T35, rats were sacrificed by a transcardial perfusion. Brains were removed, post-fixed, sectioned, and processed for Doublecortin (DCX) immunohistochemistry, which labels immature neurons in the dentate gyrus (DG). Although, we hypothesized that at T35 alcohol-exposed adolescent rats would show a decrease in DCX expression in the hippocampal DG, no statistically significant differences were seen in DCX expression between ethanol and control groups. These results suggest that the decrease in Ki67 seen at T35 does not reflect a long-term effect on adult neurogenesis, though additional time points and neurogenesis markers should be explored to fully verify this effect.

Supported by: NIAAA R01AA016959 Professional Student Mentored Research Fellowship

Group: Undergraduate Student

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#109 Abstract Title: **A Critical Period for Early-life Antipsychotic Drug Administration on Adult Behavior**

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Abstract: A dramatic rise in the number of very young children prescribed antipsychotic drugs (APDs) has been observed over the past two decades. Risperidone is the most commonly used APD for childhood behavioral disorders. Prior studies found that rats administered risperidone between postnatal days (PNDs) 14-42 were hyperactive in adulthood (Bardgett et al., 2013). The present study sought to pinpoint a critical period for risperidone exposure during development that is responsible for the observed hyperactivity. Rats received daily administration of risperidone (0.3, 1.0, or 3.0 mg/kg doses) during one of three developmental periods: PNDs 14-28, PNDs 29-42, or PNDs 14-42. The former two groups also received vehicle injections on PNDs 29-42 and PNDs 14-28, respectively. A control group was administered vehicle daily between PNDs 14-42. Beginning on PND 60, locomotor activity was tested for 60 minutes a day for five days. Consistent with previous findings, rats administered either the 1.0 or 3.0 mg/kg dose of risperidone between PNDs 14-42 were significantly more active than vehicle controls. Rats administered the high dose of risperidone between PNDs 14-28 were also more active than vehicle controls. Rats administered risperidone during PNDs 29-42 did not differ from controls. Since rats enter puberty near PND 32, the results indicate that prepubescent APD administration impacts the development of brain regions involved in locomotor activity. Our findings raise concerns about the long-term consequences of prolonged APD use in young children.

Supported by: This research was supported by grants from the National Institute of General Medical Sciences (8P20GM103436) and National Institute of Mental Health (1R15MH094955)

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#110 Abstract Title: Tomosyn Reduction Leads to Aberrant Glutamate Release in the Dentate Gyrus of the Hippocampus and a Kindling-Sensitive Phenotype in a Murine Model of Epileptogenesis

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Abstract: Epilepsy affects approximately 2.3 million adults and 500,000 children in the United States with 150,000 new cases being diagnosed each year. Despite the prevalence of epilepsy, the aberrant molecular processes that initiate and propagate epilepsy (epileptogenesis) are unknown. Dysregulation in the release of the major excitatory neurotransmitter, glutamate, as well as in the function of several presynaptic proteins associated with neurotransmitter release have been indicated as potential causes of epileptogenesis. Tomosyn, one of the presynaptic proteins implicated, is a negative regulator of glutamate release. Here we use glutamate biosensors to measure tonic, KCl evoked, and spontaneous glutamate transients in distinct sub-regions of the hippocampus (dentate gyrus [DG], CA3, and CA1) in naïve and kindled tomosyn wild type (naïve Tom+/+, n = 6; kindled Tom+/+, n = 3) and tomosyn knockout (naïve Tom -/-, n = 5; kindled Tom -/- n = 3) mice. We conducted a four-way ANOVA which revealed a significant decrease in tonic glutamate levels in kindled Tom -/- mice compared to kindled Tom+/+ mice [$F(1,13) = 6.4$, $p = 0.025$; Tukey HSD]. Our analyses also showed a significant increase in the concentration of KCl-evoked glutamate release in the DG of kindled mice compared to the DG of naïve mice and the CA3 and CA1 of both kindled and naïve mice [$F(2,26) = 6.0$; $p = 0.0073$; Tukey HSD]. Further, a significant increase was observed in the amplitude of spontaneous glutamate peaks in the DG of kindled Tom+/+ mice in the brain hemisphere ipsalateral to the kindling electrode compared to the DG in the contralateral hemisphere in kindled Tom+/+ mice [$F(1,13) = 5.3$, $p = 0.039$; Tukey HSD]. These results suggest that, in the DG, the dysregulation of proteins controlling glutamate synaptic transmission as well as aberrant glutamate release may contribute to epileptogenesis and that the hemisphere of the brain kindled is preferentially affected by stimulations.

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Group: Technician

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#111 Abstract Title: **Promoting a Targeted Neuroprotective Immune Response**

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Abstract: Macrophages, derived from resident microglia and blood monocytes, persist indefinitely at sites of spinal cord injury (SCI) and contribute to both pathological and reparative processes. More specifically, the classically activated macrophage phenotype (M1) is associated with cell loss and pathology whereas the alternatively activated phenotype (M2) is believed to promote cell protection, regeneration, and plasticity in response to injury. Unfortunately, the post-injury environment drives macrophages toward an M1 phenotype. Therefore driving and sustaining an M2 phenotype would involve either changing the environment or the way cells respond to the environment. Focusing on the later approach, our goal is to develop and refine a method for genetically engineering macrophages to utilize the M2 associated Triggering Receptor Expressed on Myeloid cells 2 (TREM2) as a means to stimulate and maintain a protective M2 phenotype. While preliminary data shows that transplanted primary macrophages transduced ex-vivo to overexpress TREM2 retain an M2 phenotype in injured spinal cord, this technique has limitations due to the variability in transduction efficiency and the stability of isolated cells. We are optimizing a method to directly target microglia / macrophages in vivo using a cell-specific promoter in a viral vector. In order to identify the optimal promoter, transduction effeciency and specificity of candidate promoter regions are being investigated with qPCR, flow cytometry, and immuno-staining. Once developed, this targeted approach will be a powerful tool to analyze the role of M2 phenotype macrophages in the dynamics of progression and repair in spinal cord injury. Further, this could lead to a clinical therapy relevant to the broad spectrum of injuries in which microglia / macrophages are involved.

Supported by: Wings For Life Individual Grant: WFL-US-012/13 University of Kentucky Start-up funding

Group: Technician

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#112 Abstract Title: Fenbendazole Improves Pathological and Functional Recovery Following Traumatic Spinal Cord Injury

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Abstract: During a study of spinal cord injury (SCI), mice in our colony were treated with the anthelmintic fenbendazole to treat pinworms detected in other mice not involved in our study. As this was not part of the original experimental design, we subsequently compared pathological and functional outcomes of SCI in female C57BL/6 mice who received fenbendazole (150 ppm, 8 mg/kg body weight/day) for 4 weeks prior to moderate contusive SCI (50 kdyn force) as compared to mice on the same diet without added fenbendazole. The fenbendazole-treated mice exhibited improved locomotor function, determined using the Basso mouse scale, as well as improved tissue sparing following contusive SCI. Fenbendazole may exert protective effects through multiple possible mechanisms, one of which is inhibition of the proliferation of B lymphocytes, thereby reducing antibody responses. Autoantibodies produced following SCI contribute to the axon damage and locomotor deficits. Fenbendazole pretreatment reduced the injury-induced CD45Rpositive B cell signal intensity and IgG immunoreactivity at the lesion epicenter 6 weeks after contusive SCI in mice, consistent with a possible effect on the immune response to the injury. Fenbendazole and related benzimadole antihelmintics are FDA approved, exhibit minimal toxicity, and represent a novel group of potential therapeutics targeting secondary mechanisms following SCI.

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Group: Professional Staff

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#113 Abstract Title: **Neuropsychiatry of Anti-NMDA-receptor Autoimmune Encephalitis**

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Abstract: Introduction: Anti-NMDA-receptor encephalitis is an autoimmune encephalitis, with neoplasm in 50% of the cases, characterized by acute onset of neuropsychiatric symptoms. These patients often recover after timely intervention. However, post-treatment neuropsychological status varies widely. Methods/Case Study: This is the case of a 33-year-old right handed woman who experienced two probable bouts of anti-NMDA receptor encephalitic episodes in 10 years. The first episode occurred at age 24, when she presented with acute headaches, hallucinations, violent outbursts, and seizures. She was comatose for 8 weeks until high dose prednisone. Nine years later, she presented with another episode, now accompanied by multiple status epilepticus. IVIG transfusion and plasmapheresis were initiated. Although teratoma was ruled out, laboratory findings revealed anti-NMDA receptor encephalitis. After plasmapheresis, neurological signs improved rapidly, but she remained cognitively impaired. Results: Post-plasmapheresis, the patient still had deficits in intelligence, memory, mental flexibility, language, visuospatial skills, and motor dexterity. Most notable deficits were in her verbal fluency and mental flexibility. Depression and anxiety levels were mildly elevated. Discussion: Once largely unknown, anti-NMDA-receptor encephalitis is no longer considered a rare neurologic autoimmune disorder. Although recent literature is finding higher prevalence of this condition, data on post-treatment neuropsychological status remain limited. This case study revealed frontally loaded cognitive deficits accompanied by mood disturbance status post-plasmapheresis.

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Group: Professional Staff

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30th Annual BGSFN Spring Neuroscience Day
POSTER ABSTRACTS

Thursday, March 27, 2014 **Lexington Convention Center**

#114 Abstract Title: **Neuropsychology of PARK2-associated Parkinson's Disease**

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Abstract: INTRODUCTION: Cognition is thought to be resilient in patients with early-onset Parkinson's disease (EOPD) with PARK2 mutation on chromosome 6. Evidence for reduced cognitive risk in PARK2-related EOPD is based on dementia-specific clinical screenings and group means of broad index scores insensitive to individual, domain-specific performance. Screening and in-depth neuropsychological testing used in combination, though, have revealed significant cognitive differences between two brothers with PARK2 mutations, one with mild dementia and the other largely intact. METHODS/CASE STUDY: Two sisters with PARK2 EOPD were examined, a 35-year-old left-handed woman (S1) and a right-handed 53-year-old (S2). Premorbid status, memory, processing speed, language, visuospatial skills, and executive skills were assessed. RESULTS: S1 evinced baseline reading disorder and learning difficulty, with nonverbal capacities slightly stronger than verbal. Learning was weaker than retention. Verbal slowing was evident, and semantic fluency was impaired more than phonemic. Line orientation was impaired, but block design was intact. S2 displayed stronger verbal than nonverbal capacities, with intact processing speed, learning, and recall. She was within normal limits on language and visuospatial skills, with relative weakness confrontation naming. High-level executive functions were relatively preserved for both sisters. DISCUSSION: Variance in cognitive phenotype in PARK2 EOPD shows the importance of baseline cognitive factors, so far absent in extant literature, in estimating cognitive performance in genotype groups. Both sisters displayed relatively intact high-level executive functions, perhaps reflecting the smaller cognitive impact of PARK2 found elsewhere in the literature.

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Group: Professional Staff

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POSTER ABSTRACTS

Thursday, March 27, 2014 **Lexington Convention Center**

#115 Abstract Title: **Characterization of volitional behavior after orofacial incision and trigeminal nerve injury in the rat: anxiety, depression-like behavior and widespread hypersensitivity**

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Abstract: Chronic constriction injury of the infraorbital nerve (ION-CCI) has been used to model clinical orofacial neuropathic pain for 20 years. ION-CCI produces decreased head withdrawal thresholds to evoked mechanical, cold and heat stimulation while sham injury (incision) produces no such hypersensitivity. Long-term effects of ION-CCI and orofacial incision injury (OII) on volitional exploratory behaviors such as open-field, light-dark exploration; together with the conjunctive effects of peripheral and facial mechanical stimulation and restraint stress have not been investigated. We sought to determine if ION-CCI or OII resulted in anxio-depressive behavior and thermal and/or mechanical hypersensitivity distal to injury. Compared to naïve rats, OII and ION-CCI produced significant but divergent effects in: anxio-depressive behavior in the open-field test, anxiety-like behavior in the light-dark box test-exacerbated by restraint, facial von Frey and somatic pain stress, paradoxical behavior in the sucrose feeding test for anhedonia, paradoxical behavior in the splash-test for depression, anxiety-like behavior after a facial cold allodynia test, thermal place-preference, mPFC pERK-immunoreactivity and forebrain reactive microglia. OII produced anxiety and depressive-like behavior in addition to altered sensitivity to thermal stimuli and increased sensitivity to noxious and non-noxious mechanical stimuli. In summary, ION-CCI produced anxiety-like behavior, but significantly less than OII, mild sensitivity to thermal stimuli, and increased sensitivity to noxious and non-noxious mechanical stimuli. OII results in long-term symptoms of anxiety, depression and widespread hypersensitivity. Secondly, the OII model may be useful in delineating the pathogenesis of widespread hypersensitivity as a result of orofacial injury, clinical depression and widespread pain disorder (fibromyalgia).

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#116 Abstract Title: **Effects of Acetyl-l-carnitine on volitional pain-related behavior after acute visceral and somatic nociceptive stimulation**

Author(s): K.N. Westlund, Dept of Physiology, College of Medicine, U of Kentucky
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Abstract: Acute pancreatitis pain presents as unremitting and often incapacitating abdominal pain, for which there is no specific therapy. Acetyl-L-Carnitine is an acetylated derivative of L-Carnitine and available as an over-the-counter nutritional supplement. ALC has been shown to alleviate acute pancreatitis by increasing glutathione content and by inhibition of lipid peroxidation, to be antinociceptive in models of inflammatory and neuropathic pain through the upregulation of mGluR2, and reduce reactive oxygen species through anti-inflammatory mechanisms. ALC may protect against cell degeneration and pain in pancreatitis by preventing mitochondrial injury. In the present study, we sought to determine the effects of ALC on anxiety-related behaviors in the light-dark box test and volitional pain-related behavior using a 10oC-45oC thermal preference task after 1) induction of acute visceral pancreatitis-related pain with DBTC and 2) induction of acute somatic pain using a thermal conditioning stimulus. Analgesic effects of ALC were also tested using the 44oC hotplate test in naïve rats for comparison to a mu-opiate analgesic. DBTC produced thermal hypersensitivity and anxiety-like behavior. ALC prevented thermal sensitivity accompanying DBTC chemically induced pancreatitis, but enhanced DBTC-induced anxiety-like behavior. A conditioning somatic pain stressor also produced thermal hypersensitivity and anxiety-like behavior. ALC reduced subsequent thermal sensitivity without effects on stressor-induced anxiety-like behavior. ALC produced morphine (~5mg/kg) equipotent analgesia on the 44oC hotplate test. These results demonstrate 1) short-term visceral and acute somatic pain produce anxiety-like behavior and decreased heat-pain tolerance; 2) ALC protected against thermal hypersensitivity secondary to visceral pain, 3) ALC acts well as an analgesic.

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30th Annual BGSFN Spring Neuroscience Day
POSTER ABSTRACTS

Thursday, March 27, 2014 **Lexington Convention Center**

#117 Abstract Title: **Carpe Datum! Enzyme Based Microelectrode Arrays Offer Novel Insights into Mechanics of Epilepsy**

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Abstract: Aberrant regulation of glutamate has been strongly implicated in epilepsy, a chronic neurological condition affecting about 50 million people worldwide. Nearly 30% of epileptic patients do not respond to current treatments, therefore novel therapies and therapeutic targets are being heavily investigated. These studies illustrate the use of three different microelectrode array (MEA) designs to elucidate more information about glutamate dynamics in different animal models of epilepsy. Enzyme-based MEAs, coupled with real-time amperometry, can reliably measure resting levels of glutamate as well as dynamic glutamate release and clearance events. Acute recordings of glutamate were conducted in different animal models of epilepsy including kindled, traumatic brain injured (TBI) and genetic models. In addition, chronic, awake recordings were completed in 4-aminopyridine (4-AP) treated rats. Microelectrode arrays offer better spatial resolution than traditional approaches to investigate in vivo neurotransmission, allowing us to record glutamate dynamics in discrete areas of the hippocampus. MEAs can also record on a sub-second basis, allowing us to detect never before seen, real-time, spontaneous and highly rhythmic bursts of glutamate we term “transients”. These transients were seen in all sub-regions of the hippocampus, and in all models. The amplitude of the transients was increased in anesthetized, kindled models, and increased during status epilepticus in awake animals. In chronically implanted rats, the transients coincided with behavioral signs of status epilepticus, and both transients and seizure behavior ceased upon administration of TTX. Future studies are needed to determine the timing of the seizure behavior and corresponding glutamate transients. If the glutamate transients precede the seizure behavior, this could be a powerful clinical tool in the prediction of seizures.

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Group: Professional Staff

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#118 Abstract Title: **Contralateral Hypersensitivity in TNFR KO mice with Trigeminal Inflammatory Compression of the Infraorbital Nerve**

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Abstract: The TNFα is a proinflammatory cytokine involved in inflammatory pain through its receptors TNFR1/2. TNFα is increased in our animal models with orofacial pain and patients with temporomandibular joint disorders. Although several models have been used in TNF receptor deficient animals to test TNFα in inflammation, the role of TNFα in nerve injury induced orofacial pain is not clear. In a mouse model we developed recently with trigeminal inflammatory compression of infraorbital nerve, TNFR1/2 knockout mice were tested behaviorally and serologically to explore TNFα's role in orofacial neuropathic pain mice. Chromic gut suture induces ipsilateral whisker pad mechanical allodynia in wild type mice. TNFR1/2 knockout mice have mechanical hypersensitivity. Severity of ipsilateral mechanical hypersensitivity is equivalent in TNFR1/2 knockout and wild type mice. P38 inhibitor reversed ipsilateral mechanical allodynia significantly at 1 hour in TNFR1/2 knockout mice which is delayed and shorter than its effect in wild type mice. There is no p38 inhibitor effect on contralateral side in TNFR1/2 knockout mice with trigeminal inflammatory compression. Cytokine panel shows increased basal TNFα in serum in TNFR1/2 knockout mice but not after nerve injury. Microglial activation is evident in trigeminal nucleus after trigeminal inflammatory compression. In conclusion, the current study shows severe pain-like behavior in TNFR1/2 knockout mice with the trigeminal inflammatory compression of infraorbital nerve. Pharmacological manipulation effective in wild type mice is less effective in TNFR1/2 knockout mice. Microglial activation is implicated as a trigger of increased circulation TNFα.

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Group: Professional Staff

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#119 Abstract Title: **Cannabinoid Receptor 2 Agonist Attenuates Pancreatic Inflammation and Pain-Related Behavior in Rats with Alcohol and High Fat Induced Chronic Pancreatitis**

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Abstract: Chronic Pancreatitis (CP), due to complex and multifactorial pain aetiology, involved many factors including structural abnormalities of the pancreatic gland as well as dysfunction of peripheral and central pain processing. In past, some drugs were developed to treat different painful pathological states. Despite their commercial success these medicines are falling short to fulfill the medical need due to either a partial pain relief or side effects. Recently availability of selective pharmacological tools enabled a great advance of our knowledge of a cannabinoid receptor2 (CB2) role in pathophysiology. In particular CB2 emerged as an attractive target for treatment of inflammatory and neuropathic preclinical pain models. In this study, a novel CB2 receptor agonist (LY02) was investigated for the treatment efficiency of alcohol/high fat (AHF) pancreatitis pain in a rat CP model. Rat fed AHF developed a series of visceral pain-like behaviors started from week 3; reached maximum at week 5 and lasted as long as 16 weeks. The pancreatic gland global degeneration (cell atrophy), vacuolization formation (fat deposition) and fibrosis featured their AHF chronic pancreatitis. In rats with AHF chronic pancreatitis treated with LY02, 10mg/kg, oral feeding, twice a day, 7 days for entire treatment course. LY02 attenuated pain-related behaviors after 3 days applications: recovered paw withdrawal threshold (PWT), prolonged abdominal withdrawal latency (ABWL), attenuated nocifensive responses to noxious 44°C hotplate stimuli. LY02 significantly protected pancreatic tissue damage and fibrosis. Compared all the parameters above between AHF drug treatment group and HFA non-drug treatment group there is a statistic significant difference.

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POSTER ABSTRACTS

Thursday, March 27, 2014 **Lexington Convention Center**

#120 Abstract Title: **Rearing Environment Modulates the Effect of a Glucocorticoid Receptor Antagonist on Cocaine Self-Administration in Rats**

Author(s): R. S. Hofford, Dept of Psychology, U of Kentucky
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Abstract: Isolation rearing is often used as a model of early life stress in rodents. Consistent with other chronic stressors applied early after weaning, isolation rearing increases stimulant self-administration. Studies suggest that the stress hormone corticosterone and its receptor, the glucocorticoid receptor (GR), modulate self-administration. The present studies tested the hypothesis that rats raised in isolation (IC) would demonstrate a diminished response to a GR antagonist and would express decreased GR in the stress-relevant prefrontal cortex compared to rats raised in an enriched environment (EC). For experiment 1, male Sprague-Dawley rats were placed in IC and EC conditions immediately following weaning. Rats were then trained to self-administer cocaine (0.03, 0.1, or 0.3 mg/kg) on a FR1 schedule. Once stability was reached, rats were pretreated with the GR antagonist, RU486 (20 mg/kg, s.c.) or vehicle. For experiment 2, a separate group of rats were placed in IC and EC conditions and then were killed and medial prefrontal cortex, orbitofrontal cortex, and amygdala were removed for semi-quantification of GR levels using Western blot. Pretreatment with RU486 decreased responding in EC rats at the lowest dose of cocaine (0.03 mg/kg) but did not affect responding in IC rats. No significant differences in GR expression were found in any brain area examined. The subsensitivity to RU486 observed in IC rats at a low unit dose of cocaine may reflect GR overactivity by corticosterone rather than a specific alteration in GR protein expression.

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Group: Postdoctoral Fellow
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#121 Abstract Title: Mitochondria Associated miRNA Expression After Traumatic Brain Injury

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Abstract: Traumatic brain injury (TBI) is a major cause of death and disability worldwide. However, the molecular events contributing to the pathogenesis are not well understood. Mitochondria serve as the powerhouse of cells, respond to cellular demands and stressors, and play an essential role in cell signaling, differentiation, and survival. There is clear evidence of compromised mitochondrial function following TBI, however, the contributing underlying mechanisms are not well known. Recent studies suggest a dynamic relationship exists between mitochondrial function and microRNA (miRNA) activity. MiRNAs are small non-coding RNA molecules that regulate gene expression at the post-transcriptional level, and function as important mediators of many biological processes including neuronal development, synaptic plasticity, and neurodegeneration. In the current study, we report that miRNA processing machinery, including dicer and argonaute (Ago2), as well as a number of miRNAs are associated with hippocampal mitochondria, and that the mitochondria associated miRNA profile is altered following TBI. In particular, we determined that dicer and Ago2 are located in mitochondria isolated from brain, spinal cord, heart, liver, and kidney and to a lesser extent in lung. In addition, dicer and Ago2 were located in both synaptic and non-synaptic mitochondria and enriched in fractions containing the mitochondrial membrane and matrix. Following TBI in rats, we observed that 1) the levels of several miRNA are differentially expressed in hippocampal mitochondria compared to cytoplasmic fractions; 2) miR-155 and miR-223, two inflammatory/immunity-related miRNAs, are highly elevated in both the hippocampal mitochondrial and cytoplasmic fractions; and 3) there was no change in mitochondrial dicer or Ago2 levels. We hypothesize that mitochondria serve as a platform for miRNA function, and play an important role in regulating miRNA activities in response to pathophysiological signaling events following TBI.

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30th Annual BGSFN Spring Neuroscience Day
POSTER ABSTRACTS

Thursday, March 27, 2014 **Lexington Convention Center**

#122 Abstract Title: **Role of the calcineurin/NFAT pathway in astrocytic glutamate uptake: Implications for Alzheimer's disease**

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Abstract: One of the essential functions of astrocytes is the prevention of excitotoxicity via the removal of excess glutamate from the extracellular milieu. Astrocytic glutamate uptake, carried out primarily by the type 2 excitatory amino acid transporter (EAAT2), accounts for as much as 90% of total glutamate uptake in some brain regions, like the hippocampus. During the progression of Alzheimer's disease (AD), hippocampal EAAT2 protein levels drop off by nearly 75% and correspond to increased activity of the protein phosphatase calcineurin (CN) and the transcription factor, NFAT. Moreover, loss of EAAT2 levels in primary astrocytes in response to inflammatory insults or pathogenic amyloid-b (Ab) peptides is largely prevented by inhibition of CN/NFAT activity. In the present set of studies, we used primary astrocyte cultures and intact APP/PS1 (5XFAD) mice to further investigate the role of astrocytic CN/NFAT signaling in AD-related glutamate dysregulation. Whole-cell voltage clamp recordings revealed that CN/NFAT activity directly leads to reduced glutamate uptake in primary cortical astrocytes, whereas selective inhibition of astrocytic CN/NFAT signaling in 5XFAD mice using adeno-associated virus (AAV) vectors led to a significant ($p < 0.05$) increase in hippocampal protein levels for EAAT2, but not EAAT1. These results are generally very consistent with our earlier studies on primary astrocyte cultures and postmortem human brain tissue and suggest that astrocytic CN/NFAT activity negatively affects glutamate regulation during the progression of AD. Moreover, these findings may explain why astrocyte specific inhibition of CN/NFAT signaling improves hippocampal synaptic plasticity and cognitive function in 2XFAD mice, as demonstrated by our recently published work. Ongoing studies are using glutamate sensitive microelectrode arrays and patch clamp electrophysiology to directly determine the extent to which astrocytic CN/NFAT activity regulates basal and synaptically-released glutamate levels in 5XFAD mice.

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Group: Postdoctoral Fellow

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30th Annual BGSFN Spring Neuroscience Day
POSTER ABSTRACTS
Thursday, March 27, 2014 Lexington Convention Center

#123 Abstract Title: **Increased inhibition in the dorsal vagal motoneurons after streptozocin-induced diabetes**

Author(s): C.R. Boychuk, Dept of Physiology, U of Kentucky
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Abstract: Neurons in the dorsal motor nucleus of the vagus (DMV) comprise the preganglionic parasympathetic motor output to much of the viscera and critically contribute to autonomic regulation of energy homeostasis. Gamma-aminobutyric acid (GABA) is the main inhibitory neurotransmitter mediating both tonic (extrasynaptic) and phasic (synaptic) inhibition to the DMV. A small body of evidence suggests that GABAA receptor activity may be abnormal following diabetes, which is known to disrupt autonomic function. The present study investigated the effect of chronic hyperglycemia on GABAA receptor-mediated inhibition in the DMV using whole-cell patch-clamp recordings. CD-1 mice were injected with either streptozotocin (STZ; 200mg/kg; i.p.) to induce hyperglycemia or saline. DMV neurons from diabetic mice only demonstrated subtle alternations in phasic currents, including increased spontaneous inhibitory postsynaptic current amplitude and THIP-sensitivity (3μM; a δ-subunit selective GABAA receptor agonist). Application of the non-specific GABAA receptor agonist, muscimol, to recorded DMV cells evoked an “inducible” outward current in DMV neurons from control and diabetic animals. This response was increased in diabetics both in amplitude and the number of neurons demonstrating it. Tonic GABA current evoked by THIP was significantly increased in STZ-treated compared to control mice ($p<0.05$). Application of a low concentration of gabazine (1μM), a γ-subunit selective GABAA receptor antagonist, revealed a significant increase in gabazine-sensitive tonic current density in neurons from STZ-treated mice. Moreover, STZ treatment increased the proportion of neurons with a gabazine-sensitive tonic current. Quantitative RT-PCR indicated message for γ-, α1 and α4-subunits was increased in the dorsal brainstem of diabetic mice. These data indicate that hyperglycemia 1) increases tonic current density in the DMV; 2) increases the proportion of neurons expressing tonic current; and 3) these changes are likely linked to increased transcription of specific subunits. Results suggest that plasticity of GABAA receptor-mediated signaling related to changes in receptor subunit composition accompanies chronic hyperglycemia in diabetes. The enhanced tonic GABAA receptor current in STZ-treated mice could contribute to autonomic and metabolic dysfunction in diabetes.

Supported by: NIH Award: RO1 DK056132

Group: Postdoctoral Fellow

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#124 **Abstract Title:** **Age-Related Neuprinflammatory Responses in Spinal Cord Injury**

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Abstract: The incidence of spinal cord injury (SCI) among older individuals has increased in recent years. According to the Kentucky Injury Prevention and Research Center, in 2007, 61% of all non-fatal SCIs were sustained by individuals >45 years old. Aged animals have reduced rates of recovery, residual locomotor deficits, and increased areas of pathology and demyelination after SCI compared to young animals, but the mechanisms behind these age-related differences are not well understood. Macrophages are a hallmark of CNS trauma and can facilitate repair or pathology in the injured spinal cord. Age is a key regulatory of macrophage function and aging is associated with increased activation of pathological macrophage phenotypes. Therefore, we hypothesize that age-related differences in the macrophage response may contribute to functional recovery after SCI. To address this hypothesis, we compared the inflammatory response in young (3-4 month old) and aged (10-16 month old) mice after laminectomy receiving either a sham or a moderate contusion SCI (50-75 Kdyne Infinite Horizons). We detected a significantly dampened pro-reparative macrophage response to SCI in aged vs. young animals (indicated by decreased expression of Arginase-1 and Fizz1). We also investigated the effect of age on functional recovery with the Basso mouse scale (BMS), grid walk, and DigiGait system. Our results indicate that aged mice exhibited worse functional deficits when compared to young mice. Collectively, these data demonstrate an important role for age in changes of inflammatory responses and functional recovery in the context of SCI. Most clinical therapies are being examined in individuals regardless of age and are based upon data generated almost exclusively using young animals. Our data highlight the potential for immunomodulatory therapies to have decreased efficacy in aged individual receiving SCI and highlight the need to elucidate the cellular mechanisms contributing to age-related differences in functional recovery.

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Group: Postdoctoral Fellow

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Thursday, March 27, 2014 **Lexington Convention Center**

#125 Abstract Title: **Post-operative electrode mapping in DBS surgery**

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Abstract: Deep brain stimulation (DBS) has been a widely accepted surgical treatment for medically refractory Parkinson's disease (PD) since its FDA approval in 1997. One of the major advantages to this treatment modality is the versatility it offers in terms of physician choice for anatomical stimulation target. Experience has shown that a multitude of diseases may be treated by targeting different structures, and similarly a single disease may be effectively treated by singular stimulation at multiple different locations. With regards to PD, stimulation at either the subthalamic nucleus (STN) or Globus Pallidus internal segment (GPi) has proven to be effective. Each of these locations present differing side effect profiles that can influence surgeon choice. Correlation between side effects or suboptimal symptom control and precise location of stimulation has been limited to relatively large anatomical borders. We have developed a postoperative targeting methodology combining CT and MRI imaging modalities with the aim of more precisely localizing the specific anatomic areas being stimulated at each of the four leads implanted within the target nucleus. We will present several cases demonstrating this technique and the specific locations of stimulation correlated to side effects and symptom control.With this information, we hope to better understand the side effect profiles and effectiveness of stimulation at specific areas of the target nuclei. Additionally, this information will help to compare different intraoperative targeting strategies by providing a radiographic means to evaluate their accuracy.

Supported by: NA

Group: Postdoctoral Fellow

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POSTER ABSTRACTS

Thursday, March 27, 2014 **Lexington Convention Center**

#126 Abstract Title: **The behavioral and physiological effects of nicotine on crayfish**

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Abstract: In many areas of the world where smoking is permitted, cigarette butts are often not properly disposed of. They get tossed onto the ground, where they eventually get washed away by precipitation and enter streams and rivers. Organisms often inhabit these streams and suffer from the nicotine still present in the butts. Nicotine is a known sedative, which depresses the passage of nerve impulses and increases the effect of serotonin. Depending on the exposure level nicotine can even inhibit important neurological functions. Many stream and lake borne animals are dependent on proper neurological function for escape responses and survival. Since crayfish are readily accessible and relatively easy to work with for physiological and behavioral experiments as well as having a rich history in neurophysiological studies we chose to work with them. Crayfish are known as sentinels of water quality in streams as many studies have been designed around them. The effects of nicotine on the behavior and physiology of crayfish during an escape response was examined. The results indicated that nicotine caused the crayfish to lose the ability to respond to their environment from sensory stimuli. Nicotine correlated with a decrease in physiological function in response to stimuli. Central neural control on the tail flip behavior, cardiac regulation and control of motor units to ventilatory muscles appear to be altered depending on exposure dosage. Further studies are underway to identify Ach receptor subtypes within defined neural circuits which correlate to particular behaviors.

Supported by: Personal funds (RLC)

Group: High School Student

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Thursday, March 27, 2014 **Lexington Convention Center**

#127 Abstract Title: **Characterization of an Insm1 mutant in the zebrafish**

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Abstract: Insm1a, the zebrafish ortholog of mammalian INSM1, is a known regulator of pancreatic beta cell differentiation, sympatho-adrenal development, and is upregulated in many cancers. Using morpholino-mediated knockdown, our lab has shown a requirement for insm1a in proper timing of photoreceptor differentiation. Because the knockdown only persists for 4 days, we have an incomplete picture of the effect of insm1a after 4 days post fertilization (dpf). Examining the function of insm1a later in development, and in the adult retina, will require an insm1a mutant. Here, we present initial characterization of a zebrafish line carrying a putative null mutation in insm1a. We hypothesize that the mutant will phenocopy the insm1a morphant during the first 4 days of embryonic development, and that survival of the homozygous mutants will not be adversely affected. Preliminary data shows that homozygous mutant survival is not affected at 3 and 5 days post fertilization (dpf), as mutants survive as well as wild types. At 3dpf and 5dpf, a decrease of rod photoreceptor cells was observed in a subset of embryos by fluorescent microscopy. Genotyping studies revealed that these defects occurred only in individuals carrying at least one copy of the insm1a mutation. Preliminarily, these results suggest that the insm1a mutants may be a good alternative to the insm1a morphants for studying the function of insm1a in late development and in the adult zebrafish retina.

Supported by: Current Funding from: NIH award RO1 EY021769 (ACM) and the Pew Biomedical Scholars Program (ACM). Previous funding from: Fight For Sight (ACM), and the Gertrude Flora Ribble Graduate Fellowship (MAFO)

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30th Annual BGSFN Spring Neuroscience Day
POSTER ABSTRACTS
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#128 Abstract Title: A novel reagent modulates CN/Cx43 interactions during the progression of Alzheimer's disease

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Abstract: Alzheimer's disease (AD)-associated neuroinflammation is characterized by microglial and astroglial activation that arises in the early stages of the disease. Upon activation, astrocytes upregulate calcineurin (CN), a protein phosphatase involved in inflammatory signaling and in the production of pro-inflammatory cytokines. These inflammatory mediators can disrupt gap junction (GJ) coupling through impairment of GJ proteins, including the most abundant astrocytic GJ protein connexin 43 (Cx43). Previous work has shown that Cx43 is selectively dephosphorylated at Ser 368 in primary astrocytes by CN. However, the functional implications of this dephosphorylation event in AD are not well-understood. In the current study, we treated primary astrocyte cultures with the Ca2+ mobilizers ionomycin and phorbol ester (Ion/PE), or with the pro-inflammatory cytokine IL-1β, in the presence or absence of the CN inhibitor cyclosporine. Using Western blot to measure the levels of dephosphorylated Cx43, we found that treatments with Ion/PE and IL-1β resulted in a significant increase in the level of dephosphorylated Cx43 relative to untreated samples ($p<0.05$). Similarly, we prepared human hippocampal membrane fractions from non-demented subjects (n=10), subjects with mild cognitive impairment (MCI) (n=14), and subjects with AD (n=21), and used Western blot to measure the levels of dephosphorylated Cx43. The results showed a significant increase in the level of dephosphorylated Cx43 in MCI samples relative to non-demented samples ($p<0.01$), which occurred in parallel to elevated CN signaling. These results suggest that activation of CN leads to increased levels of dephosphorylated Cx43 which occurs selectively in MCI, and may contribute to early clinical progression of AD through disruption of astrocytic gap junctions. Furthermore, we developed a novel mimetic peptide reagent that mirrors a portion of the C-terminus of Cx43. Preliminary work reveals that our peptide reagent significantly reduces levels of dephosphorylated Cx43, measured using Western blot ($p<0.001$), but does not interfere with other CN substrates (e.g. NFAT), measured using an NFAT-Luciferase reporter assay. These results suggest that our mimetic peptide may selectively interfere with CN/Cx43 interactions. Ongoing studies are being completed to further characterize the mimetic peptide and to observe its functional ramifications on GJ coupling during the progression of AD.

Supported by: NIH award: R01 AG027297, The PhRMA Foundation, and a gift from Jeff and Patti Tautenhan

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#129 Abstract Title: **Superselective Intra-arterial Administration of Verapamil is Profoundly Neuroprotective in Experimental Ischemic Stroke**

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Abstract: While intravenous and intra-arterial thrombolysis are mainstays in acute ischemic stroke therapy, clinical outcomes lag significantly behind improving rates of revascularization. In this setting, we explore adjunctive, targeted pharmacotherapy for reducing ischemic injury. Previous neuroprotective studies failed due to long intervals between symptom onset and drug administration, lack of concordant thrombolytic revascularization, and lack of targeted administration to the affected vessel. Despite known neuroprotective properties, verapamil, a calcium channel blocker (CCB) that is already safely injected intra-arterially (IA) for vasospasm, has never been rigorously investigated as a stroke therapy. To determine whether verapamil might be an effective stroke therapy when administered in this fashion, we have developed a novel method to mimic the clinical condition of superselective IA pharmacotherapy administration after vessel recanalization in rodent models after experimental ischemic stroke (transient middle cerebral artery occlusion, MCAO). Specifically, after 1 hour MCAO in three month old male C57/Bl6 mice, we examined the potential neuroprotective effects of verapamil administered via the external carotid artery (10mg/kg) to the internal carotid artery or intraperitoneal injection (IP, 15mg/kg). On post stroke day three (3), Tetrazolium chloride (TTC) staining of sectioned brains and subsequent infarct volume measurement with NIH Image J software demonstrated a significant reduction in infarct volume with IP verapamil that was even further reduced with IA administration, both as compared to controls injected IA or IP with 0.9% saline. These results suggest that IA administration of verapamil following recanalization after acute large vessel occlusion, may be an effective neuroprotective stroke therapy that could be readily employed in human ischemic stroke patients.

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#130 Abstract Title: **A novel statistical procedure for identification of individual differences in drug abuse**

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Abstract: About half of individuals that receive treatment for drug addiction relapse (NIH, 2012). Researchers have used sign and goal tracking models to study the vulnerability of drug taking. Sign trackers are presumably more sensitive to the cues that become associated with drug taking. In this study adult male quail (N=15) were presented with a light (CS) on one end of a 4ft x 2ft chamber. After a variable amount of time (90 sec VT), a door at the opposite end of the chamber was opened and male quail had visual access to a female quail (US) for 8 sec. Birds that spent significantly more time near the light were categorized as sign trackers. Those that spent more time near the window were categorized as goal trackers and those that did not show a difference in their time spent near the light versus the window were categorized as intermediates. A novel statistical procedure that involved using individual t-tests on the scores of individual birds was used to determine significance. Five subjects were found to be goal trackers, [t (89), p<.0001].Two subjects were found to be sign trackers, [t (89), p < p < .0001-.002], and one subject showing a trend of sign tracking, [t (89), p < .06]. There were 8 subjects that showed neither sign tracking nor goal tracking behavior, [t (89) p < .12-p < .98]. This model adds a less arbitrary method of identification for sign and goal tracking behavior to current research in drug addiction.

Supported by: NIDA Grant DA 022451

Group: Graduate Student

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#131 Abstract Title: **Sox4 Regulates Ocular Development Upstream of Hedgehog Signaling in Zebrafish**

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Abstract: Sox4 is a member of the group C SRY-box containing transcription factors. It has been reported to regulate retinal neurogenesis in mice and Xenopus. Zebrafish have two co-orthologs of the mammalian sox4 gene: sox4a and sox4b. Their functions during zebrafish ocular development are not clear. The purpose of this project was to study the role of sox4 during oculogenesis in zebrafish. Using fluorescent in-situ hybridization, sox4a and sox4b transcripts were detected in the developing zebrafish brain and periocular mesenchyme but not the eye prior to 24 hpf. Sox4a/b expression was initiated within the retina by 36 hpf and thereafter spread to the ganglion cell layer (GCL) and inner nuclear layer. Sox4 knockdown caused ocular coloboma, ectopic cell proliferation and reduced numbers of rod photoreceptors. The rod lineage transcription factor Nr2e3 showed prolonged expression in sox4 morphants, suggesting that rod photoreceptors were specified but did not terminally differentiate. Expression of the Hedgehog (Hh) signaling ligand ihhb was strongly upregulated in sox4 morphants. Consistent with elevated Hh pathway activity, the expression of pax2a in the optic stalk, which is induced by midline Hh signaling, was expanded in sox4 morphants. Treatment of sox4 morphants with the Hh inhibitor cyclopamine or co-injection of an ihhb morpholino rescued the coloboma phenotype. Overexpression of sox4 in WT embryos caused cyclopia. Coloboma and cyclopia are known diseases related to increased or reduced Hh signaling, respectively. Based on the fact that sox4 knockdown causes coloboma with elevated ihhb expression while sox4 overexpression causes cyclopia, and the coloboma phenotype can be rescued by Hh inhibitor or ihhb co-knockdown, we conclude that sox4 controls ocular development by negatively regulating Hh signaling.

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Previous funding: Knights Templar Eye Foundation.

Group: Graduate Student

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#132 Abstract Title: **Binge alcohol elicits increases in nestin expression: Teasing apart hippocampal neural progenitor subtypes versus reactive astrocytes**

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Abstract: Excessive alcohol consumption produces neurodegeneration and cognitive impairments that may recover with abstinence. Previous work suggests that “reactive neurogenesis” in abstinence may contribute to recovery. Specifically, alcohol-induced reactive neurogenesis appears to be due to an increased activation of neural stem cells 7 days into abstinence. Nestin, a universal stem cell marker, is strikingly increased following 4-day binge alcohol exposure. However, it is not known if nestin+ cells are neural progenitor cells or reactive astrocytes. Therefore, to examine the effects of binge alcohol on neural progenitor cells, alcohol was administered to adult male Sprague Dawley rats via gavage for 4 days (3xday). After 7 days of abstinence, rats were transcardially perfused and the brain collected. Tissue sections (1:12 series at 40μm thick) were processed for triple fluorescent immunohistochemistry for nestin , GFAP, and doublecortin. Z-stack confocal images were taken on nestin+ cells exhaustively around the dentate gyrus. 3D images were reconstructed and analyzed in ImageProPlus. Location and morphology of nestin and GFAP expression was utilized to differentiate neural progenitor cells from reactive astrocytes. Relative to controls, alcohol elicits an 8-fold increase in the number of nestin+/GFAP+ co-labeled cells with a circular expression pattern (Type 1) and a 5-fold increase in the number of nestin+/GFAP- cells (Type 2) in the subgranular zone (SGZ). Binge alcohol exposure appears to increase the number of both Type 1 and Type 2 progenitor cells in abstinence. Interestingly, nestin expression in Type 1 cells in the SGZ exhibits a distinct circular pattern which may be useful in distinguishing neural progenitor cells from reactive astrocytes.

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Thursday, March 27, 2014 **Lexington Convention Center**

#133 Abstract Title: **Sox11 is required to maintain proper levels of Hedgehog signaling during vertebrate ocular development**

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Abstract: The SRY (sex determining region Y)-box 11 (SOX 11) gene, codes for a transcription factor that is required for a variety of developmental processes including organogenesis, neurite outgrowth and neural cell survival. Previously, we have shown that Sox11 is required to maintain proper levels of Hedgehog signaling and the absence of which causes microphthalmia, coloboma, and specific reduction in rod photoreceptor cells. The goal of this study is to determine the mechanism by which Sox11 regulates shha transcription during ocular development in zebrafish and characterize the functional activity of human SOX11 sequence variants. Translation blocking morpholinos were injected into 1-cell stage zebrafish embryos. The embryos were collected at different time points and processed for whole-mount in situ hybridization and quantitative real time PCR. DNA samples from probands with MAC (microphthalmia, anophthalmia, and/or colobomata) were screened by sequencing the SOX11 coding sequence. In vitro transcribed sox11 mRNA was co-injected with sox11 morpholinos into zebrafish embryos. Dual-luciferase assay was performed on transfected COS-7 cells.sox11 morphants have significantly lower levels of BMP7b at 12 and 24 hpf. Two MAC patients with heterozygous sequence variations (p.G145C and p.351S-S354dup.) in SOX11 were identified. In contrast to wild type human SOX11 mRNA, mRNA containing either mutation could not rescue the abnormal eye phenotypes in the zebrafish sox11 morphants and both the mutant proteins had poor transactivation capabilities. Our results reveal that Sox11 regulates early ocular and photoreceptor development in part by maintaining proper levels of Hedgehog signaling and that perhaps Sox11 is required to activate BMP7b transcription which in turn is attenuates shha transcription in the ventral mid line.

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#134 Abstract Title: **Stopping Orofacial Pain: Re-purposing Old Drugs for New Use**

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Abstract: Approximately 1/3 of the U.S. population suffers from a chronic orofacial/headache pain condition. Trigeminal neuropathic pain is one such unilateral orofacial pain syndrome characterized by constant aching and burning thought to be caused by unintentional injury or vascular mechanical irritation of the trigeminal nerve. Patients with this type of pain are currently treated with analgesics combined with anticonvulsants and/or antidepressants due to their anxiety related to pain. However, these drugs are proving to be unsatisfactory in relieving pain. The proposed studies demonstrate alleviation of chronic neuropathic orofacial pain- and anxiety-like behaviors by administering peroxisome proliferator-activated receptor gamma (PPARγ) agonist, pioglitazone (PIO), and NMDA receptor (NMDAR) partial agonist, D-Cycloserine (DCS) in the Trigeminal Inflammatory Compression (TIC) injury mouse model we devised to mimic chronic neuropathic orofacial pain. PIO is FDA approved as Actos® for treatment of Type II diabetes. Recent studies show that this drug is effective in reducing inflammation and other types of neuropathic pain. Likewise, DCS is FDA approved under the name Seromycin® as a broad spectrum antibiotic for tuberculosis which coincidentally also has unique binding ability for the glycine binding site of NMDAR. Studies show that DCS reduces hypersensitivity as well as anxiety through an NMDAR blocking mechanism in pre-limbic forebrain in certain neuropathy models. However, PIO and DCS have never been used to treat orofacial pain. Our findings determined that Pioglitazone and D-cycloserine each reduce trigeminal neuropathic pain in mice when administered solely and have a potentiated effect when combined.

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#135 Abstract Title: **How CO2 Suppresses Synaptic Transmission: Changing in Glutamate Sensitivity**

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Abstract: Glutamate receptors sensitivity is altered upon exposure to CO2 at the Drosophila and crayfish neuromuscular junction (NMJ); therefore, we suggest that the sensitivity of the glutamate receptor is influenced by CO2 either directly or indirectly. Synaptic transmission at the NMJ and response to glutamate is decreased with lowered pH extracellularly but does not result in cessation of transmission and complete decreased sensitivity to glutamate. Thus, we investigated the drop in intracellular pH and the time domain in association with sensitivity to eEPSP. Exposing a NMJ to CO2 results in blockage of transmission within 1 or 2 minutes. Upon exchanging the tainted saline with fresh saline, transmission comes back in 1 or 2 minutes and completely recovers by 3 to 5 minutes. However, monitoring intracellular pH with pH sensitive fluorescent dye (pyranine or BCECF-AM), intracellular pH rapidly drops with exposure to CO2 but stays low for several minutes upon washing away the CO2. The pH recovers with a very slow rise over 20 to 60 minutes in these muscles. Thus, the proton exchange is slow in these cells at room temperature. Also, synaptic responses return prior to intracellular pH recovering. Thus, the muscle does not buffer the drop in pH well nor does the cell recover quickly when CO2 exposure is removed. The rapid synaptic changes suggest that the block in synaptic transmission may be due to molecular CO2 itself. We speculate molecular CO2 maybe blocking the inotropic glutamate receptor directly within the pore or in the binding domain for glutamate.

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#136 Abstract Title: **Brain Insulin Exposure: Intranasal and Acute Effects on Calcium Electrophysiological Biomarkers of Aging and Memory.**

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Abstract: Metabolic syndrome is generally defined as a constellation of symptoms consisting of insulin resistance, compensatory hyperinsulinemia, dyslipidemia, hypertension, and central obesity. While the impact of at least one of these components, type 2 diabetes (T2DM) is recognized in the periphery, it is also becoming clear that insulin resistance exists in the brain of aging and Alzheimer's disease (AD) patients. To combat this decreased insulin signaling in the brain, a successful approach has been to use intranasal insulin therapy. Results from several trials show improved cognition and memory in AD patients treated with insulin. Here, we tested the impact of daily short-acting Humalog® or long-acting Levemir® on cognitive function in 21 months-old F344 rats. Treatment lasted for approximately 18 days and in a subset of animals, the impact of intranasal insulin on the well-characterized electrophysiological marker of brain aging was measured (the Ca2+-dependent afterhyperpolarization-AHP). Using zinc-free insulin Apidra®, age-dependent changes in hippocampal insulin sensitivity were seen. Our results show that the AHP is sensitive to insulin and that intranasal delivery improves memory recall on the Morris water maze. Taken together, the AHP may represent a novel cellular target of insulin in the brain which may underlie a mechanism of improved performance in response to intranasal insulin therapy. The sensitivity of this structure to insulin places the hippocampus at the nexus between peripheral metabolic dysregulation and aging and memory processes, and also suggests a mechanism for at least partially reversing aspects of the aging phenotype.

Supported by: NIH award: R01AG033649

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POSTER ABSTRACTS

Thursday, March 27, 2014 **Lexington Convention Center**

#137 Abstract Title: Sleep Alterations In 5XFAD Mice, A Model Of Alzheimer's Disease

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Abstract: Sleep perturbations including fragmented sleep with frequent night-time awakenings and daytime naps are common in patients with Alzheimer's disease (AD), and constitute a major factor for institutionalization of these patients. The extent to which these changes in sleep-wake patterns contribute to AD progression is poorly understood. This study examined alterations in sleep-wake patterns in a double-transgenic mouse model of AD, called 5XFAD. These mice have five distinct human mutations in amyloid precursor protein (APP) and Presenilin1 (PS1) engineered into two transgenes driven by a neuron specific promoter (Thy1), and thus develop severe amyloid deposition at an early age. Age-matched (4-6 months old) male and female 5XFAD mice (males: N=10; females: N=7) were monitored and compared to wild-type littermate controls (males: N=7; females: N= 11) for various sleep traits using a non-invasive, high throughput, automated piezoelectric system. Sleep-wake patterns were recorded under baseline conditions for 3 days and after sleep deprivation of 4 hours. Under baseline conditions, 5XFAD mice exhibited shorter bout lengths (14% lower values for males, 21% for females) as compared to controls ($p<0.001$). Female 5XFAD mice also showed 11% less sleep than WT ($p<0.01$). After sleep deprivation, reduced bout length was also found in 5XFAD mice of both sexes during the succeeding 8 hours ($p<0.05$ at multiple time points). Bout length reductions were greater during the night than during the day, which does not model the human condition of disrupted sleep at night. However, the overall decrease in bout length suggests increased fragmentation and disruption in sleep consolidation that may be relevant to human sleep. The AD mice may serve as a useful model for testing therapeutic strategies to improve sleep consolidation in AD patients.

Supported by: NIH award: R01AG13418 and Internal funding

Group: Graduate Student
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#138 Abstract Title: **Markov Modeling of Sleep-Wake Dynamics Following Acute Neural Injury**

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Abstract: Traumatic brain injury (TBI) disrupts normal physiological rhythms. The ability to track changes in the microstructure of post-traumatic sleep could help assess intervention and perhaps the likelihood of epileptogenesis. However, convenient metrics that track sleep-wake dynamics—beyond simplistic measures like the percent time spent in different vigilance states or their mean bout durations—are lacking. Here, a methodology based on hidden Markov models (HMMs) is used to characterize transient sleep-wake dynamics in mice. With IACUC approval, adult C57BL/6J mice were implanted with EEG/EMG preamplifiers and monitored round-the-clock for four weeks. HMMs mapped values of signal features (EEG delta/theta power ratio and root-mean-squared EMG) in sequential 4s epochs onto REM, non-REM, and Wake states. HMMs tracked sleep-wake state with 92% sensitivity and 95% specificity (n = 6 mice), and were re-estimated every four hours. Trends in HMM properties were inspected to characterize changes in behavior following surgery. An HMM is parameterized by a vector of marginal state probabilities P and a matrix S of state transition probabilities. The Wake probability Pw and trace Tr of S were used as measures of sleep quality. Pw was abnormally low following implantation, as expected after general anesthesia and mild head trauma from EEG surgery. Although this suggested increased somnolence, Tr was low as well, consistent with fragmented sleep. Pw and Tr took 7-10 days to stabilize, with normal diurnal cycles indicative of recovery. These results suggest that models estimated from physiological measurements could provide quantitative markers of transient behavior and recovery from TBI.

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Group: Graduate Student

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#139 Abstract Title: **Altered Neural Responses to Affective Repetition in Persons with Mild Cognitive Impairment**

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Abstract: Human memory involves multiple subcomponents, and these components are asymmetrically affected in the clinical course of Alzheimer's disease (AD). Aspects of memory that are robust to Alzheimer's disease can be leveraged to reduce the functional impact of the disease on behavior. Emotional enhancement effects (EEE) and repetition effects (RE) are aspects of memory believed to be relatively robust to the course of AD, but another aspect of memory, working memory, declines early in the course of AD. Understanding the concomitant neural processing of EEEs and REs will inform the incorporation of EEE-relevant content into existing RE-based cognitive interventions for early AD. 16 participants – 8 with mild cognitive impairment (MCI), 8 with normal cognitive status – participated in an affective repetition task while electrophysiological data was collected. Images from the International Affective Picture System (IAPS) image set were shown to participants, and participants indicated whether low arousal positive (LAP) and high arousal negative (HAN) images included human body parts. ERPs showed discrete temporal and spatial neural processing of emotional and repetition components of stimuli, ps = 0.002. Additionally, individuals with MCI showed disproportionately large effects of HAN and repeated stimuli. Only neural processing data identified group differences. The current study provided new evidence of changes in emotional processing and repetition effect processing in the earliest stages of clinical change due to Alzheimer's disease, which challenges the view that these effects are unresponsive to the course of aging and dementia.

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Group: Graduate Student

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#140 Abstract Title: **Binge alcohol administration does not inhibit alcohol-induced reactive proliferation**

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Abstract: Previous research has shown that 7 days after binge alcohol exposure (T7) there is a reactive increase in neural progenitor cell (NPC) proliferation. Since alcohol has been shown to inhibit proliferation in a variety of cell types and organs, we hypothesized that binge-like administration of alcohol at T7 would reduce alcohol-induced reactive proliferation. Adult male rats were fed a nutritionally complete diet containing 25% ethanol (w/v) or isocaloric dextrose. Diet was administered via gavage every 8 hours for 4 days and the ethanol dose was titrated to behavioral intoxication scores. On the evening of the 6th day of abstinence and the following morning (8 hours later, T7), rats were gavaged with 5 g/kg ethanol or control diet. The S-phase/proliferation marker bromodeoxyuridine (BrdU) was injected 1 hour following the second 5 g/kg ethanol dose (T7) and rats were perfused 2 hours after BrdU injection. Brains were removed and processed for BrdU immunohistochemistry. BrdU+ cells within the subgranular zone of the hippocampal dentate gyrus were counted. Alcohol administration during alcohol-induced reactive proliferation did not inhibit NPC proliferation; alcohol-treated animals showed a 139% increase ($p < 0.005$) in the number of BrdU+ cells (103 ± 15 cells/section) compared to controls (43 ± 5 cells/section). These values are similar to previous results that show an increase in NPC proliferation at T7 and a resultant increase in neurogenesis after 14 days of abstinence. Therefore, reactive NPC proliferation at T7 in the dentate gyrus is robust and surprisingly resistant to alcohol inhibition of cell proliferation.

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#141 Abstract Title: **Middle-Aged Rats Demonstrate Variable Sleep, Cognition, and Hormone Responses to Acute Psychosocial Stress**

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Abstract: Psychosocial stress is a non-physical form of stress caused by major life changes, such as loss of a job or spouse or social isolation, and strongly influences multiple systems (e.g., corticosterone level, body temperature regulation, sleep and cognition). Psychosocial stress is of particular interest to us because humans are both more likely to experience it, and have a stronger negative reaction to that exposure, as we age. Previous work in our lab has shown an age-related shift in psychosocial stress sensitivity. However, little is known about acute middle-aged subjects' stress response. We hypothesize that this age-range should serve as a transition point from the young to the aged phenotype. Thus, we expect middle-aged animals to be more variable in their stress responses. To test this, we used middle aged (12 mos) male Fischer 344 rats implanted with wireless telemetry from DSI (Data Sciences International) to monitor electroencephalogram and electromyography output for sleep architecture analysis. To assess cognition, rats were tested using the Morris water maze: 3 days of training (3, 60 second trials/day) and the probe trial on day 4 (1, 60 second trial, platform removed). Prior to the probe, rats were split into two groups: control and stressed (8/group). Stressed rats were restrained in a Rat Snuggle® (Harvard Apparatus) in the water maze room for 3 hours in their home cage immediately preceding the probe trial. The following day, trunk blood was collected for corticosterone and adrenocorticotrophic hormone analysis. We examined relationships between corticosterone levels, water maze performance and sleep architecture.

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Group: Graduate Student

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#142 Abstract Title: **A Mouse Model of Chronic Pancreatitis Induced by an Alcohol and High Fat Diet**

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Abstract: Background/Aims: The study of acute pancreatitis in chemically-induced rodent models has provided useful data. Models of alcoholic chronic pancreatitis have been called for by those prominent in the field of pancreatitis research. The aim is to produce an alcohol and high fat (AHF) diet-induced mouse model of chronic pancreatitis for laboratory study. Methods: Mice are fed ad libitum normal chow, or a liquid diet containing 6% alcohol as well as a high fat supplement over a period of five months. Hindpaws of mice were tested for mechanical hypersensensitivity with von Frey filaments, while thermal hypersensitivity was tested using a 44oC hotplate. Mice also underwent mechanical and thermal testing both with and without pharmacological treatment. Pharmacological agents tested were a peripherally restricted mu-opiate (loperamide) and a TRPV4 antagonist. Results: Mice on the AHF diet exhibited mechanical and heat hypersensitivity as well as histopathology indicative of chronic pancreatitis. The peripheral mu-opiate attenuated both mechanical and thermal hypersensitivity, while only thermal hypersensitivity decreased after TRPV4 antagonism. Conclusion: Mice fed an alcohol and high fat diet develop histopathology consistent with chronic pancreatitis, and opiate sensitive mechanical and heat hypersensitivity.

Supported by: NIH award: RO1 NS39041-01

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#143 Abstract Title: **Firing-rate plasticity in sensory-evoked motor output.**

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Abstract: Our lab is interested in the physiological mechanisms of behavioral plasticity. We have characterized mechanosensory behavior and habituation to tactile stimuli in Drosophila melanogaster larvae. Light brushes to the anterior segments of crawling larvae evoke a limited repertoire of stereotypical behavioral responses, and the probability of animals responding to the stimulus decreases by about 60% after 25 stimulations at 5s inter-stimulus intervals (ISI). The neural correlate of sensory-evoked motor responses was measured from segmental nerve roots and from single muscle fibers. Touching dissected larvae with an insect pin evoked short bursts of activity in the segmental nerve (6-10s on average, depending on where the stimulus was delivered). Bursts of similar duration and frequency were evoked in a muscle fiber by stimulating sensory nerve roots with an electrode. The duration of these bursts was comparable to endogenous activity patterns that resemble fictive crawling, but the firing rate was significantly slower, suggesting that different patterns of activity convey crawling and the sensory-evoked behaviors. We applied repetitive nerve root stimulations at different ISIs to investigate habituation at the cellular level. Surprisingly, the average frequency of responses increased in response to repetitive stimulations, possibly because simultaneous activation of all sensory neurons in the nerve root was perceived by the CNS as noxious. The time course of this sensitization-like behavior varied with respect to ISI, with longer ISIs evoking a more substantial increase in frequency than shorter ISIs. With the extensive neurogenetic tools available in Drosophila, we are now investigating the cellular and molecular mechanisms of plasticity in this mechanosensory circuit.

Supported by: NA

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Thursday, March 27, 2014 **Lexington Convention Center**

#144 Abstract Title: **Calpain 5 is an atypical calpain highly expressed in the CNS, possesses dual nuclear localization signals, and is associated with Promyelocytic Leukemia nuclear bodies**

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Abstract: Calpain 5 (CAPN5) is an atypical member of the calpain family. It lacks the EF hand motif characteristic of classical calpains but retains catalytic and Ca2+ binding domains, and contains a unique C-terminal domain. Tra-3, an ortholog of CAPN5, has been shown to be involved in necrotic cell death in C. elegans. CAPN5 is expressed throughout the CNS, but its expression relative to other calpains and subcellular distribution have not been investigated previously. This study shows that, based on relative mRNA levels, CAPN5 is the second most highly expressed calpain in the CNS, with CAPN2 mRNA being most abundant. Unlike typical calpains, CAPN5 is a non-cytosolic protein, present in the nucleic acid binding fraction of rat brain cortex homogenates. CAPN5 possesses two nuclear localization signals (NLSs): an N-terminal monopartite NLS and a unique bipartite NLS closer to the C-terminus. The C-terminal NLS contains a SUMO-interacting motif that contributes to nuclear localization, and mutation or deletion of both NLSs renders CAPN5 exclusively cytosolic. Dual NLS motifs are common among transcription factors and other DNA-binding proteins, and one NLS often overlaps with a DNA-binding domain. Interestingly, CAPN5 is found in punctate domains associated with promyelocytic leukemia (PML) protein within the nucleus. PML nuclear bodies are implicated in transcriptional regulation, cell differentiation, cellular response to stress, viral defense, apoptosis, cell senescence, as well as protein sequestration, modification, and degradation. The insights from this study provide clues regarding the function of CAPN5 and its association with PML bodies, which remain to be elucidated.

Supported by: Kentucky Spinal Cord and Head Injury Research Trust (KSCHIRT)

Group: Graduate Student

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#145 Abstract Title: **The pharmacological profile and actions of cholinergic system in larval Drosophila: Behavior, development, CNS activity, and heart.**

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Abstract: We investigated the role of acetylcholine on the Drosophila larval heart and CNS to identify its functional roll and receptor pharmacology in this model organism. Genomic screens have revealed that there are ten receptors in Drosophila that are very similar to the nicotinic acetylcholine receptors (nAchRs) of mammals. In Drosophila acetylcholine is a transmitter within the CNS and is the neurotransmitter for sensory neurons but not motor neurons, as in mammals. A distinctive advantage of Drosophila larvae is the short developmental time (~4 days) in which the development of the CNS can be investigated. The alteration in neural activity related to circuits is particularly important during neural development for formation and stabilization of neural connections. In addition, the Drosophila larval heart offers a play ground for future experimentation on the ionic regulation and modulation of pacemaker activity. We will report on the stimulatory effect of nicotine on the larval heart and on a sensory-CNS-motor circuit. The significance of this study is presenting a testable model preparation for ion channels and Ca2+ transport function in regulating pacemaker potentials for cardiac cells and pacemaker cells as well as the pharmacological profile of AchRs in the CNS of the Drosophila model.

Supported by: This work was supported by the NSF.

Group: Graduate Student
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#146 Abstract Title: **Association of PICALM Gene Polymorphism with Expression of PICALM and Alzheimer's Disease.**

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Abstract: GWAS have identified a series of single nucleotide polymorphisms (SNP)s that are associated with Alzheimer´s disease (AD). We studied SNP, rs3851179, near the gene phosphatidylinositol-binding clathrin assembly protein (PICALM) for its effect on expression and splicing of PICALM. Expression: Quantified total PICALM mRNA in 56 brain cDNA samples, using qPCR. In linear regression analyses of PICALM that included cell type specific markers, AD,and rs3851179; rs3851179 ($p<6.9 \times 10\text{-}3$) and cell type specific markers ($p<0.01$) associated with PICALM expression. Splicing: Over 700 clones were sequenced to evaluate the abundance and relative distribution of splice variants present. PICALM has multiple splice variants, which lack exons encoding functional protein motifs. Sequencing the cloned isoforms we found that exons 13, 14,15,18 and 19 were variably spliced and isoform lacking exon 13 is the most abundant isoform. Expression of isoforms lacking exon 13 associated with rs3851179 genotype ($p<8.1 \times 10\text{-}3$), AD, and cell type specific markers. We targeted the latter part of the gene, exon 17-20, to investigate allelic expression imbalance (AEI) using semiconductor-sequencing technology. Individuals heterozygous for rs76719109, located in exon 17, were used to study the ratio of G/T allele in cDNA and genomic DNA. We analyzed the G : T allelic ratio, the variant lacking exons 18 and 19 showed unequal allelic expression in 8 individuals (p-value < 0.001). One individual was an outlier, showing overall AEI. The isoform lacking exon 18-19 appears to be under genetic control and is the subject of current investigation.

Supported by: NIH award: P01-AG030128

Group: Graduate Student

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#147 Abstract Title: **Gene Expression Changes in Response to Selenium Diet in Spinal Cord Injured Rats.**

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Abstract: Certain groups at high risk for spinal cord injury groups may benefit from a prophylactic supplement, such as dietary selenium, that would intervene in the secondary neurodegenerative cascade immediately following trauma. Selenium was supplemented in the diets of female Sprague-Dawley rats prior to receiving a moderate (150kdyn) contusive spinal cord injury or sham laminectomy. Twenty-four hours following injury, 5mm of spinal cord directly surrounding the injury epicenter was collected from animals on both diets, sham and injured. Later, RNA was isolated from these tissues, converted to cDNA, and utilizing the Affymetrix genome array platform, hybridized to rat microarray genome chips with probe sets representing 31,097 genes. Raw signal intensities from Affymetrix scanner were converted to gene expression summary values using RMAExpress. Genes underwent a rigorous selection process, which resulted in a 14,907 filtered gene list. These genes were sorted into templates ($p<0.017$) based on their expression patterns in the four treatment groups. A total of 4301 and 4812 genes were consistently down-regulated and up-regulated, respectively, across diet groups in response to the injury. Of particular interest, a template that isolated 78 genes specifically down-regulated in the control injured group showed these phenotypes rescued in selenium injured animals, including genes associated with transcriptional regulation and cell cycle arrest. Additionally, another template showed 111 genes up-regulated in selenium injured animals when compared to control injured animals. These genes include pathways associated with DNA repair. These tools will help us to understand mechanisms of selenium in the central nervous system in response to injury.

Supported by: C. Crowdus was supported by NIH training grant: 1T32NS077889. Alltech provided support for supplies and rat diets.

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#148 Abstract Title: **Using Social Cues for Cocaine Self-Administration and Cued Reinstatement**

Author(s): V. G. Weiss, Dept of Psychology, U of Kentucky
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Abstract: Although drug taking in humans is commonly engendered within a social context, animal models of addiction are conducted typically in the absence of social cues. The present experiments determined if cocaine self-administration and reinstatement in rats is influenced by a social partner. The apparatus was a custom-built 2-lever operant conditioning chamber that was adjacent to another identical chamber, with a wire mesh barrier. In Experiment 1, rats were initially trained to respond on a FR5 schedule for food pellets. Rats then underwent surgery to implant a jugular catheter in their right jugular vein to allow for self-administration of i.v. cocaine. Rats were then re-trained to self-administer cocaine, during which time a social partner rat was present in the adjacent chamber. After acquisition, the rats underwent extinction in the absence of a social partner. Following extinction, the partner rat was re-introduced into the adjacent chamber for one session and lever responses were recorded. Experiment 2 used similar procedures, except that acquisition consisted of pairing the one social partner when cocaine was available and pairing a different social partner on alternate sessions when only saline was available. Following a period of extinction, in which neither partner was present, each partner was tested individually as a cue for reinstatement following a period of extinction. Results from Experiment 1 showed the presence of the social partner led to reinstatement of responding, $p<0.05$. However, results of Experiment 2 showed that there were no significant differences between the reinstatement induced by the cocaine-paired and saline-paired partners. Results indicate that social cues provided by a conspecific can reinstate cocaine seeking after a period of extinction. However, the presence of a conspecific alone may be sufficient to reinstate cocaine seeking, at least using the current procedures.

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#149 Abstract Title:	**Development of Ethanol Dependence Requires Activation of mGlu1-and-5 Containing Receptors In Vitro**

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Abstract: Multiple periods of withdrawal from ethanol (EtOH) dependence are associated with accelerated neurological outcomes in the clinical population. Studies conducted in our laboratory demonstrate that exposure to chronic, intermittent ethanol (CIE) produces N-methyl-D-aspartate (NMDA) receptor-mediated cytotoxicity during periods of ethanol withdrawal (EWD). However, the mechanistic underpinnings associated with increases in NMDA receptor function that likely confer sensitivity to the cytotoxic effects of CIE have yet to be characterized. The present studies assessed the hypothesis that EtOH activates the metabotrophic glutamate receptor 1 and/or 5 (mGluR1/5) to promote PKA-dependent neuroadaptations in glutamatergic signaling to, further potentiating EWD neurotoxicity. Rat hippocampal explants were exposed to EtOH (50 mM) for 3 cycles of CIE that involved 5 days of exposure with or without the addition of 1) PKA inhibitor KT-5720 (0-1 μM), 2) MGluR1 antagonist SIB-1893 (0-20 μM), or 3) MGlur5 antagonist CPCCOEt, followed by a 24-hour period of EWD. Cytotoxicity was assessed using immunohistochemical labeling of NeuN (Fox-3), a marker of mature neuron content. NeuN immunoreactivity was significantly reduced (>20%) in each examined hippocampal cell layer, while this effect was not demonstrated in the absence of EWD. Exposure to KT-5720 (1 μM) during EtOH treatments significantly attenuated the loss of NeuN immunoreactivity produced by 3 cycles of CIE. Further, exposure to the SIB-1893 (20 μM) and CPCCOEt (3 μM) during EtOH treatment prevented the loss of NeuN immunoreactivity produced by 3 cycles of CIE. These findings demonstrate that while EWD is required for hippocampal cytotoxicity, development of EtOH dependence requires activation of hippocampal mGluR1-and-5 containing receptors.

Supported by: Supported by NIAAA (AA013388 awarded to MP).

Group: Graduate Student
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#150 Abstract Title: **The Pivotal Role of mitoNEET in Pioglitazone-Mediated Neuroprotection Following TBI**

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Abstract: Traumatic brain injury (TBI) is a devastating healthcare problem in the United States affecting hundreds of thousands annually. Regrettably, no pharmacological agents are approved for the clinical treatment of this horrendous disease. Therefore, treatments options for TBI are urgently needed. Pioglitazone, an FDA approved drug for type 2 diabetes, has previously been shown to increase mitochondrial function, cortical sparing and cognition following TBI, however the mechanism of action is still undetermined. Additionally, pioglitazone has been found to bind to a novel mitochondrial protein called mitoNEET, which has also been shown to mediate oxidative phosphorylation. This study examines the hypothesis that pioglitazone is able to provide neuroprotection following TBI through direct interactions with mitoNEET. Consistent with this theory, preliminary results indicate that pioglitazone is unable to ameliorate TBI related mitochondrial dysfunction and is not neuroprotective in mitoNEET knockout animals. Additionally, treatment with a specific mitoNEET ligand (NL-1) has been shown to be neuroprotective following TBI. These data support the theory that pioglitazone's ability to improve mitochondrial bioenergetics, thereby decreasing tissue loss and improving functional recovery following TBI, hinges on binding mitoNEET and that the protective effects of pioglitazone can be reproduced by NL-1, an exogenous mitoNEET ligand.

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#151 Abstract Title: Intranasal Delivery of DNSP-11in Normal and Parkinsonian Fischer 344 Rats

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Abstract: Studies involving neurotrophic factors, such as glial cell line-derived neurotrophic factor (GDNF), have shown promising results in treating patients with Parkinson's disease (PD). However, their large size and inability to cross the blood brain barrier has resulted in their invasive surgical delivery limiting their widespread application and success. A smaller, functional molecule amendable to non-invasive procedures, such as intranasal delivery, could be a viable treatment option for PD and other neurodegenerative diseases. Our team has shown that DNSP-11, an amidated, synthetic 11-amino acid peptide derived from the proregion of GDNF, exhibits neurotrophic-like effects both in vivo and in vitro. To test the efficacy of intranasal delivery, a dose response was conducted in normal animals that received DNSP-11for 3 weeks. A significant increase in dopamine turnover was observed at 300 µg in the substantia nigra and striatal tissue as measured by HPLC-EC. Tracking studies examining a one-time dose of I125-labeled DNSP-11 have elucidated its rapid uptake into cerebrospinal fluid, blood and brain tissue. Additionally, a rostral to caudal gradient was observed in serial coronal brain slices as measured by gamma counting and autoradiography. Intranasal administration of DNSP-11was further tested in a unilateral 6-hydroxydopamine (6-OHDA) striatal lesion model. Animals were treated daily with 300 µg of DNSP-11 or vehicle 1 week prior to 6-OHDA injection and 5 weeks post-surgery. A significant decrease in amphetamine induced rotation was observed at 2 and 4 weeks. These are the first studies to support the efficacy of intranasally administered DNSP-11in normal and 6-OHDA lesioned rats.

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Group: Graduate Student

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#152 Abstract Title: Methylglyoxal Produces Pain and Activates Spinal Neurons via TRPA1

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Abstract: Increases in methylglyoxal (MG) are positively correlated with painful diabetic neuropathy (PDN) in patients and streptozotocin and db/db diabetic mouse models. We extended MG measurements to the Zucker Diabetic Fatty rat model of type 2 PDN and found, compared to control ZDFfa/+, diabetic ZDFfa/fa rats had elevated MG and were hypersensitive to mechanical stimulation. Recent reports indicate that nociception and activation of dorsal root ganglion sensory neurons produced by MG are reduced in TRPA-/- mice. To determine the effect of MG on activity of nociceptive neurons in the dorsal horn of the spinal cord, we evaluated behavior, phosphorylation of extracellular signal-regulated kinase (pERK), and Fura-2 calcium imaging after application of MG. To test the hypothesis that spinal sensitization and pain occurred via TRPA1, we evaluated responses to MG after genetic or pharmacologic disruption of TRPA1. MG produced dose-dependent nociceptive responses in SD rats and C57BL6 mice and increases in calcium mobilization in ex vivo spinal cord slices . MG-induced nociception and pERK were diminished in TRPA1-/- mice or by intrathecal pre-treatment with the TRPA1 antagonist HC030031. Our current findings suggest that MG produces pain and spinal sensitization through a mechanism dependent upon spinal TRPA1. This, along with our finding that MG is elevated in type 2 PDN, lead us to speculate that elevation of MG in type 2 diabetes sensitizes nociceptive afferents and/or spinal pain transmission neurons. Future studies in rodent models of type 2 diabetes will evaluate the contribution of this MG-TRPA1 system to the generation of pain-like behavior.

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Group: Graduate Student

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#153 Abstract Title: **Identifying candidate genes for variation in Sleep QTLs**

Author(s): S. Joshi, Department of Biology, U of Kentucky
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Abstract: Quantitative trait loci (QTL) analysis is a powerful tool to study variations of complex traits. The Collaborative cross and diversity outcross projects have made it possible to identify novel QTLs with higher resolution. A non-existent gene ontology and lack of a dedicated database containing a comprehensive list of sleep related genes and their function presents a hurdle for sleep researchers. We are applying a two pronged approach to solve this problem. The GEO (Gene Expression Omnibus) database at NCBI (National Center for Biotechnology Information) website provides more than one thousand results for microarray datasets for keyword “sleep” in Mus musculus species. Currently, the datasets for sleep deprivation studies for their effects on gene expression in the brain are being analyzed but we intend to look at gene expression differences in peripheral tissues as well. At the end of these investigations, we will have a list of candidate genes that may influence sleep related traits. Alongside, information is collected and collated for previously identified QTLs. The SNPs present in these QTL regions are identified using Mouse Genome Informatics (MGI) database. A list of genes containing these SNPs is created which present potential candidates causing variations in the QTL trait. Our aim is to combine this information about potential candidate genes with the results obtained from meta-analysis of microarray datasets. The association of information about genes with their function and role in sleep can help in forming sleep specific gene ontologies, which would be useful for sleep researchers.

Supported by: Internal funds from U of Kentucky

Group: Graduate Student

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#154 Abstract Title:	**Entorhinal Cortex and Hippocampal Damage are Amplified by Concussions Repeated at 24hr Intervals**
Author(s):	A. N. Bolton, Dept of Physiology, Spinal Cord and Brain Injury Research Center, U of Kentucky K. E. Saatman, Depts of Physiology and Neurology, Spinal Cord and Brain Injury Research Center, U of Kentucky

Abstract: Most traumatic brain injuries (TBI) that occur every year are mild, concussive head injuries that may be repeated multiple times in individuals involved in high risk activities. Outward indicators, such as loss of consciousness, are used to determine the initial severity of a concussion and aid in determining how much time should be spent recuperating. In this study we characterize a mouse model of concussion to compare the acute physiological and histopathological consequences of repeated concussions and the effects that time interval variation between impacts have on these responses. A single concussion resulted in a brief period of apnea and unconsciousness as measured by righting response and minimal gliosis in the entorhinal cortex without overt cell death. When the concussive impact was repeated every 24hrs, apnea and righting reflex diminished with subsequent impacts, such that by the final impact the righting reflex response mirrored the sham response. Despite reduced physiological responses with repeated injuries, multiple concussions resulted in a hemorrhagic lesion in the entorhinal cortex, accompanied by an increase in inflammation, cell death, and the size of axonal swellings. When the interval between concussions was increased to 48hrs, the pathological consequences were comparable to a single concussion. Combined, this data suggests an evolution of acute physiological responses with repeated head injuries that may mask the pathological consequences occurring in the brain.

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Group: Graduate Student

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#155 Abstract Title: **Cotinine Induced Upregulation of Nicotinic Acetylcholine Receptors: A Potential Role in Nicotine Addiction**

Author(s): A. M. Fox, Department of Chemistry, University of Kentucky
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Abstract: Nicotinic acetylcholine receptors (nAChRs) are cation-selective membrane receptors that express throughout the central and peripheral nervous systems. They form pentameric structures containing alpha (α1-α10) and beta (β2-β4) subunits, with each subunit encoded by a distinct gene. Receptor assembly into the correct stoichiometry and composition is essential for proper subcellular localization, agonist sensitivity, and Ca2+ permeability. Changes in nAChR assembly and stoichiometry resulting from nicotine exposure and subunit composition have previously been linked to nicotine addiction. However, differences in expression and trafficking as a result of cotinine exposure, the primary metabolic product of nicotine, have not been investigated. Cotinine has a half-life in the bloodstream almost 10 times longer than nicotine, meaning a potential role in addiction is feasible but not explored. My current work focuses on ligand induced upregulation of the nAChRs α4β2 and α3β4 with and without an auxillary α5 subunit. We utilize a pH sensitive fluorophore, super ecliptic phluorin, to differentiate between intracellular nAChRs and those expressed on the plasma membrane. This can be utilized to determine the relative percentage of receptors on the plasma membrane compared to the peripheral endoplasmic reticulum, as well as resolve individual insertion events of a single vesicle arriving at the plasma membrane. We have found that there is an overall increase in total number and percentage of receptors on the plasma membrane when exposed to 1 μM cotinine. Also, α4β2, α4β2α5, and α4β2α5D398N show clear differences in response to nicotine and cotinine.

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Group: Graduate Student

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#156 Abstract Title: mTOR Inhibition After Traumatic Brain Injury Alters Dentate Neurogenesis and Hilar Interneuron Excitability

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Abstract: Traumatic brain injury (TBI) is among the most common causes of acquired temporal lobe epilepsy (TLE). The latent period after head injury and prior to the expression of seizures includes plasticity events that support epileptogenesis, including cell loss and synaptic reorganization in the dentate gyrus. A murine model of TBI using controlled cortical impact (CCI) injury was used to examine the effect of rapamycin on hilar gamma-aminobutyric acid (GABA) systems and dentate neurogenesis. The number of surviving GABAergic hilar interneurons was assessed in mice that express GFP in a subset of inhibitory neurons (GIN mice; FVB-Tg(GadGFP)4570Swn/J). Cell counts were made in sham-operated controls, CCI-injured, and CCI-injured + rapamycin treatment (3 mg/kg) 48-72 hours after surgery. Rapamycin did not affect hilar interneuron loss ipsilateral to injury after CCI. Dentate granule cell (DGC) layer area was measured in these same mice using Image J. There was a significant decrease in DGC area ipsilateral to injury in rapamycin treated mice after CCI compared to CCI and sham ipsilateral hemisphere. CD-1 mice treated for 2 weeks with rapamycin also show decreased DGC area in the ipsilateral hemisphere relative to CCI and sham ipsilateral hemisphere. Preliminary data show when rapamycin treatment is discontinued for one week, DGC area trends back to CCI and Sham operated control levels. Doublecortin immunohistochemistry was used to assess whether the reduced DGC area was related to neurogenesis. In the hemisphere ipsilateral to injury or sham surgery, rapamycin treated mice had less doublecortin expression compared to CCI but not different than shams. CCI-injured mice had increased doublecortin expression relative to shams. There was no change in doublecortin expression in the contralateral hemisphere of tested groups. Whole cell patch-clamp and on-cell electrophysiology recordings in vitro were used to examine the spontaneous excitatory post-synaptic currents (sEPSCs) and spontaneous firing rate of GFP-positive hilar inhibitory interneurons in GIN mice with rapamycin treatment for 8-12 weeks after CCI injury. Preliminary data indicate no significant change in either the sEPSCs or spontaneous firing rate, which was previously reported to increase in interneurons ipsilateral to CCI injury (Hunt et. al. 2011). These data suggest that rapamycin inhibits neurogenesis in the dentate gyrus, which could contribute to reduced abberant axonal sprouting after head injury and reduced seizure susceptibility/ epileptogenesis. Ongoing experiments will further assess the effect of rapamycin on hippocampal circuitry after CCI.

Supported by: DoD USAMRMC grant W81XWH-11-1-0502

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30th Annual BGSFN Spring Neuroscience Day
POSTER ABSTRACTS

Thursday, March 27, 2014 **Lexington Convention Center**

#157 Abstract Title: **DMXB-A Reduces Cell Damage following Developmental ETOH Exposure in a Rodent Hippocampal Slice Model**

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Abstract: Prenatal alcohol exposure can have life-long consequences for the developing offspring. Alcohol can damage the developing brain through excitotoxicity caused by ethanol (ETOH) withdrawal (EWD). Targeting this excitotoxicity has been shown to be a promising approach for improving outcomes following developmental ETOH exposure. Activation of nicotinic acetylcholine receptors (nAChR), in the central nervous system is protective against various excitotoxic challenges, including EWD. In this study, we examined whether the administration of DMXB-A, an α7 nAChR agonist, could reduce the neurotoxicity caused by EWD in the hippocampus. To test this hypothesis, a neonatal organotypic hippocampal slice culture model was used in which hippocampal slices were harvested from postnatal day 8 male and female Sprague Dawley rat pups. Slices were exposed to an average of 65mM ETOH for 10 days and treated with one of two doses of DMXB-A (3 or 10uM DMXB-A) during EWD. A subset of slices were also exposed to 5uM NMDA to potentiate excitotoxicity. After 24 hours of EWD, cell damage in three areas of the hippocampus was measured. EWD + NMDA exposure in the CA1 region of the hippocampus produced neurotoxicity/cell damage. The 10uM DMXB-A attenuated this effect, suggesting that DMXB-A was protective against EWD induced neurotoxicity. These findings are particularly exciting since this drug is currently being assessed in clinical trials for a variety of other CNS conditions and so has significant translational potential. Further work is ongoing to determine whether this drug can also reduce behavioral deficits in our rodent model of fetal ethanol effects.

Supported by: Supported in part by a Pilot Grant Program from University of Kentucky

Group: Graduate Student

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POSTER ABSTRACTS

#158 Abstract Title: **Effects of Immunotherapy and Behavioral Enrichment on Beta-Amyloid Pathology in a Canine Model of Aging**

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Abstract: Alzheimer's disease (AD) is characterized by cognitive decline and a hallmark neuropathology, including β-amyloid (Aβ). Therapeutic strategies for AD focus on reducing the production or deposition of Aβ. Canines develop Aβ neuropathology and cognitively decline with age similar to AD patients making them a useful model for testing potential therapeutic agents. Immunization with Aβ1-42 (IMM) in aged canines shows a significant decrease in brain Aβ and maintains executive function. However, behavioral enrichment (BEH) improves cognition without reducing brain Aβ. We hypothesized that IMM combined with BEH would provide larger cognitive benefits and further reduce neuropathology, as compared to controls or IMM and BEH alone. Aged beagles (10.5-13.6 y) were placed into four groups: controls (Alum adjuvant only), fibrillar Aβ1-42 + Alum vaccine, BEH with Alum, and combination treatment. Animals were treated for 18 months. Insoluble Aβ (formic acid extracted) and Aβ plaque load (6E10, anti-Aβ 1-42, Pyro Glu3) in the prefrontal cortex were measured by sandwich ELISA and immunohistochemistry, respectively. IMM significantly reduced both insoluble Aβ1-40 ($F(1,34)=8.79$ $p=0.006$) and 1-42 ($F(1,34)=5.61$ $p=0.024$), as well as all forms of measured plaque load, 6E10 ($F(1,34)=56.51$ $p<0.0005$), Aβ 1-42 ($F(1,34)=33.04$ $p<0.0005$), and Pyro Glu3 ($F(1,34)=10.00$ $p=0.004$). An overall reduction in 6E10 ($F(1,34)=4.08$ $p=0.052$) and Aβ 1-42 ($F(1,34)=3.87$ $p=0.058$) plaque load due to BEH was also seen. A significant additive affect from BEH and IMM was seen in clearance of Aβ 1-42 plaque load ($F(1,34)=6.54$ $p=0.016$). Changes in cognition, extent of neurogenesis, and growth factor levels will be measured.

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POSTER ABSTRACTS

#159 Abstract Title:	**In Vivo Microelectrode Recordings: Increased Glutamate Release and Memory Deficits in a TauP301L Mouse Model of Alzheimer's Disease.**
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Abstract: The purpose of this study was to examine glutamate dysregulation in a TauP301L mouse model of Alzheimer's disease (AD). Glutamate is the primary excitatory neurotransmitter in the brain responsible for learning and memory. However, overstimulation of glutamate receptors can result in cell death, a process termed excitotoxicity. Extracellular glutamate can accumulate to reach pathological levels through several mechanisms, including an increase in glutamate release or a decrease in removal of glutamate from the synapse by astrocytic glutamate transporters. Preliminary data from the Reed lab shows a 65% increase in hippocampal vesicular glutamate transporter (VGLUT) expression in TauP301L. Because VGLUTs impact the amount of glutamate released into the synapse and increased VGLUT expression causes excitotoxic neurodegeneration, we hypothesized that the neurodegeneration observed in our AD model is due in part to an increase in extracellular glutamate levels. Here, we used the hippocampal-based Barnes maze test to assess memory performance in TauP301L mice at five months of age. At six months of age, microelectrode arrays were used to examine resting glutamate levels and stimulated glutamate release in the CA1, DG, and CA3 regions of the hippocampus. Our results confirmed previous reports of memory deficits in TauP301L mice. We also showed, for the first time, that stimulated glutamate release in the CA3 region of the hippocampus is increased 9-fold in TauP301L mice, despite similar resting glutamate levels. Findings of increased CA3 glutamate release in our mouse model corroborate findings of CA3 hyperexcitability in memory-impaired aged humans and patients with mild cognitive impairment (MCI).

Supported by: N/A

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POSTER ABSTRACTS

#160 Abstract Title: **Total cholesterol to high-density lipoprotein ratio is associated with ventricular volume in healthy seniors**

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Abstract: Dyslipidemia is a prevalent cardiovascular risk factor among U.S. adults. Although there is an abundance of evidence related to dyslipidemia and cardiovascular disease, less is known about the relationship between abnormal lipid levels and brain health. Interestingly, low HDL levels have been associated with reduced gray matter volume in both animals and cognitively intact humans. However, to our knowledge, no studies have explored the relationship between total cholesterol-to-HDL ratios (THR) and ventricular volume in cognitively healthy seniors. This is of interest for two reasons: 1) THR is a useful index of the joint effects of total cholesterol and HDL; and 2) reductions in ventricular volume are one of the most consistent pathologic findings in Alzheimer's disease. Thirty-six community dwelling healthy volunteers (24 female) participated in this study (mean age = 63.90, SD = 2.9). All participants had blood laboratory tests collected and laboratory tests performed, which included a two-hour fasting lipid panel. MRI data were collected on a 3T Siemens TIM scanner. Ventricular volume was quantified by using the semi-automated software program FreeSurfer. Individual ventricular volumes were normalized to total intracranial volume. After controlling for age, sex, and socioeconomic status, total cholesterol-to-HDL ratios demonstrated a significant positive relationship with both left ($r = 0.41$, $N = 36$, $p < 0.05$) and right ($r = 0.30$, $N = 36$, $p < 0.05$) lateral ventricular volume. These findings demonstrate that cholesterol, a prominent risk factor associated with cardiovascular disease, may also play an important role in the preservation of cortical tissue in healthy seniors.

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9th Annual CCTS Spring Conference and 4th Annual ATRN Summit

Thursday, March 27, 2014 Lexington Convention Center

POSTER ABSTRACTS

#161 Abstract Title: **Clinical features of mild cognitive impairment of the cerebrovascular type (MCI-CVD)**

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Abstract: Objectives: To evaluate the clinical features of mild cognitive impairment (MCI) in subjects with high and low cerebrovascular disease (CVD) burden on brain imaging. Background: While MCI has historically been considered a predementia form of Alzheimer's disease (AD), the diagnosis now includes multiple types of amnestic and non-amnestic MCI with the intent of distinguishing different pathological disease states at the earliest signs of cognitive decline. Available data support this diagnostic algorithm for distinguishing MCI with low CVD burden (MCI-AD) from MCI due to early Lewy body disease and frontotemporal dementia. More limited data exist on the utility of this algorithm in distinguishing MCI with high CVD burden (MCI-CVD) from MCI-AD, despite the recognition that CVD may be more prevalent than AD as a cause for dementia in the population at large. Design/Methods: Case control study of community-based research subjects with MCI that have either low (n=43) or high (n=45) CVD burden on brain imaging. Standard descriptive and comparative statistics were used to evaluate demographic, clinical, and genetic features of MCI-CVD. Results: Subjects with MCI-CVD were older (83.1 ± 6.3 vs. 74.8 ± 9.7, $p<0.001$), had more advanced cerebral atrophy ($p<0.001$, and this remained significant when analyzing only those between the age of 70-80 years to account for age related effects on atrophy), were more likely to carry an ApoE e2 allele (20.0 vs. 4.7%), and had higher prevalence of CVD risks including a history of hypertension, smoking (pk/yrs), MI, arrhythmia, PVD, TIA, stroke, and depression than subjects with MCI-AD (27.7 vs. 14.9). Neurologic exam findings and an extensive battery of neuropsychologic tests were unable to distinguish MCI-CVD from MCI-AD in this cohort. Conclusion/Relevance: These findings suggest that: 1) CVD is a prominent cause/contributor to MCI in community-based populations, 2) premortem identification of MCI-CVD rests on history of CVD risk factors and brain imaging, 3) standard neurological/neuropsychological examination cannot distinguish MCI-CVD from MCI-AD

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POSTER ABSTRACTS

#162 Abstract Title: **The Pathway to Grandparenting Stress: Trauma, Relational Conflict and Emotional Well-Being**

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Abstract: Over the past two decades, the number of grandparents serving as primary caregivers for their grandchildren has steadily increased. Caregiver substance abuse, child abuse and neglect, intimate partner violence, and other forms of trauma exposure in biological families contribute to the need for grandparents to serve as custodial parents. Although such adverse experiences can lead to traumatic stress symptoms, few programs developed for grandfamilies address trauma-related needs. Methods: Interviews and surveys were conducted with 297 grandparents who were raising their grandchildren through kinship care or relative caregiving programs. Respondents completed questions that included the Parenting Stress Scale (Berry & Jones, 1995) modified for grandparents, the conflicts scale from the Child-Parent Scale (Pianta, 1992), the RAND 36 (Hays, Sherbourne, & Mazel, 1993), and other items regarding demographics, child trauma exposure, and trauma diagnoses. Results: Approximately two-thirds (72%) of the sample of children experienced at least one type of traumatic exposure. A full structural model shows that the number of different types of trauma exposures experienced by the child indirectly affected grandparental stress, and was mediated by child-grandparental conflict. Examination of goodness of fit indices suggests a good fit for the model. A higher level of child-grandparent conflict was also associated with a lower level of emotional well-being among custodial grandparents. Implications: This study reinforces the importance of the nature of trauma exposure and provides support for a trauma-informed approach to service delivery.

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POSTER ABSTRACTS

#163 Abstract Title: **Effects of Gender and Velocity on the Lumbopelvic Rhythm**

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Abstract: Background: Low back pain (LBP) is a significant socio-economical problem. Current research is focused on development of objective tools that can distinguish LBP patients from healthy individuals. One suggested approach based on kinematics of the spine is the assessment of lumbopelvic (LP) rhythm. The objective of this study was to investigate whether LP rhythm is sensitive to known risk factors for LBP (i.e., velocity and gender). Method: Sixteen asymptomatic subjects (9 males and 7 females) with average (SD) age of 24.3 (2.3) years, height of 167.9 (9.2) cm and weight of 62.6 (7.3) Kg participated in this study after completing a consenting procedure approved by the UKY's IRB. Each participant completed two data collection sessions. During each session, subjects performed three repetitions of free trunk flexion-extension movements at two velocities: 1) slow (lasting ~6 sec per repetition) and 2) fast (lasting ~ 1 sec per repetition). Kinematic data were obtained using two accelerometers strapped on the subjects' trunk and pelvis. LP rhythm, as the ratio of lumbar rotation (i.e., thorax minus pelvic) over pelvic rotation, was obtained in three time windows over the flexion phase of each repetition. Results and Conclusion: LP rhythms were significantly ($p<0.03$) higher among males for the second and third time windows of the trunk flexion. During the same time windows, faster trunk motion was associated with significantly ($p<0.001$) lower LP rhythms. Since lower LP rhythms are associated with an elevated risk of LBP, LP rhythm appeared sensitive to risk factors studied here.

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POSTER ABSTRACTS

#164 Abstract Title:	**Neonatal Abstinence Syndrome (NAS): Neurobehavioral Outcomes, Methadone vs. Morphine**

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Abstract: Background: The prevalence of Neonatal Abstinence Syndrome (NAS) is increasingly exponentially. Many treatment options are suggested including opioids (morphine, methadone and buprenorphine) and non-opioids drugs. Neurobehavior performance has been systematically evaluated in babies treated with morphine but not in those treated with methadone. Objective: To evaluate the neurobehavioral performance of infants on methadone. Methods: Study period was between October 2012 and February 2013. Informed consent was obtained for infants who were treated with methadone for NAS and met additional criteria of gestational age >35 weeks. Infants with congenital malformations and prenatal exposure to cocaine were excluded. NICU Network Neurobehavioral Scale (NNNS) evaluation was done between days 2 to 7 after starting methadone and repeated between 39 - 44 weeks post menstrual age. NNNS summary scores were computed and compared to our NICU cohort of morphine treated infants (n =15). Linear mixed model with random effects (SAS Institute, Cary, NC) were used for statistical analysis. Results: 53 infants of 333 consecutive NICU admissions were exposed to opioids in utero. 30 infants were eligible for enrollment out of which 24 infants were enrolled. 1st NNNS was done in 20 and repeated in 13 infants. On initial assessment, methadone treated infants scored lower in attention and higher in stress abstinence, non-optimal reflexes and lethargy. On further assessment differences were also noted for handling, height of arousal, excitability (high scores) and regulation (low scores) for methadone treated infants. Conclusion: Findings suggest methadone treatment did not result in better neurobehavioral performance when compared to morphine.

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POSTER ABSTRACTS

#165 Abstract Title: **The relationship between sensation seeking and impulsivity on d-amphetamine taking behavior**

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Abstract: Aims: This study investigated the relationship between impulsivity and sensation seeking, and the behavioral and physiological effects of d-amphetamine. Methods: Forty young healthy adults scoring in the upper and lower median of population norms on impulsivity and sensation seeking items of the Zuckerman-Kuhlman Personality Questionnaire participated in a randomized, double-blind, placebo-controlled study designed to examine the subjective effects of oral d-amphetamine (8, 16 mg). During the first 'sample' session on each of 4 two-session blocks, subjects received 8 identical capsules all containing 0, 1 or 2 mg of d-amphetamine. During the second 'self-administration' session of each block, subjects could earn up to 8 capsules from the previously sampled d-amphetamine dose. The first capsule was earned by completing 50 responses, with the response requirement for each subsequent capsule being doubled, such that 12,750 responses were required to earn all 8 capsules.

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POSTER ABSTRACTS

#166 Abstract Title:	**A Comparison of Medical Student Opinions of Ultrasound in Medical Education Before and After Exposure to Ultrasound Education in Ultrasound-Naïve Emergency Medicine Oriented Students and Non-Emergency Medicine Oriented Students**
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Abstract: Background: Emergency medicine (EM) frequently utilizes point of care ultrasound (US). At the same time medical student exposure to ultrasound education is on the rise. With US's valuableness to EM and increased medical student exposure, students considering EM may place more value and respond more positively to US education than other medical students. Objectives: In our study we evaluated US-naïve medical students' opinion of US in medical education before and after exposure to US education. Methods: 75 students participated in a hands-on US workshop. 57 subjects participated in our study. 35 subjects indicated they were considering EM (EM students) and 22 subjects indicated they were not (non-EM students). Surveys assessed agreement with US positive statements on a Likert scale before and after workshop participation. Responses were compared between EM and non-EM students. Results: Before US education, both groups agreed with all 7 undergraduate US education statements. EM students agreed with 2 of 3 graduate US education statements, while non-EM students agreed with 1 of 3. Following US education, agreement increased in both groups for 7 of 7 undergraduate US education statements. EM student agreement increased for all 3 graduate US education statements. Non-EM student mean agreement increased for 2 of 3. Conclusion: Medical students clearly want US education. However, exposure to US education increases students' value of US education even more. Medical students entering US-utilizing specialties value graduate US education and respond more positively to US education than their peers.

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POSTER ABSTRACTS

#167 Abstract Title: **Sex differences in subjective and physiological responses to oral Δ9-THC in regular cannabis users**

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Abstract: Aim: Limited evidence suggests that there are sex differences in endocannabinoid function and the response to exogenous cannabinoids. The purpose of this study is to further explore these differences by determining the influence of sex on the subjective, cognitive/psychomotor, and physiological effects of oral Δ9-THC in cannabis users. Methods: Data from 30 subjects (N=18 M, 12 F) who completed Δ9-THC discrimination studies are being combined for this retrospective analysis. In each of the studies, subjects learned to discriminate between Δ9-THC and placebo. Subjects then received a range of Δ9-THC doses (0, 5, 15 and a “high” dose, either 25 or 30 mg). Responses on a subjective effects questionnaire, cognitive/psychomotor performance tasks and physiological measures were assessed. Data from individual outcomes are fit to a linear mixed model with Δ9-THC dose and sex included as predictors. Results: Initial analyses reveal expected dose-dependent effects of Δ9-THC. Specifically, Δ9-THC increased ratings on “positive” VAS items (e.g., Good Effects, Like Drug, Take Again) and those related to intoxication (e.g., High, Stoned). Δ9-THC also impaired performance, elevated heart rate and reduced temperature. Despite comparable current cannabis use patterns in male and female subjects, sex differences emerged on physiological outcomes, and interestingly, female subjects were more likely to report negative subjective effects. Conclusions: Ongoing post-hoc analyses will assess dose-related differences in the response to Δ9-THC as a function of sex. The influence of substance use history on Δ9-THC effects will also be determined. Retrospective analyses that combine data across multiple studies are useful for investigating factors that might impact the response to drugs but cannot typically be evaluated in individual studies having small sample sizes, and can be used to guide the design of future prospective studies to more rigorously investigate specific variables contributing to increased vulnerability to drug use.

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POSTER ABSTRACTS

#168 Abstract Title: **Resident-Initiated Educational Exchange: Merging Academic Productivity with Surgical Humanitarianism**

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Abstract: Background: International surgical rotations are increasingly popular electives for general surgery residents. Global surgery experiences vary from extreme rural locations to tertiary care centers in developing countries. Visiting residents undoubtedly benefit from exposure to unique pathology and challenging surgical situations; however, we hypothesized that the experience can be enhanced for all involved by encouraging individual project proposal, development, and implementation as a prerequisite for participating in international elective surgical rotations. Methods: Residents participating in global surgical experiences are put in direct contact with faculty at the international location and expected to offer project proposals for curriculum development, surgical skills courses, or didactic sessions for the local residents. Projects are approved by both the program director and the institutional review board with anticipation of formal publication upon the resident's return to the home institution. Discussion: Projects from formal implementation of low-fidelity laparoscopic skills curriculum to literature reviews on critical care have been undertaken by this institution with success and greeted with great enthusiasm from local residents. Projects are initiated and often completed within each resident's rotation. This serves to facilitate formal completion reports and manuscript submission/publication, enhancing academic productivity among general surgery residents. Conclusion: Individual project development as an expectation for participation in international surgical electives selects dedicated residents with genuine interest in surgical humanitarianism towards patients and colleagues. Mandating a true educational exchange requires visiting residents to acknowledge the vast disparities in surgical resources, allows unique opportunities for resident-driven academic productivity, and enhances the international experience for all involved.

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POSTER ABSTRACTS

#169 Abstract Title: Personality Influences on the Cognitive Effects of D-amphetamine

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Abstract: Aims: To determine how personality influences objective cognitive response to d-amphetamine. Methods: A randomized, double-blind, placebo-controlled, outpatient study of forty healthy, young adults was designed to examine how impulsivity and sensation seeking mediate cognitive enhancement response to d-amphetamine. Sensation seeking and impulsivity were measured with the Zuckerman-Kuhlman Questionnaire. Participants scored in the upper and lower median of population norms. Cognitive effects of d-amphetamine at two randomized dosages (8mg, 16mg) and placebo were measured by performance on the N-back, CuedRT, and DSST tasks.

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POSTER ABSTRACTS

#170 Abstract Title: **The Young Child Brief Behavioral Screen: Preliminary Results**

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Abstract: Background: Early identification of disruptive behavior problems is crucial to reduce the serious long-term consequences of this public health problem. Accurate brief screening methods could improve low rates of physician recognition of young children with behavioral issues. This abstract reports preliminary results of an ongoing validation study of the 7-item parent-report Young Child Brief Behavioral Screen (YCBBS). Method: Parents (N=98) of children ages 3-5 seen at a university pediatric primary care clinic completed the YCBBS at baseline and at 2-week follow up and rated its acceptability. Physicians (N=27) in the same clinic also rated acceptability of the YCBBS in practice. Preliminary descriptive and psychometric analyses are reported. Results: Internal consistency of the YCBBS was .78. Test-retest reliability was high (ρ=.78, $p<.001$). Baseline YCBBS scores were significantly higher among parents who believed their child has emotional or behavioral problems (M=4.80, SD=3.05) compared to those who did not (M=2.74, SD=2.33), $t(35.168)=3.05$, $p<.01$. Most parents agreed/strongly agreed that the YCBBS was short enough for use during their child's appointment (86%), that it would be a good idea for their child's doctor to ask these questions (77%), and that primary care would be a good place to ask these questions (88%). Most physicians agreed/strongly agreed that the YCBBS was short enough for use in primary care (100%), that primary care is an appropriate venue for this tool (96%), and that they would use this tool in their own practice (74%). Conclusions: Parents and physicians are still being enrolled in this ongoing study. Early results of the psychometric properties of the YCBBS are promising. Future analyses will examine construct and criterion-related validity to determine its potential utility in early identification of young children with behavior problems.

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POSTER ABSTRACTS

#171 Abstract Title: **Differences in Drug Use, Mental Health, and Physical Health among Rural and Urban Criminal Offenders in Residential Substance Abuse Treatment & Recovery**

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Abstract: Rural women and urban women have been shown to differ in multiple ways. The purpose of this presentation is to examine the differences and similarities among women from rural and urban areas entering residential substance abuse treatment and recovery programs directly from incarceration. As part of an ongoing CSAT-funded evaluation of enhanced services provided to offenders reentering the community, face-to-face interviews were conducted with 199 women in residential substance abuse treatment/recovery. Data were collected on topics including drug use, mental health, health, income sources, sexual contacts, and criminality. Of the 199 women who consented to the evaluation between February 2013 and January 2014, Beale codes determined that 107 were from rural areas and 92 were from urban areas. Rural women were more likely than urban women to report abusing substances including Oxycotin (t=5.545, p=.012); Benzodiazepines (t=3.264, p=.002) and barbiturates (t=2.516, p=.017). Rural women also reported better overall health than urban women (t=1.979, p=.049), but reported more memory problems (t=2.291, p=.023) and were more likely to have income from disability (t=3.390, p=.001) than urban women. On the other hand, urban women reported more sexual contacts (t=-2.035, p=.044), and more criminal convictions (t=-2.401, p=.018) than rural women. Rural and urban women reported no differences in alcohol use, violence and trauma experiences, social support, educational attainment, lifetime incarceration, or housing. Understanding the similarities and differences among rural and urban women offenders in substance abuse treatment and recovery programs can significantly impact the effectiveness of programming women complete before returning home.

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POSTER ABSTRACTS

#172 Abstract Title: **Cocaine Images Impact Inhibitory Control: A Within- and Between-Subjects Comparison**

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Abstract: Cocaine users display impaired inhibitory control after viewing cocaine images compared to neutral images. Examining the effect of image type on inhibition has been limited by the need to use between-subjects designs. This study developed within-subjects methods to assess the impact of cocaine images on inhibitory control. We predicted subjects would show significantly impaired inhibitory control following cocaine images, but not following neutral images or a non-image cue (i.e., a rectangle as presented in the cued go/no-go task). One group of subjects (n=20) completed the Attentional Bias-Behavioral Activation (ABBA) task wherein cocaine images were the go cue. A second group (n=20) completed the ABBA task wherein neutral images were the go cue. Both groups completed the cued go/no task. The cocaine go condition produced more inhibitory failures on the ABBA compared to the cued go/no-go task. Performance did not differ when subjects performed the ABBA with neutral images and the cued go/no-go task. Subjects who completed the ABBA task with cocaine images performed more poorly than their counterparts who completed this task with neutral images. The two groups did not differ significantly when they performed the cued go/no-go task. The consistent rate of inhibitory failures between the neutral image condition of the ABBA task and cued go/no-go task suggests that the cued go/no-go task can be substituted for the neutral go condition of the ABBA task, allowing a within-subjects design to evaluate the influence of other manipulations on inhibitory control. Research supported by a NIDA grant R01 DA025032 (PI: CRR).

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POSTER ABSTRACTS

#173 Abstract Title: **Microlinguistic and Cognitive Contributions to the Proportion of Main Events Relayed**

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Abstract: Microlinguistic and Cognitive Contributions to the Proportion of Main Events Relayed Investigations of narrative discourse ability help us understand changes in language structure that occur across the adult lifespan. In this cross-sectional study, we addressed two questions: (1) what are the relative influences of episodic memory and working memory on lexical diversity (VOCD), informativeness (%IU), syntactic complexity (SynC) and the ability to relay main events (ME)?; and (2) what are the relative contributions of VOCD, %IU and SynC to the proportion of ME relayed? Language samples were elicited from the two single and two sequential pictures from Nicholas and Brookshire (1993). Picture description was the task of interest since it is frequently used to elicit language samples in age-related studies of language production. Two hundred forty healthy adults participated and comprised six decade cohorts, 20 through 70. Participants completed standardized measures of memory and picture descriptions. Results suggest that for single picture descriptions, working memory scores and %IUs are significant predictors of MEs relayed. For sequential pictures, age, episodic memory, %IUs, and SynC are significant predictors of MEs relayed. Significant age-related differences were found for LD, SynC, and MEs relayed, regardless of task; 60 and 70 year olds demonstrated significantly less lexical diversity, simpler syntax and relayed fewer main events as compared to the other cohorts. Memory scores were not significant predictors of any of the microlinguistic processes. Findings suggest that the relative impact of memory on MEs relayed is influenced by discourse task. Although age related changes in LD, SynC and %IUs were present, memory was not a significant predictor.

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POSTER ABSTRACTS

#174 Abstract Title: **The Relationship between Labial Vibrotactile Detection Thresholds and Low-Level Force Control Capabilities in Healthy Adults**

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Abstract: Although speech motor control theories have demonstrated the general importance of sensation for learning, maintaining and correcting articulatory motion, little is currently known about the specific relationship between sensory-related control strategies and parameters of fine force regulation in the orofacial region. This original research study was designed to characterize the relationship between labial vibrotactile threshold capacity and low-level force control (<2 N) capabilities of healthy young, middle-aged and aging adults. Sixty healthy adults (19-84 yrs.) completed vibrotactile detection threshold (VDTs) testing of the left lower lip vermillion using 5 and 10 Hz inputs. Low-level labial static and ramp-and-hold force control data was collected at a 0.5 N force endpoint. We hypothesized a significant difference for VDTs and force measures between age groups and that a negative correlational relationship would exist between orofacial sensation and force production measures as a function of advancing age. Non-parametric Kruskal-Wallis tests were used to compare the difference between groups, including variables of age, sex, speech use and smoking history. Spearman correlations were conducted to assess the relationship between sensory and force measures in comparison to various group data. This study identified a significant (or trending) correlation between the 5 Hz test frequency and force measures of rise time, peak force, and mean force hold (during static and ramp force conditions). Our findings demonstrated that as vibrotactile detection thresholds increase (less sensitivity), select measures of low-level force control decrease. Further research is needed to determine the clinical utility of these basic results.

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POSTER ABSTRACTS

#175 Abstract Title:	**Utilization of the Oswestry Disability Index in Primary Care: A Part of Kentucky Pain Referral and Outcomes Studies (KYPROS)**
Author(s):	S. R. Nester, College of Medicine, U of Kentucky W.G. Elder, Dept of Family and Community Medicine, U of Kentucky

Abstract: Chronic low back pain (CLBP) is a common complaint in primary care setting. Clinical presentations are heterogeneous and research is just beginning to stage or otherwise categorize psychological and functional factors for purposes of treatment selection. This project aims to determine if the Oswestry Disability Index (ODI) can differentiate patients who will utilize primary care provide (PCP) recommended treatments, in this case, complementary and alternative medicine (CAM) therapies. Our hypothesis is that more disabled CLBP patients will be less likely to utilize PCP recommended CAM to address their condition. The ODI assesses the patient's perception of the impact of low back pain on their function and quality of life. It is scaled so that higher scores are equated to more disability. In our study, the patients filled out the ODI during an initial baseline visit, and again after their CAM intervention 12 weeks later. Recently collected data from an NIH funded study will be analyzed to determine whether there is a relationship between ODI score and utilization of PCP recommended CAM. Additional exploratory analysis will examine if patient and physician attitudes, medications, BMI, gender and other variables mediate the relationship. In our results thus far, there do appear to be clinically significant differences showing that more severely functionally impaired CLBP patients are less likely to accept referral. Analyses are pending for examination of the mediating variables.

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POSTER ABSTRACTS

#176 Abstract Title: **Effects of Vigilance State on Clinical Seizure Predictability: A Pilot Analysis**

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Abstract: The ability to predict seizures would greatly benefit individuals with intractable epilepsy. Most seizure prediction algorithms (SPAs) extract “prediction variables” from the electrocorticogram (ECoG) and take abnormal trends as signs of impending seizures. However, changes in vigilance state (REM or R, NREM or N, Wake or W) are known to limit SPA performance, but a detailed investigation of its effects on seizure predictability is lacking. Polysomnography (PSG) is needed to determine vigilance state, but is not routinely acquired with ECoG. Here, we examine the effects of vigilance state on ECoG prediction variables. We analyzed prospectively acquired ECoG and PSG (EEG, EOG, EMG) data from patients undergoing invasive presurgical evaluation. A hidden Markov model (HMM) mapped sleep variables based on the relative spectral power of conventional EEG rhythms (delta, theta, etc.) onto W/N1, N2, N3, and R states. Then, prediction variables typical of those in published SPAs, specifically the linear cross-correlation peak and mean phase coherence, were computed from differential ECoG contacts near the seizure focus and correlated with HMM-scored vigilance state. Both ECoG prediction variables were strongly correlated with sleep variables and varied significantly with vigilance state ($p < 0.001$) across subjects. In conclusion, univariate and bivariate ECoG prediction variables were found to vary significantly with vigilance state as determined by PSG. Hence, such algorithms should correct for normal changes in vigilance state in order to minimize false predictions. Further analysis of ECoG-PSG recordings is ongoing and may yield more definitive ways to correct for state and improving SPA performance.

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POSTER ABSTRACTS

#177 Abstract Title: **Implantation of Autologous Peripheral Nerve Grafts into the Substantia Nigra of Subjects with Parkinson's Disease undergoing Deep Brain Stimulation Surgery**

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Abstract: In Parkinson's disease (PD), the substantia nigra undergoes a loss of dopaminergic cells and cell function that, in part, manifests into the outward symptoms of PD. One avenue of intense efforts to treat this disease involves the delivery of neurotrophic factors to restore dopaminergic cell function. A potential source of these neurotrophic factors are Schwann cells from the peripheral nervous system. After injury, Schwann cells release a host of growth factors including GDNF, NGF, BDNF, and NT-3. We have begun a pilot study to examine the safety and feasibility of implanting an autologous peripheral nerve graft into the substantia nigra of PD patients undergoing deep brain stimulation (DBS) surgery. Multi-stage, DBS surgery targeting the subthalamic nucleus was performed using standard procedures. After the DBS leads were implanted, a section of sural nerve (approximately 5mm in length) containing Schwann cells was excised and unilaterally delivered, using a custom-designed cannula, into the area of the substantia nigra. Adverse events were continuously monitored. Subjects have undergone or will undergo a Unified Parkinson's Disease Rating Scale (UPDRS) evaluation before surgery and at 1, 3, 6, 9, and 12 months after surgery. We have successfully completed peripheral-nerve-graft surgery in 5 of 5 participants. Immediate, post-operative magnetic resonance scans did not indicate evidence of abnormal tissue disruption. Participants who have completed six months in the study reported comparable adverse effects to standard DBS surgery. In addition, UPDRS Part III scores off medication/off stimulation remained mostly unchanged after 6 months (36 ± 8 baseline vs. 33 ± 9, mean ± SD; N=4), but two of the participants, under 60 years old, showed an 11 point improvement. Scores on medication and on stimulation improved by 6 points (16 ± 11 baseline vs. 10 ± 7 six months), and daily levodopa equivalents decreased from a mean of 844 ± 691 mg at baseline to zero after six months. During the initial months of the study, we have observed a limited number of adverse events along with some improvements on UPDRS evaluations but on-going assessments will help gauge the safety and feasibility of implanting peripheral nerve tissue in conjunction with DBS surgery and the potential benefits these grafts may provide.

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POSTER ABSTRACTS

#178 Abstract Title: **A Retrospective Chart Review Of Patients Treated For Chlamydia And Gonorrhea In The Emergency Department**

Author(s): S. Desai, Dept of Emergency Medicine, U of Kentucky
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Abstract: Background: In the emergency department the decision to treat chlamydia and gonorrhea infections (STIs) is based on the H&P. Chlamydia and gonorrhea infections are common, easily transmissible and pose serious complications if untreated. Therefore, it is important to not miss these diagnoses and the opportunity to treat. Objectives: Determine whether there are any correlations between H&P findings and a positive STI screen that could be used to accurately diagnose STIs in the emergency department. Methods: Data was gathered from EMR. Patients included were males and females seen in the emergency department in the past three years, who received treatment and testing for chlamydia or gonorrhea, and were between the ages of 18 and 50. 181 females and 32 males were included. History and physical findings were recorded. The percentage of patients with any given sign/symptom was calculated. If relevant, sensitivity and specificity was calculated using the H&P sign/symptom compared to PCR. Results: Women There was no one H&P item or combination that occurred a significant amount of time and only in the positive group. Chart 1 shows that H&P findings occurred at a similar rate in both groups. Men From Chart 2, a majority (91.7%) of men who tested positive for an STI were positive for penile discharge, compared to 20% of those who tested negative. For penile discharge: Sensitivity 91.7% Specificity 80.0% Conclusion: STIs cannot be accurately diagnosed based on H&P in the emergency department. There are two possible actions based on this conclusion. One being treatment is reserved until after confirmatory testing. Second, due to patient unreliability and lack of follow up, treatment is based on suspicion and confirmatory testing is not ordered. Because a significant proportion of our population is as above, and due to the prevalence and potential dangers of STIs this writer would tend to suggest the latter.

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POSTER ABSTRACTS

#179 Abstract Title: **Treatment Outcomes for Prescription Drug Misusers: The Negative Effect of Client Residence and Treatment Location Geographic Discordance**

Author(s): C.B. Oser, Dept of Sociology, Center on Drug & Alcohol Research, U of Kentucky
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Abstract: This is the first known study to examine geographic discordance (traveling from one's home residence to a different geographic location to receive substance abuse treatment) as a predictor of clinical and social functioning treatment outcomes (i.e., relapse, self-help attendance, anxiety, and incarceration) among a sample of prescription drug misusers. Substance abuse treatment entry and 12-month follow-up client-level survey data was collected from 187 clients who misused prescription drugs, and organizational-level survey data was collected from the supervisors at treatment centers attended by the clients. Multivariate models reveal that geographic discordance significantly increased the odds that prescription drug misusers would report relapse to prescription opioid misuse (O.R. = 2.97, 95% C.I. = .84, 10.53), anxiety (O.R. = 4.94, 95% C.I. = 1.72, 14.15), and any incarceration at follow-up (O.R. = 2.29, 95% C.I. = .92, 5.68). Moreover, discordant clients were significantly less likely to have attended a self-help group (O.R. = .39, 95% C.I. = .14, 1.09), net of the effect of other individual- and organizational-level factors. Implications for clinical practice and substance abuse treatment policy are provided.

Supported by: This project was supported by grants K01-DA021309 (PI: Oser) and T32-DA035200 (PI: Rush; Post-doctoral trainee: Harp) from NIDA. Funding for the client-level data was provided by the Kentucky Department of Behavioral Health, Developmental and Intellectual Disabilities, Division of Behavioral Health under a contract with the University of Kentucky Center on Drug and Alcohol Research (PI: Logan). Neither NIDA nor the Kentucky Department of Behavioral Health had a role in the study design, data collection, analysis and interpretation of data, and in the writing of the paper. The opinions expressed are those of the authors. The authors would like to acknowledge the contributions of Dr. TK Logan, Dr. Jennifer Cole, and Robert Walker, MSW in the collection/management of the KTOS data.

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POSTER ABSTRACTS

#180 Abstract Title: **The Relationship Between State Prescription Drug Monitoring Program Characteristics and Controlled Substance Dispensing to Medicaid Beneficiaries**

Author(s): A. Goodin, Martin School of Public Policy & Administration, Institute for Pharmaceutical Outcomes & Policy, U of Kentucky

Abstract: Objectives: Prescription Drug Monitoring Programs (PDMPs) have been enacted by several states to combat the abuse and diversion of controlled substances (CS). The study objective is to measure the impact of state PDMP characteristics on the dispensing of opioids and benzodiazepines to Medicaid beneficiaries. Methods: Medicaid dispensing and reimbursement data for each state (1990-2011) was obtained from the Medicaid Drug Rebate Program. Opioid and benzodiazepine prescriptions dispensed were isolated from the data and standardized to morphine milligram equivalents (MMEs) and diazepam equivalents (DMEs), respectively. Data was merged with state PDMP characteristics obtained from the National Alliance of Model State Drug Laws and several potential explanatory variables were identified; including, operational program, compulsory provider participation, interstate data sharing, and proactive notification of potential abuse. A random effects model using GLS regression was employed to generate estimates of the impact of state PDMP characteristics over time on MMEs dispensed of Schedule II opioids (CII), dispensing of Schedule III opioids (CIII), and DMEs of benzodiazepines. MMEs, DMEs, and Medicaid reimbursement dollars per MME dispensed were log transformed. Results: States with operational PDMPs dispensed on average 0.29 fewer logged MMEs of CII opioids ($p<0.05$). States with PDMPs housed in law enforcement agencies dispensed 0.11 more logged MMEs of CII opioids ($p<0.05$) on average and a 1-unit increase in Medicaid reimbursement resulted in 0.39 more logged MMEs of CII opioids dispensed ($p<0.001$). States with PDMP interstate data sharing dispensed 0.11 more logged MMEs of CII opioids ($p<0.05$). Results for CIII opioids and benzodiazepines were similar. Conclusions: States with operational PDMPs dispense fewer CII and CIII opioids, and benzodiazepines, to Medicaid patients. The amount of Medicaid reimbursement and data sharing with other states is associated with increased dispensing, but compulsory PDMP use and proactive reporting to health providers were not found to impact dispensing.

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POSTER ABSTRACTS

#181 Abstract Title:	**Prescription Drug Monitoring Program Utilization in Community Pharmacies**
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Abstract: Objective: Identify characteristics of Kentucky community pharmacists and community pharmacists' practice associated with utilization of the Kentucky All Schedule Prescription Electronic Reporting Program (KASPER), the state's prescription drug monitoring program (PDMP). Methods: Anonymous surveys were mailed to all 1,018 Kentucky pharmacists with a KASPER account and an additional 1,000 licensed pharmacists without an account. Bivariate analyses examined the association between KASPER utilization and practice type (independent or chain) and practice location (rural or urban). A Poisson regression model with robust error variance estimated risk ratios (RR) of KASPER utilization by characteristics of pharmacists' practice. Results: Responses were received from 563 pharmacists (response rate 27.9%). Of these, 402 responses were included in analyses. A majority of responding pharmacists (84%) indicated they or someone in their pharmacy had requested a patient's controlled substance history since KASPER's inception. Independent pharmacists reported greater KASPER utilization (94%) than chain pharmacists (75%; $p<0.001$). Responding pharmacists perceive KASPER as an effective tool to reduce drug abuse/diversion (92%) and doctor shopping (90%) in Kentucky. Utilization of KASPER varies significantly among community pharmacists; practicing in an urban location (RR: 1.11; [1.01–1.21]) or at an independent pharmacy (RR: 1.27; [1.14–1.40]) increased the likelihood of KASPER utilization. Conclusion: Utilization of KASPER varies among community pharmacists and is influenced by characteristics of the pharmacist's practice including practice type and location. Understanding characteristics associated with PDMP use is necessary to remove barriers to access and increase utilization.

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POSTER ABSTRACTS

#182 Abstract Title: **Hypercalciuria in Patients with Osteoporosis is Independent of the Underlying Bone Turnover**

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Abstract: Introduction: Osteoporosis (OP) is classified as being either high bone turnover (HBT; i.e., excessive bone resorption) or low bone turnover (LBT; i.e., decreased bone formation). Hypercalciuria is well known to be associated with OP. However, this is thought to be related to increased bone resorption and calcium release to the blood circulation seen in HBT OP. To date, it is not known whether LBT OP, which is increasingly prevalent in older patients, is associated with hypercalciuria. Hypothesis: The purpose of this study is to test the hypothesis that hypercalciuria in patients with OP is independent of the underlying bone turnover. Methods: This is a retrospective study of patients with osteoporosis who underwent bone biopsy and 24-hour urine calcium measurement at the University of Kentucky between January 2010 and December 2012. Patients were divided into two groups based on whether they had HBT or LBT OP. Demographic data and standard lab values were obtained from the medical records. Results: A total of 153 patients with OP were identified (66 HBT and 87 LBT). Patients' age was (Mean ± SD): HBT = 56 ± 15 and LBT = 61 ± 12 ($p < 0.05$). Total urinary calcium (mg/day) was: HBT = 236 ± 126 and LBT = 214 ± 107 (NS). Hypercalciuria defined as > 250 mg/day for men and > 200 mg/day for women was present in 59% and 51% of HBT and LBT patients, respectively. The urine calcium/creatine ratio, another measure of urinary calcium, was also not significantly different between the two groups. Conclusion: Hypercalciuria is very frequently present in patients with OP. It appears to be independent of the underlying bone turnover status. Further studies are needed to explain the mechanism of hypercalciuria in osteoporotic patients.

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POSTER ABSTRACTS

#183 Abstract Title: **Three-dimensional flow contrast imaging of deep tissue using noncontact diffuse correlation tomography (ncDCT)**

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Abstract: Introduction: Blood flow distribution in tissues can provide vital information to healthcare professionals including clinicians and research investigators. We have recently developed a noncontact diffuse correlation spectroscopy (DCS) flowmetry system using a lens-focusing technique to monitor the relative change of blood flow at a spot of interest. This study extended the noncontact DCS system into noncontact diffuse correlation tomography (ncDCT) for three-dimensional flow imaging of deep tissue. Methods: A linear array of 15 photodetectors and two identical laser sources coupled with a lens-focusing probe and a motion translation system enabled automatic and noncontact scanning of flow in a region of interest. These boundary measurements were combined with a finite element method based DCT image reconstruction algorithm which was accomplished through integration into an open software package termed NIRFAST, thus promoting ncDCT to image objects with arbitrary geometry and optical properties. The ncDCT technique then was tested in computer simulations and using a tissue-like phantom design with a pump connected tube as the inducer of anomalous flow contrast. Results: The cylindrical tube-shaped anomaly was clearly reconstructed in both simulation and phantom experiments. Recovered and assigned flow contrast changes in anomaly were found to be highly correlated: regression slope = 1.00, R2 = 1.00 and $p < 10\text{-}5$ in simulation and regression slope ≥ 0.97, R2 ≥ 0.96 and $p < 10\text{-}3$ in phantom experiments. Conclusion: The noncontact breakthrough design enables potential imaging of deep blood flow contrast in real human tissues (e.g., breast tumor, pressure ulcer) without distorting hemodynamic properties.

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Classification / Health Topic Area: Basic Science / Cancer

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POSTER ABSTRACTS

#184 Abstract Title: **Genotype Effect on Differential CD33 Exon 2 Splicing in Leukemia Cells**

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Abstract: Introduction: CD33 is a myeloid-lineage cell surface receptor. There is evidence of locus rs12459419 genotype effects on levels of CD33 transcripts with exon 2 skipped (D2-CD33) in brain samples. Gemtuzumab ozogamicin is a monoclonal antibody-based chemotherapeutic for acute myeloid leukemia (AML) and was developed from a clone that recognizes an exon 2 epitope. This study set out to characterize CD33 splicing in AML lineages. Methods: RNA extracts were prepared from 26 lines of acute (n=24) or chronic (n=2) myeloid leukemia. Libraries of cDNA were created and full-gene PCRs were conducted on a pooled sample. Results were visualized on a polyacrylamide gel and sequenced. Cell lines were genotyped for the rs12459419 locus. Each cell line then underwent quantitative PCR (qPCR) for total CD33 cDNA (tCD33) and D2-CD33 cDNA copy numbers. Results were compared by two-tailed Student's T test with a = 0.05. Results: Multiple splice isoforms were found in the pooled cDNA sample. Of the cell lines tested, half (n = 13) were homozygous for the major rs12459419 allele and half (n = 13) were heterozygous. Numbers of tCD33 copies (p = 0.48) and D2-CD33 copies (p = 0.44) were not significantly different between the two genotype groups. The percentage of total CD33 expressed as D2-CD33 (D2-CD33/tCD33) was different between the genotype groups (p = 4.2 x 10-5). Conclusions: CD33 genotype impacts proportions of D2-CD33 transcripts in myeloid leukemia lineages. Further studies are needed to determine if rs12459419 genotype exerts a similar effect on CD33 protein expression.

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POSTER ABSTRACTS

#185 Abstract Title: **RORα Binds to E2F1 to Induce Cell Quiescence and Regulate Mammary Gland Branching Morphogenesis**

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Abstract: RAR-related orphan nuclear receptor alpha (RORα) is a potent tumor suppressor that induces cell quiescence and inhibits tumor growth. However, the molecular mechanism by which it induces cell quiescence remains unknown. We demonstrate a non-canonical nuclear receptor pathway that RORα binds to E2F1 to inhibit cell cycle progression. We showed that RORα bound to the heptad repeat and marked box region of E2F1 and suppressed E2F1-regulated transcription in epithelial cells. Binding of RORα inhibited E2F1 acetylation and its DNA-binding activity by recruiting HDAC1 to the protein complexes. Knockdown of HDAC1 or inhibition of HDAC activity at least partially rescued transcription factor activity of E2F1 that was repressed by RORα. Importantly, RORα levels were increased in mammary ducts compared to terminal end buds, and reversely correlated with expression of E2F1 target genes and cell proliferation. Silencing RORα in mammary epithelial cells significantly enhanced cell proliferation in the ductal epithelial cells and promoted side-branching of the mammary ducts. These results reveal a novel link between RORα and E2F1 in regulating cell cycle progression and mammary tissue morphogenesis.

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POSTER ABSTRACTS

#186 Abstract Title: **The Protective Role of aMSH-MC1R Signaling in Reducing Oxidative Stress in Human Melanocytes**

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Abstract: There has been an increase in the incidence of skin cancer in the US, particularly that of melanoma. Nonfunctional human melanocortin receptor (Mc1r) is a known risk factor for melanoma. Because of the crucial role of oxidative damage to DNA and its inadequate removal in skin carcinogenesis, we take a closer look at the role of the Mc1r pathway in the activation of enzymes that are known to reduce and remove UV-mediated DNA oxidative damage. Previous data shows that the Mc1r pathway initiates a rise in base excision repair enzyme 8-oxoguanine glycosylase (0GG-1). However, this mechanism is not understood. We used Mc1r deficient melanocytes to study OGG-1 expression and to measure DNA oxidative products. We used forskolin, a drug that is able to activate adenylate cyclase, which is a downstream target of Mc1r, to study to induction of OGG-1 in Mc1r deficient human melanocytes. We expect an increase in OGG-1 after activation of the secondary messenger cyclic AMP. Our data show a twofold increase in OGG-1 levels after forskolin treatment 3 and 6 hours prior to UV irradiation, compared to untreated cells. We also show a significant increase in apurinic/apyrimidic (AP) sites, a marker for oxidative DNA damage, in Mc1r defective cells that were not protected by forskolin prior to UV irradiation. The pharmacologic activation of cAMP in Mc1r deficient cells induces a rise in OGG-1 and a decrease in AP sites on DNA. These data suggest a possible role of functional αMSH-Mc1r signaling in the removal of UV-mediated DNA oxidation.

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POSTER ABSTRACTS

#187 Abstract Title: **Effect of Withaferin A, an anti-cancer agent from a medicinal plant on lymphoma and leukemia cells**

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Abstract: Withaferin A, a withanolide from the plant, Asvagandha (Withania Somnifera) used in Ayurvedic medicine, has been found to be valuable in the treatment of several medical ailments. Withaferin A has been found to have anticancer activity in various solid tumors, but its effects on hematological malignancies have not been studied in detail. Here we examined the effect of highly purified Withaferin A on the survival of multiple B cell lymphoma lines and leukemia. Withaferin A strongly inhibited the survival of several human (SUDHL-6, LY10, Ramos, Mino), and murine (BKS-2, A20) lymphoma cells. The drug also inhibited the survival of chronic lymphocytic leukemia cells from the Emu-Tcl1 transgenic mice. Our data suggests that WA inhibits proliferating lymphoma cells and quiescent CLL cells. We demonstrated that Withaferin A inhibited nuclear translocation of NF-κB in diffuse large B cell lymphomas and found that Withaferin A treatment resulted in a significant decrease in protein levels of Akt and Src family kinases. Since previous studies implicated Withaferin A affects heat shock proteins and their chaperone activity via ATP-independent mechanisms, and Akt and Src are some of the target kinases of HSP90, we are investigating if the growth inhibition in lymphoma cell lines and B-CLL is also dependent on this pathway. (Supported by NIH)

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POSTER ABSTRACTS

#188 Abstract Title: **Tobacco Exposure, Perceived Risk, and Lung Cancer Worry**

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Abstract: Background. This study examined the association between demographic factors, perceived risk, tobacco exposure and lung cancer worry at baseline of a dual home screening trial to reduce home exposure to radon and secondhand smoke (SHS). Lung cancer is preventable through the elimination of tobacco smoke and radon exposure. It was hypothesized that smokers and those exposed to SHS in the home would have higher perceived risk and be more worried about lung cancer. Methods. A purposive sample of homeowners (N=113) were recruited in an outpatient clinic in the South. Recruitment is ongoing through 12/14. Self-reported race, education, income, age, gender, marital status, perceived risk of lung cancer, smoking status, past 7-day secondhand smoke exposure in the home, and lung cancer worry were assessed via iPad survey. An 11-point ordinal scale assessed perceived risk. Lung cancer worry was measured using a 4-item scale. Results. Preliminary findings indicate that Caucasian participants had lower lung cancer worry than those in other ethnic/racial groups. Those who perceived their lung cancer risk to be higher also had higher worry scores, as did current smokers. Interestingly, lung cancer worry was unrelated to other demographic factors and secondhand smoke exposure in the home. Conclusions. Although SHS is the third leading cause of lung cancer, those exposed in the home did not have higher scores on the lung cancer worry scale than those who were non-exposed. More research is needed to examine ethnic/racial variations in lung cancer worry and perceived risk for lung cancer.

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POSTER ABSTRACTS

#189 Abstract Title: **3-D Blood Flow Imaging of Breast Tumor Using Noncontact Diffuse Correlation Tomography (ncDCT): Computer Simulations**

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Abstract: Background: Since aggressive cancers are frequently hypermetabolic with angiogenic vessels, quantification of blood flow can be vital for cancer diagnosis. Our lab has recently developed a noncontact diffuse correlation tomography (ncDCT) to image blood flow contrasts in deep tissues. This study is to evaluate the ncDCT system for 3-D imaging of tumor-to-normal contrasts in tissues with different geometries using computer simulations. Methods: A homogeneous flat-slab mesh and a breast-shape mesh (node distance = 2 mm) were generated respectively to simulate the background tissues with different geometries. A sphere anomaly mesh (diameter = 10 mm) with a 5-fold flow contrast higher than the background tissue was placed 7 mm beneath the background surface to mimic an anomaly/tumor. The line-shape ncDCT probe with 2×15 source-detector pairs was scanned rotationally over the anomaly to collect boundary data, which was then input to the inverse process for the reconstruction of anomaly flow contrast distribution. Results: For the flat-slab mesh, the peak and average flow contrasts inside the reconstructed anomaly were underestimated by 15.4% and 37.8 ± 9.76% respectively while the reconstructed anomaly center was deviated to 4.8% of the anomaly diameter. For the breast-shape mesh, the peak and average flow contrasts were underestimated by 3.6% and 33.6 ± 10.6% while the reconstructed anomaly center was deviated to 7.4%. Conclusions: Our results demonstrate that the ncDCT system can reconstruct anomaly blood flow contrast and location in both regular (slab-shape) and arbitrary (breast-shape) geometries with similar accuracies.

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POSTER ABSTRACTS

#190 Abstract Title: **Lung Cancer Screening: Evaluation of a Pilot Continuing Education Program for Primary Care Providers**

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Abstract: The National Lung Screening Trial (NLST) demonstrated a significant reduction in lung cancer mortality following lung cancer screening (LCS) based on low-dose computed tomography (LDCT) as compared to chest x-ray (CXR). However, the NLST also revealed potential harms including substantial rates of false positive test results, raising the need for shared decision making (SDM) in implementing LCS. However, healthcare providers may not be adequately informed about the potential benefits, harms, and uncertainties associated with LCS. This pilot study examined the impact of a continuing education (CE) program designed to provide primary care providers with accurate information about LCS and to improve their ability to engage in SDM about LCS. The sample consisted of 45 primary care providers (N=45; male=51%; mean age 40.6±12.3) who completed a survey directly before and after the CE program, which assessed feasibility and acceptability of the program as well as knowledge, attitudes, and practices. A majority of participants (82%) reported that they were satisfied and would recommend (82%) the CE program to their colleagues, supporting acceptability. Paired-samples t-tests demonstrated significant improvement in self-efficacy to engage in SDM about LCS ($p<.01$). McNemar's tests demonstrated significant improvement in objective knowledge of key facts regarding LCS ($p<.01$). However, self-efficacy regarding tobacco cessation counseling showed no significant improvement. These results suggest that the CE program is an acceptable and effective approach to disseminate information and skills about LCS and SDM. Efforts are underway to enhance the program by delivering content online and examining longer-term effects on provider behavior.

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POSTER ABSTRACTS

#191 Abstract Title: **Local Delivery of Imiquimod in Hamsters by Mucoadhesive Films.**

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Abstract: Oral squamous cell carcinoma, estimated to affect 42,440 patients in the United States of America in 2014, progresses from untreated precancerous dysplastic lesions. Hence, mucoadhesive films loaded with the immune response modifier imiquimod were developed for potentially halting progression or promoting disease reversal. Several properties, such as sustained release of drug, adhesive properties, permeability, and transport kinetics of drug, were characterized in vitro. The objective of the present studies was to investigate performance characteristics of two types of films in vivo. Due to a lack of information regarding suitable small animal models for testing long-residing mucoadhesive films, the residence time of films at different application sites in hamster cheek pouches was first investigated. Films applied to the cheek, outside surface of the pouch, or deep inside the pouch resided up to 0.5, 4, or 9 hours, respectively, with no difference between film types. Local delivery of imiquimod and its retention in oral mucosal tissue, and systemic distribution in blood were then determined for mucoadhesive films and compared to commercially available imiquimod cream. The films delivered imiquimod to oral mucosal tissue and helped localize the drug while they remained adherent for 4 hours, after which tissue drug content decreased through 12 hours. Although imiquimod cream resulted in higher drug contents through 8 hours half of the animals showed systemic absorption of imiquimod. In humans, the residence time of the mucoadhesive films depended on the application site, increasing in the order of tongue < cheek < gingiva.

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POSTER ABSTRACTS

#192 Abstract Title: Cardiac Mechanics of Diet-Induced Obese Mice: A Complex Time Course of Dysfunction

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Abstract: Obesity is an epidemic that is associated with increased cardiovascular mortality. Medical imaging-based assessments of cardiac mechanics, such as myocardial strains, are good predictors of mortality and are known to be altered in obesity. However, the time course of dysfunction and the contributions of other factors (e.g., hypertension) are poorly understood. We hypothesized that diet-induced obesity in mice leads to reductions in left ventricular (LV) mechanics, which develop subsequent to hyperglycemia, hypertension, and ventricular remodeling. Twenty 3-week-old C57BL/6J mice were randomized (n=10 per group) to a high-fat (60% kcal from fat) or sucrose-matched control (10% kcal from fat) diet for 40 weeks. LV mechanics were quantified every 6 weeks using cine displacement encoding (DENSE) MRI on a 7T magnet. Blood pressure and glucose tolerance were assessed every 4 weeks. Mixed effects modeling was used for statistical analyses.Measures of fasting blood glucose (202 vs. 112 mg/dL for high-fat and controls, respectively; $p<0.05$), LV mass (88 vs. 79 mg) and systolic blood pressure (172 vs. 162 mmHg) exhibited diverging patterns as a function of time on diet. LV mechanics were significantly different, with some changes observed after only 4 weeks on diet; however, significant variations were observed over time with no obvious diverging time point. There was no difference in ejection fraction through 40 weeks. Diet-induced obesity in mice is associated with reduced left ventricular mechanics; however, the time course of this dysfunction is complex such that assessments at individual time points may not be representative of overall functional status.

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POSTER ABSTRACTS

#193 Abstract Title: **High Resolution Magnetic Resonance Imaging of Cardiac Motion and Mechanics in Humans**

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Abstract: Purpose: Displacement Encoding with Stimulated Echoes (DENSE) is a magnetic resonance imaging (MRI) technique that is used for quantifying cardiac strain and torsion. DENSE has been implemented with a resolution limited to 4 pixels across the heart wall. This resolution may limit the ability of DENSE to quantify strains and torsion within thin regions of the left ventricular wall. We hypothesize that a higher resolution will provide more accurate estimates of cardiac strain and torsion. Methods: Ten healthy subjects were consented. A Siemens MRI was configured with a navigator feedback system. The feedback system projected a navigator image to the subject in real time. Standard resolution and high resolution DENSE were acquired with a pixel size of 2.8mm and 1.4mm, respectively. Left ventricular strains and torsion were calculated and compared between the two resolutions using paired t-tests and Bland-Altman statistics. Results: The volunteers had a navigator efficiency of 73%±10%. The high resolution demonstrated excellent image quality with noticeable improvement over the standard resolution. Radial strain and torsion were significantly different between the two resolutions for each region of the left ventricle. Circumferential and longitudinal strains were similar between the two resolutions and only demonstrated significant differences in the outer regions of the left ventricle. Conclusions: High resolution DENSE produces images with superior image quality. A navigator feedback system produces high efficiency scans. Measures of radial strain and torsion are sensitive to the image resolution and are likely improved with higher resolution imaging. This improvement should be further tested for ability to predict serious outcomes like mortality.

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9th Annual CCTS Spring Conference and 4th Annual ATRN Summit

Thursday, March 27, 2014 Lexington Convention Center

POSTER ABSTRACTS

#194 Abstract Title: **Two-Dimensional Estimates of Left Ventricular Strains are Significantly Affected by Through-plane Motion**

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Abstract: Advanced measures of cardiac mechanics such as left ventricular (LV) strains can be used in conjunction with classical biomarkers to gauge cardiovascular health and improve prediction of patient outcomes. Several imaging techniques, including displacement-encoded magnetic resonance imaging (DENSE), are used to non-invasively assess cardiac mechanics. These data are predominantly acquired in two dimensions (2D) due to simplified post-processing and shorter acquisition times; however, this type of acquisition cannot account for through-plane motion caused by longitudinal contraction of the LV. We hypothesized that through-plane motion significantly affects 2D strain estimates. DENSE data were acquired in eight healthy volunteers (Age: 27±3 years) and 3D displacement of the LV myocardium was measured throughout the cardiac cycle. Cardiac strains were computed from the 3D displacement data and compared to strains derived from only 2D displacement data (ignoring through-plane motion) using a two-tailed paired t-test. Two-dimensional imaging consistently overestimated radial strain and underestimated circumferential strain. Circumferential strain was significantly different at the basal and mid-ventricular segments (p=0.001 and 0.009, respectively). Radial strain decreased from the base to the apex in both 2D and 3D analyses; however, 2D significantly overestimated radial strain at the mid-ventricular and apical slices compared to 3D (p=0.002). Two-dimensional imaging methods for assessing left ventricular mechanics consistently overestimate radial strain and underestimate circumferential strain when compared 3D imaging. This limitation of two-dimensional imaging is likely due to the through-plane motion of the heart, which is ignored in two-dimensional techniques. Future research needs to determine the clinical and prognostic significance of this difference.

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9th Annual CCTS Spring Conference and 4th Annual ATRN Summit

Thursday, March 27, 2014 Lexington Convention Center

POSTER ABSTRACTS

#195 Abstract Title: **Effect of Variable Breath-hold Positions During Cardiac Magnetic Resonance Imaging on Measures of Heart Function**

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Abstract: Purpose: Cardiac magnetic resonance (CMR) can be used to quantify measures of cardiac function, for example strains and torsion, using methods such as cine Displacement Encoding with Stimulated Echoes (DENSE). Images are generally acquired during an end-expiratory breath-hold. Unfortunately, it is difficult for subjects to hold their breath at the exact same position during the required series of breath-holds of a typical CMR study; normal end-expiratory breath-hold positions have a range of about 8 millimeters (mm). We hypothesized that the normal variability in breath-hold positions would significantly affect the quantification of left ventricular strains and torsion. Methods: Eight healthy volunteers were consented. The CMR scanner utilized a feedback system to enable subjects to view their diaphragm position in real time during acquisition. We acquired DENSE images at three different breath-hold positions equally spaced across 8mm with a narrow acceptance window of ±2mm. Left-ventricular strains and torsion were calculated and compared between diaphragm locations using a repeated measures ANOVA with a Huynh Feldt correction. Results: Diaphragm position had a minimal effect on left ventricular radial strain, circumferential strain, and torsion. The only significant difference between navigator positions was for the mid-ventricular and global peak radial strains ($p = 0.01$ for both). Estimated power for detecting a difference was adequate between 70 and 100% suggesting a low probability for Type II errors. Conclusions: Breath-hold positions had minimal effects on calculated peak left ventricular cardiac strains and torsion from two-dimensional DENSE CMR. It will be important to determine whether this result holds true in a future study which includes patients with potentially heterogeneous contraction patterns in the left ventricle.

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POSTER ABSTRACTS

#196 Abstract Title: **Myocardial Recoil at the End of Systole Quickens Diastolic Relaxation**

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Abstract: Diastolic dysfunction is associated with cardiac morbidity and mortality. The mechanisms that control diastolic relaxation are not yet clear. Classical ex vivo experiments suggest that the relaxation of cardiac muscle depends on afterload, with lower afterloads producing faster relaxation. These original experiments used protocols in which the muscle recoiled to its original length before beginning diastolic relaxation. In this experimental mode, reducing afterload increases the velocity of the muscle when as returns to its original length (late systolic strain rate). In this work, we used electrically simulated rat trabeculae to test the hypothesis that the strain rate, and not the afterload, controls relaxation. We varied the late systolic strain rate by allowing the trabeculae to recoil at different strain rates at a fixed afterload. Relaxation was slowest when recoil was prevented and fastest when strain rate was highest. Preload did not influence this effect. We have confirmed this mechanism exists in a right ventricular trabecula from a human donor heart. Identically to the rat trabecule, faster late systolic strain rate quickens diastolic relaxation in human hearts. This data may have clinically translatable impact in the diagnosis and treatment of diastolic dysfunction.

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POSTER ABSTRACTS

#197 Abstract Title: **Accurate Extraction of Diffuse Correlation Spectroscopy Flow Index by Integration of Nth-order Linear Model with Monte Carlo Simulation**

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Abstract: Conventional semi-infinite solution for extracting blood flow index (BFI) from diffuse correlation spectroscopy (DCS) measurements may cause errors in estimation of BFI (αDB) in tissues with small volume and large curvature. We proposed an algorithm integrating Nth-order linear model of autocorrelation function with the Monte Carlo simulation of photon migrations in tissue for the extraction of αDB. The volume and geometry of the measured tissue were incorporated in the Monte Carlo simulation, which overcome the semi-infinite restrictions. The algorithm was tested using computer simulations on four tissue models with varied volumes/geometries and applied on an in vivo stroke model of mouse. Computer simulations shows that the high-order (≥ 5) linear algorithm was more accurate in extracting αDB (errors < ±2%) from the noise-free DCS data than the semi-infinite solution (errors: -5.3 to -18.0%) for different tissue models. Although adding random noises to DCS data resulted in αD-B variations, the mean values of errors in extracting αD-B were similar to those reconstructed from the noise-free DCS data. In addition, the errors in extracting the relative changes of αDB using both linear algorithm and semi-infinite solution were fairly small (errors < ±2.0%) and did not rely on the tissue volume/geometry. The experimental results from the in vivo stroke mice agreed with those in simulations, demonstrating the robustness of the linear algorithm. DCS with the high-order linear algorithm shows the potential for the inter-subject comparison and longitudinal monitoring of absolute BFI in a variety of tissues/organs with different volumes/geometries.

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POSTER ABSTRACTS

#198 Abstract Title: **Transmural heterogeneity of cellular level power output is reduced in human heart failure**

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Abstract: Heart failure is a complex pathophysiological condition associated with pump dysfunction and remodeling. The aims of this study are to test (a) whether non-failing human samples exhibit transmural heterogeneity of cellular level contractile properties, and (b) if heart failure alter these region specific changes in contractile function. Chemically permeabilized samples were prepared from the sub-epicardial, mid-myocardial, and sub-endocardial regions of the left ventricle of non-failing (n=6) and failing (n=10) human hearts. Mechanical and biochemical assays were then performed on these permeabilized samples. The results of the study demonstrates that non-failing mid-myocardial samples have a higher power output (0.59 ± 0.06 μW mg-1) than samples from the sub-epicardium (p=0.021) and the sub-endocardium (p=0.015). The nonfailing mid-myocardial samples also produced more isometric force (14.3 ± 1.33 kN m-2) than samples from the sub-epicardium (p=0.008) and the sub-endocardium (p=0.026). The results from the heart failure samples demonstrated reduced power (p=0.009) and force (p=0.042) with the greatest decrease occurring in the mid-myocardial samples. Heart failure samples also demonstrated an increase in fibrosis (p=0.021) with mid-myocardial samples from failing hearts containing more collagen than the matching sub-epicardial (p<0.001) and sub-endocardial (p=0.043) samples. The main conclusions are that (a) non-failing human hearts exhibit transmural heterogeneity of contractile properties, and (b) failing hearts demonstrate more fibrosis in the mid-myocardial tissue, which leads to the greatest contractile deficit.

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POSTER ABSTRACTS

#199 Abstract Title: **An Examination of the Role of Cathepsin B in the Shear Stress Regulation of CD11/CD18 Surface Levels by Neutrophils**

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Abstract: Previously, cathepsin B (catB) was identified as a key cysteine protease involved in shear-induced CD18 cleavage, a putative anti-inflammatory control mechanism for neutrophils. But mechanistic insight regarding catB involvement remains elusive, particularly due to limitations of using human neutrophils for molecular analyses. To address this, we explored the use of HL60-derived neutrophilic cells (dHL60NCs) as a model cell line for characterizing the molecular dynamics of catB-related CD18 cleavage. We tested the hypothesis that flow-related CD18 cleavage by catB is phenotypic of neutrophils. Based on flow cytometric analyses, dHL60NCs exposed to 5 dynes/cm2 shear stress for 10 minutes were observed to exhibit reduced expression of CD18 and CD11a, but not CD11b. E64, a cysteine protease inhibitor, attenuated CD18 and CD11a cleavage under shear. Notably, while human neutrophils and dHL60NCs exhibited similar CD18 cleavage under shear, we previously reported that primary neutrophils preferentially cleave CD11b over CD11a. This difference, however, may be explained by the minimal expression of catB detected for dHL60NCs, in contrast to its abundance in primary neutrophils. Moreover, shear stress stimulated catB release by primary neutrophils in a temporal fashion similar to that reported for shear-related cleavage of CD18 and CD11b. Collectively, our results suggest that, although shear-induced cleavage of CD18 subunits is characteristic of a neutrophilic phenotype, catB may not be the only cysteine protease responsible for cleaving CD11/CD18 integrins on sheared neutrophils. Future work will utilize the apparent differential cysteine protease expression patterns of human neutrophils and dHL60NCs to explore the role of catB in shear-induced CD18 cleavage.

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POSTER ABSTRACTS

#200 Abstract Title: **Voluntary Exercise Reduces Risk Factors Associated with Polychlorinated Biphenyl -Induced Cardiovascular Disease**

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Abstract: Cardiovascular disease is the leading cause of mortality in developed countries. Polychlorinated biphenyls (PCBs) are persistent environmental pollutants that contribute to the initiation of cardiovascular disease. Previous work in our laboratory has examined the role of nutrition in modulating the toxicity of PCBs in vascular endothelial cells. We hypothesize that, in addition to nutrition, exercise also can modulate the vulnerability to environmental insults. There is strong evidence that exercise can reduce the risk of cardiovascular disease; however, whether exercise can modulate PCB-induced cardiovascular inflammation and endothelial dysfunction is unknown. Male ApoE-/- mice were divided into sedentary and exercise groups and developed atherosclerosis over a 12 week period. Half of each group was exposed to PCB 77 at a dose of 170 μmoles/kg mouse during weeks 1, 2, 9 and 10. Exercise significantly reduced several risk factors associated with cardiovascular disease including glucose intolerance, hyperlipidemia, hypertension, systemic inflammation, and oxidative stress in PCB77-treated animals. Exercise upregulated antioxidant enzymes including phase II enzymes, suggesting enhanced metabolism and clearance of PCB77 and its metabolites, measured through LC MS/MS. Ex vivo vascular reactivity studies were performed to measure endothelial function. Sedentary animals exposed to PCB77 exhibited endothelial dysfunction as demonstrated by significant impairment of endothelium-dependent-dilation (EDD), which was prevented in exercised animals. Administration of tempol, a superoxide dismutase (SOD) mimetic restored endothelium-dependent vasodilation implicating increased superoxide levels as a cause of endothelial dysfunction in these animals. Results from this study provide novel findings suggesting that regular physical activity could be utilized as a therapeutic approach for the prevention of adverse cardiovascular health effects induced by environmental pollutants such as PCBs.

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POSTER ABSTRACTS

#201 Abstract Title: **Patients with Repaired Tetralogy of Fallot Suffer from Multiple Forms of Cardiac Dyssynchrony: A Cardiac Magnetic Resonance Study**

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Abstract: Background– Patients with repaired tetralogy of Fallot (rTOF) frequently have right bundle branch block. However, the contribution of cardiac dyssynchrony to dysfunction remains controversial. To better understand this phenomenon, we aimed to quantify left (LV), right (RV) and inter-ventricular cardiac dyssynchrony using standard cine CMR. Methods– 30 patients with rTOF (age 28±16) and 17 healthy controls (age 29±7) underwent cine CMR. Patients were imaged twice to assess inter-test reproducibility. Circumferential strain curves were generated with a custom feature tracking algorithm for 12 LV and 12 RV segments in 4-7 short-axis slices encompassing the ventricles. Temporal offsets (TOs, in milliseconds) of the strain curves relative to patient-specific reference curves were calculated. The intra-ventricular dyssynchrony index (DI) for each ventricle was computed as the standard deviation (SD) of the TOs (more dyssynchrony increases the SD). The inter-ventricular DI was calculated as the difference in median RV and median LV TOs. Results– Compared to controls, patients had a greater LV DI (21±8 vs 11±5ms, $p<0.001$) and RV DI (60±19 vs 47±17ms, $p=0.02$). RV contraction was globally delayed in patients, resulting in a greater inter-ventricular DI with the RV contracting 45±25ms later than the LV vs 12±29ms earlier in controls ($p<0.001$). Inter-test reproducibility was acceptable with all coefficients of variation ≤22%. The degree of dyssynchrony was correlated with measures of LV function but not RV function. Conclusions– Patients with rTOF have multiple types of cardiac dyssynchrony which can be reproducibly quantified from standard cine CMR. Future studies need to determine whether these patients may benefit from cardiac resynchronization.

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POSTER ABSTRACTS

#202 Abstract Title: **Transradial approach to cardiovascular interventions: An Update**

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Abstract: BACKGROUND: Since the first cardiac catheterization in 1929, the procedure has continually evolved with advances in understanding, capabilities, and ease of operation. Though historically performed by cutdown of the brachial artery, cardiologists soon learned that transfemoral access was both easier to perform and more efficacious with regard to patient outcome. In the last twenty years, the transradial approach has been adopted, and is being utilized with increasing frequency. METHODS: We conducted a survey of literature published concerning safety, efficacy, cost-effectiveness, and global uptake of transradial catheterization with specific attention to how transradial interventions compare to transfemoral interventions. RESULTS: This review of literature indicates that when performed by an experienced interventionalist, radial catheterization is as effective as femoral catheterization and has additional benefits of shorter length of hospital stay and reduced patient costs. Transradial access is superior to transfemoral access in some, but not all, clinical scenarios; additionally, it is an effective alternative for catheterization in patients contraindicated for transfemoral procedures. Adoption of radial access in the US is at a faster rate than previously expected, though rate of use varies drastically worldwide. CONCLUSION: The transradial approach is an excellent option for carrying out cardiovascular interventions, and will be adopted by more cardiologists in the upcoming years.

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POSTER ABSTRACTS

#203 Abstract Title: **Decline in Platelet Count or Function After TAVR Predicts Adverse Outcomes**

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Abstract: Transcutaneous aortic valve replacement (TAVR) has emerged as an important option for patients with severe AS who are unable to undergo or at high risk for conventional AVR surgery. Patients undergoing TAVR are typically treated with aspirin and clopidogrel following the procedure to reduce the risk of thromboembolic events, although the net clinical benefits of dual anti-platelet therapy post-TAVR are largely unknown. This study sought to determine if platelet number and function identified individuals who are at risk for post-procedural complications and early mortality after TAVR. Of 30 patients studied, 29 (96.7%) displayed a decrease in platelet count at 48 hours post-TAVR; platelet count was lower immediately after the procedure in 24 (80%) patients. On average, platelet count declined by 15.4%, 24.5% and 37.8% immediately, at 24 hours, and at 48 hours, respectively, post-TAVR. A decline in ADP- and thrombin-mediated platelet activation was also observed. On average, ADP-mediated activation declined by 41.2%, 63.5%, and 60.4% immediately, at 24 hour, and 48 hours post-TAVR. Thrombin-mediated platelet activation declined by 30.9%, 43.3%, and 45.2% at the same time points. The subset of patients with P2Y12 antagonist use prior to TAVR had lower baseline ADP-aggregation, as expected. Despite the lower baseline values, they also experienced a decline in TRAP-aggregation post-procedure. Survivors tended to have a higher platelet count at 72 hours post-TAVR than the individuals who expired early after the procedure (p=0.052). TAVR results in a reduction in platelet count and activity that is observed immediately after the procedure and is maximal within 24 - 48 hours. Immediate post-operative platelet activity may be useful in identifying patients that are higher risk following TAVR.

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POSTER ABSTRACTS

#204 Abstract Title: **A Rapid and Simple Method for Fatty Acid Profiling and Determination of ω-3 index in Red Blood Cells**

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Abstract: Fatty acid profiling has become a very useful and effective tool in the diagnosis, prevention and treatment of several diseases with cardiovascular disease being particularly important. In order to arrive at accurate conclusions that would help promote the health of individuals plagued by such diseases, not only are excellent laboratory methods required, but also very important in monitoring responses to treatment. Over the years, several researchers have tried to improve methods of fatty acid profiling in biological systems and even though great progress has been made, an ideal method for the extraction of lipids and accurate fatty acid analysis had not been reported. The ω-3 index (a measure of the amount of eicosapentaenoic acid, EPA, and docosahexaenoic acid, DHA, in Red Blood Cell membranes expressed as the percent of total fatty acids) is of growing interest because it has been reported to provide prognostic information regarding the risk for heart diseases. Sodium methoxide has been widely used in the determination of ω -3 fatty acids in food samples. However, to our knowledge, few studies have been able to describe in detail, the use of this reagent in determining the fatty acid profiles in biological samples such as red blood cells. In this study, we show that sodium methoxide can be used effectively in a one-step extraction and methylation procedure for high throughput analysis of fatty acids in red blood cell membranes. It is rapid with complete methylation in 20 minutes, simple and relatively safer when compared with other reported methods.

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POSTER ABSTRACTS

#205 Abstract Title: **Yamaguchi's Hypertrophic Cardiomyopathy: a Case Study in an African American Male**

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Abstract: The purpose of this paper is to present an atypical and rare case of apical hypertrophic cardiomyopathy, review relevant imaging/laboratory findings, as well as present a brief review of the literature. Individual case information was reviewed and subsequently stripped of personally identifiable information. Subsequently a PubMed search for the terms "Apical Hypertrophic Cardiomyopathy, Yamaguchi's Cardiomyopathy, and Case Study" was performed. Case studies, and review articles were then included. Data includes several laboratory values, EKG, Echo, and MRI compared to values found in the literature. Conclusion: Yamaguchi's Cardiomyopathy is a very rare disease, but knowledge of the disease presentation can help not only recognize, but also improve the quality of life for patients in the future.

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POSTER ABSTRACTS

#206 Abstract Title: **Pulmonary Hypertension in the RASopathies**

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Abstract: The RASopathies are a class of developmental disorders caused by a genetic mutation in the Ras signaling pathway and associated mitogen-activated protein kinases that control the cell cycle, differentiation and senescence. Dysregulation of these pathways have profound effects on normal development. Germline mutations in the genes encoding components of the Ras/MAPK pathway encompass a diverse set of developmental syndromes, including neurofibromatosis type 1, Noonan syndrome, autoimmune lymphoproliferative syndrome, Costello syndrome, Legius syndrome, LEOPARD syndrome and cardiofaciocutaneous syndrome, among others. Although the pathophysiological manifestations of these conditions are diverse, they share some common phenotypic features and can be considered a spectrum of neuro-cardio-facial-cutaneous syndromes. The prevalence of pulmonary hypertension in the RASopathies is not well established as compared to cardiac and neurocognitive impairments. After examining the available case reports in the medical literature, it appears that individual cases of pulmonary hypertension have been reported in all member syndromes. Due to the aggressive and often fatal nature of pulmonary hypertension, a diagnosis of a RASopathy should also include screening for pulmonary hypertension.

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POSTER ABSTRACTS

#207 Abstract Title: **A Protocol to Improve the Evaluation of Atypical Acute Coronary Symptoms**

Author(s): S. Desai, Dept of Emergency Medicine, U of Kentucky

Abstract: Background: Current AHA recommendations are to obtain and interpret an EKG within 10 mins of arrival for patients presenting with chest pain. However, not all patients presenting with ACS present with chest pain. We created a protocol to obtain EKGs rapidly in patients with potential chest pain equivalents, to better and more rapidly identify these atypical ACS's. Objectives: We assessed a new EKG protocol to identify ACS in patients without chest pain. Methods: We retrospectively identified patients seen in the ED with principle or secondary diagnosis of acute myocardial infarction between June 2010 and July 2011. 405 patients identified. We excluded patients transferred from intra and inter-facilities with suspected or known acute myocardial infarctions (n = 97). We excluded patients with inadequate data (n = 27), negative cardiac enzymes, or suspected type II myocardial infarctions (n =54). Patient's presenting with acute non-traumatic CP (n= 106) were excluded from the remaining samples. This resulted in a total of 121 MI patients seen at the ED with presenting symptoms other than non-traumatic chest pain between 6/2010 and 7/2011. The patients were then categorized to two groups under the old protocol (n = 61) and new protocol (n = 60). Desai EKG Protocol: a) SOB, b) Syncope c) Palpitations d) Stroke-like Symptoms, e) Left arm pain f) Epigastric pain, dizziness or lightheaded, if over age 40, smoker, or diabetic Results: 22/61 (36.1%) patients received a Rapid EKG under the previous protocol (triage gestalt) while 21/60 (35%) patients received a Rapid EKG under the new protocol. Conclusion: This study did not find the protocol to be beneficial. The protocol needs to be simplified, and each symptom better assessed for sensitivity. We found barriers in keeping the RN's following the protocol versus using their gestalt. There are also many barriers in obtaining an EKG on certain patients who have multiple other needs that must be addressed rapidly.

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POSTER ABSTRACTS

#208 Abstract Title: **The Effects of Trendelenburg Position on Vital Signs**

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Abstract: Background: Traditional teaching suggests that hypotensive patients benefit from being placed in the Trendelenburg (Tbrg) position. The patient is placed supine with their head lower than their feet. The theory is that gravity will increase cerebral blood flow. However, gravity plays little if any role in the delivery of blood to this organ and to properly evaluate blood flow, properties such as cardiac output and arterial resistance must be considered. Tbrg positioning may very well decrease cardiac output and arterial resistance, therefore decreasing cerebral blood flow. A 2005 review stated the literature was "…scarce…" and its use '…seemed to be guided by "expert opinion"...' (Bridges, 2005). Objectives: To measure the effect upon MAP, HR, and SpO2 upon patients placed in Tbrg in normo and hypotensive patients. Methods: Design: Prospective, non-blinded study. Subjects: 80 normotensive (MAP>70) and 40 hypotensive (Sys BP<90 or Diastolic BP<60) patients. Inclusion criteria: Age>18. Exclusion criteria: Refusal, inability to consent, pregnant, interference with patient care, already in a Tbrg position, or SBP>220 or DBP>120. Interventions: For each patient, SBP, DBP, HR, and SpO2 were measured in the supine position and placed in Tbrg position (20°). After 30 seconds, those vitals retaken. Data analysis: Averages of MAP, HR, SpO2 were obtained for supine and Tbrg position in both groups. Difference between each position was determined by subtracting the mean vitals in each position. Results: In the normotensive, the difference in MAP, HR, and SpO2 of supine vs Tbrg position is negligible with 1.81 decrease in MAP, and increase of 0.09bpm and 0.04% in HR and SpO2. In hypotensive, the difference in MAP, HR, and SpO2 of supine vs Tbrg position is also negligible with a decrease of 1.25 and 0.33% in MAP and SpO2, and increase in 1.75bpm. Conclusion: Placing normotensive and hypotensive subjects in Tbrg position does not cause any change in their BP, HR, and SpO2.

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POSTER ABSTRACTS

#209 Abstract Title:	**Performance on USMLE Step 1 but not Self-Directedness or Personality Preferences Correlate with Future Performance on In-Training Examinations During Anesthesiology Graduate Medical Education**

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Abstract: Objective predictors of performance in residency training have been elusive. As such, the purpose of this study was to explore potential predictors of future performance on the annual American Board of Anesthesiology (ASA) In-Training Examinations (ITEs) during graduate medical education in anesthesiology. Residents in the University of Kentucky Department of Anesthesiology were administered the Self-Directed Learning Readiness Scale (SDLRS-A) and the Myers-Briggs Type Inventory (MBTI). The residents' reported levels of readiness to manage self-directed learning, along with personality preference types and accomplishments on the United States Medical Licensure Examination (USMLE) in medical school, were then assessed for correlation with subsequent ITE achievements throughout residency training. In this cohort of anesthesiology residents, SDLRS scores were shown to have a minimal inverse correlation to future ITE accomplishments. Similarly, only the MBTI extroversion/introversion binary indicator correlated with improvement of ITE performance throughout residency. However, it was determined that the higher a resident's USMLE Step 1 score in medical school, the better the resident performed on his/her ITEs. This correlation between USMLE Step 1 scores could potentially be used to predict future performances on ABA ITEs, and to identify residents who might benefit from supplemental educational opportunities during residency.

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POSTER ABSTRACTS

#210 Abstract Title: **Intraoperative Teaching in Neuroanesthesiology Through Virtual Simulated Case Scenarios**

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Abstract: Intraoperative teaching, or teaching within the operating room, is an essential part of anesthesiology resident education. Individual time observing an attending physician in the intraoperative setting is the best method for residents to learn the problem solving, risk prevention, and time management skills they will need as practicing anesthesiologists. However, clinical exposure is vulnerable to a high degree of variability. Residents' exposure to common and uncommon cases in the OR inevitably varies, thus making the goal of covering a standardized list of teaching topics difficult. Simulation technology is becoming more incorporated into medical education due to its ease of instituting teaching standardization, and its ability to involve the learner in critical thinking scenarios without patient risk. However, high-fidelity human patient simulators come at the expense of specialized staff, resources, and time away from patient care. In our study, we see if we can maintain the same active teaching and learning environment of high-fidelity simulators through the use of virtual simulated case scenarios. PGY 2-4 anesthesiology residents at the University of Kentucky rotating through the Neuroanesthesia subspecialty completed case scenarios on a virtual interface like an iPad or laptop, while in the OR by the attending anesthesiologist's side. During times when the patient was under the care of the attending, the resident took a pretest assessment of knowledge on a particular subject, such as anesthesia pharmacology or hemodynamics. The resident was then given a case scenario on the same subject, followed by clinically relevant multiple-choice questions. After choosing their answers, the resident watched resultant hemodynamic effects on recorded videos of simulated clinical scenarios. These scenarios were created utilizing the CAE Human Patient Simulator and recorded with B-Line SimCapture. Taking place inside the OR with the presence of the attending by the participant's side, this teaching method is designed to stimulate discussion and immediate feedback during the modules. Upon completion of the exercise, the resident takes a post-test Likert-style survey to assess the quality of the learning experience. The pre-test, case scenario question, and post-test were all designed and tracked with REDCap (Research Electronic Data Capture), a web-based application for data capture of research studies.

Supported by: Department of Anesthesiology at University of Kentucky

Classification / Health Topic Area: Clinical Science / Education

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9th Annual CCTS Spring Conference and 4th Annual ATRN Summit

Thursday, March 27, 2014 Lexington Convention Center

POSTER ABSTRACTS

#211 Abstract Title:	**Impact of the Professional Student Mentored Research Fellowship (PSMRF) on Medical Student Training and Career Path**
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Abstract: Introduction: The past decade has demonstrated a downward trend in medical students choosing to become physician scientists. Consequently, many medical schools have developed research programs to stimulate interest and incentivize students. One such example developed at the University of Kentucky - The Professional Student Mentored Research Fellowship (PSMRF) - is unique in its 12-month duration, $3,000 stipend, and core curricular requirements. However, to date, there have been little evidence of its long-term impacts. This study, then, explores the possible effects of participation in this program on medical students' career paths. Methods: This study includes all 64 medical students (of 735 total matriculants) who completed PSMRF from 2007-2011. Data have been collected to assess demographic criteria, academic profile, and residency placement – including undergraduate college GPA, MCAT score, class ranking, AOA status, USMLE Step 1 score, residency program rank and academic status (US News and World Report). All data are pre-existing and have been properly de-identified, and the project is pending IRB approval as an exempt study. Results: Applications for PSMRF has shown an upward trend from 15 students in 2007 to 41 students in 2013. Of these, a greater percentage of PSMRF fellows matched in residency programs affiliated with academic medical centers (AMCs) – 79.7% (n=508) vs. 75.5% (n=51). In addition, a much smaller percentage of PSMRF fellows matched in UK Medical Center (UKMC) residency programs – 17.2% (n=11) vs. 27.9% (n=187). However, neither of these differences was statistically significant (p = < .05). Among those matriculants who matched into non-UKMC residency programs (n=537), the mean and median program rankings among non-PSMRF and PSMRF students was 45 vs. 36 and 42 vs. 35, respectively. A Mann-Whitney U test showed that the distributions of rankings were not the same for the two groups (p=.043). Discussion: Although the PSMRF program is early in its development, it shows an upward enrollment trend, and is modestly correlated with external (non-UKMC) residency program rankings. Additional analyses are necessary to further examine these and other long-term impacts of the program.

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Classification / Health Topic Area: Community Science / Education

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POSTER ABSTRACTS

#212 Abstract Title: **Meeting the Need to Incorporate More Nutrition Into Medical Education: An Example of a Student-Run Clinic**

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Abstract: Introduction: Even though nutrition plays an important role in many pathophysiological disease processes, it has not been strongly integrated into the medical school curriculum. Furthermore, there has been a lack of opportunities for medical students to practice nutrition counseling as part of their education. To address this need, a student-run nutrition clinic was developed. Purpose: The purpose of this pilot study is to assess the effect of the nutrition clinic on reported self-efficacy of student as they provide nutrition counseling within a healthcare context. Methods: Volunteer self-efficacy assessments were administered prior to, and after student exposure to numerous activities within the nutrition clinic. The self-efficacy survey had five areas of focus including: addressing weight issues, discussing health concerns, developing rapport, multitasking, and working under-supervision. Results: Pre and post data were complete for 10 students. On the key item of the ability to address weight issues, 90% of students reported an increase in self-efficacy. 63% reported improvement in general nutrition counseling skills. Interestingly on more complex professional skills, only 20% of students reported improvement. Conclusion: Most students reported improved self-efficacy in nutrition counseling after training and clinic involvement. Complex professional skills such as multitasking may require more experience and time to develop. The clinic experience may have made students more aware of what they still did not know. This pilot study illustrates how nutrition counseling practicums may be an effective way of incorporating more nutrition counseling into medical education.

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POSTER ABSTRACTS

#213 Abstract Title:	**VCAM-1/α4β1 Integrin Interaction Is Crucial for Prompt Recruitment of Immune T Cells into the Brain during the Early Stage of Reactivation of Chronic Infection with Toxoplasma gondii to Prevent Toxoplasmic Encephalitis**

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Abstract: T. gondii establishes a chronic infection by forming cysts preferentially in the brain, and reactivation of the infection can cause life-threatening toxoplasmic encephalitis in immunocompromised individuals. We examined the role of VCAM-1 /a4b1 integrin interaction in T cell recruitment to prevent reactivation of the infection in the brain. SCID mice were infected and treated with sulfadiazine to establish a chronic infection. VCAM-1 and ICAM-1 were the endothelial adhesion molecules detected on cerebral vessels of infected SCID and wild-type animals. Immune T cells from infected wild-type mice were treated with anti-a4 integrin or control antibodies and transferred into infected SCID or nude mice, and animals received the same antibody every other day. Three days later, sulfadiazine was discontinued to initiate reactivation of infection. Expression of mRNA for CD3d, CD4, CD8b, IFN-g, and inducible nitric oxide synthase (NOS2; an effector molecule to inhibit T. gondii growth), and numbers of CD4+ and CD8+ T cells in the brain, were significantly less in mice treated with anti-a4 integrin antibody than those treated with control antibody at 3 days after sulfadiazine discontinuation. At 6 days after sulfadiazine discontinuation, amounts of tachyzoite (the acute stage form of T. gondii)-specific SAG1 mRNA and numbers of inflammatory foci associated with tachyzoites were markedly greater in the brains of anti-a4 integrin antibody-treated than control antibody-treated animals, even though IFN-g and NOS2 mRNA levels were higher in the former than the latter. These results indicate that VCAM-1/a4b1 integrin interaction is crucial for prompt recruitment of immune T cells and induction of IFN-g-mediated protective immune responses during the early stage of reactivation of chronic T. gondii infection to control tachyzoite growth.

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POSTER ABSTRACTS

#214 Abstract Title: **Urothelial PAR4 Receptors Mediate Bladder Pain without Cystitis: A Role for Macrophage Migration Inhibitory Factor**

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Abstract: Introduction: Painful Bladder Syndrome / Interstitial Cystitis (PBS/IC) is a persistent, debilitating condition characterized by painful urination associated with increased frequency and urgency often in the absence of obvious bladder pathology. We previously showed that urothelial macrophage migration inhibitory factor (MIF) release contributes to bladder inflammation. Since stimulation of protease-activated receptors (PARs; especially PAR1 and 4) in mice also results in bladder inflammation, we hypothesized that urothelial PAR receptor activation elicits MIF release to mediate bladder pain and cystitis. Methods: MIF release was measured after exposing human benign (transformed) urothelial cells (UROtsa) to PAR1 and 4 activating peptides (AP) in dose-response experiments. Female C57BL/6 mice were instilled with PAR1 and 4-AP to determine: 1) urothelial MIF release 2) abdominal sensitivity to von Frey filament stimulation 24 hrs after AP; 3) micturition 24 hrs after AP. Bladders were collected for histology and RT-PCR. Results: PAR1 and 4-AP triggered MIF release from UROtsa cells in a dose-dependent manner, but not from mouse urothelium in vivo. Both PAR1 and 4-AP increased abdominal sensitivity after 24 hrs yet MIF inhibitor (ISO1) only prevented PAR4-mediated effects. No changes in micturition or bladder histology were observed. PAR4-AP increased mRNA levels of bladder CXCR4 (MIF receptor). However, AMD-3100 (CXCR4 antagonist) did not prevent PAR4-mediated mechanical hypersensitivity. Conclusion: Stimulation of urothelial PAR4 receptors increased abdominal mechanical hypersensitivity through a MIF-mediated mechanism in the absence of bladder inflammation. This represents an interesting model of PBS/IC where pain occurs without bladder pathology.

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Classification / Health Topic Area: Basic Science / Inflamation

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POSTER ABSTRACTS

#215 Abstract Title: **Effect of cyclic compressive loading on protein homeostasis of young and old rats.**

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Abstract: Massage is a widely used therapy for individuals seeking relief from stress, injury or various musculoskeletal disorders. Little is known about the biological mechanisms in the beneficial effects of massage, particularly in aged muscle. The purpose of this study was to identify the effect of a massage-mimetic (cyclic compressive loading, CCL) on pathways involved in protein synthesis in healthy skeletal muscle of young and aged rats. Male Brown Norway/F344 rats at 10 months (young) or 32months (old) of age were used. The right gastrocnemius muscle was subjected to a moderate load of CCL (4.5 N) for 30 minutes one time only, or rats were kept as control, non-massaged. Muscles were dissected 24 hours after the one bout of CCL. Puromycin was injected 30 minutes before euthanasia to measure protein translation. Western blot analysis showed elevated puromycin levels in gastrocnemius of old rats compared to young; in addition, CCL was associated with increased puromycin levels in old but not young gastrocnemius muscles. Phosphorylated GSK3β was significantly higher in gastrocnemius muscles with CLL in both young and old animals and eIF2BƐ was increased with CCL in both young and old animals potentially leading to the increased protein synthesis. RBM3, a protein known to enhance protein translation, was elevated with CCL by 29% in old animals but unchanged in young. MurF1, a muscle atrophy protein, was 36% higher in young compared to old animal and was increased in CCL in both young and old muscle. These results suggest that massage in the form of CCL is associated with a potential change in muscle remodeling through the activation of protein homeostatic pathways which seems to be particularly beneficial in the aged muscle. Supported by NIA AG042699.

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Classification / Health Topic Area: Basic Science / Muscle

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POSTER ABSTRACTS

#216 Abstract Title:	**Effects of a Cavity-Filling Mutation in the Enzyme Choline Acetyltransferase**
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Abstract: Choline acetyltransferase (ChAT) synthesizes the neurotransmitter acetylcholine, and point mutations in the enzyme cause an often fatal neuromuscular disorder known as congenital myasthenic syndrome with episodic apnea (CMS-EA), the condition that results in severe muscular weakness and respiratory insufficiency. We hypothesize that the susceptibility of ChAT to point mutations at sites distributed over the enzyme is due to its unusually large number of core packing defects or cavities. Using site directed mutagenesis, we have tested our hypothesis by introducing single cavity filling mutation S106I near a known congenital mutation site L102. The cavity-filling mutation increases the thermal stability of the enzyme by almost 5 degrees Celsius, indicating that it has reduced cavity volume as expected. Importantly, filling the cavity largely restores the activity of the L102P CMS-EA mutation to wild type levels, providing a link between cavities and the effects of the congenital mutations. We are screening to identifying small ligands that bind in cavities and stabilize ChAT to a number of congenital mutations. These compounds will represent a new therapeutic approach for treating the disease, and we have identified a number of candidate molecules. We are also in the process of further testing the role of cavities in PC12 cells and a Drosophila model. The ability to rescue the CMS mutants in an animal model will be an important step in validating the long-term goal of developing a therapy for the disorder by targeting ChAT packing defects.

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POSTER ABSTRACTS

#217 Abstract Title: The Effect of Cyclic Compressive Loading on Immune System Related Responses in Young and Old Rats

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Abstract: Massage is a therapeutic tool that has been used clinically to facilitate muscle recovery and reduce muscle edema. We have shown previously that a massage-mimetic (cyclic compressive loading, CCL) modulates the immune response in skeletal muscle from young rats in a load dependent manner. However, whether similar effects are observed in aged rats is unknown. In this study we hypothesized that massage in the form of CCL will change the immune response in aged muscle. Male F344/Brown Norway rats at 10 (young) and 30 (old) months of age were divided into two groups: control, non-massaged (n=6) and massaged (n=6) for each age. The right gastrocnemius muscle of the massage groups was subjected to one bout of CCL for 30 minutes at 4.5N; tissues were harvested 24 hours post CCL. Muscles were sectioned at 8 □m and immunohistochemistry was performed to stain for CD68 (ED1+ macrophages), CD163 (ED2+ macrophages), and CD43 (neutrophils). Images were obtained and positive cells and muscle fibers were counted using Zeiss AxioVision image analysis software. Western blot analysis was used to determine the effect of CCL on Hsp70 and Hsp27 protein abundance. There was no difference in the number of ED1+ cells with age, but ED2+ cell number and neutrophils were elevated in aged muscles ($p<0.05$). CCL was associated with a trend for elevated numbers of ED1+, ED2+ and neutrophils in aged, but not young muscle. This however did not reach statistical significance. Hsp70 has recently been shown to be involved in immune regulation in skeletal muscle and we found that it was upregulated with CCL in gastrocnemius muscle in aged, but not young rats. Similarly, CCL application was associated with an increase in Hsp27 in aged muscle only. Results therefore indicate that the inflammatory environment is different between young and old muscle and that massage may be especially useful in modulating the immune response in the aged. Supported by NIA AG042699.

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POSTER ABSTRACTS

#218 Abstract Title: **Tissue Metabolic Rate of Oxygen Consumption in Calf Muscle Measured by Arterial and Venous Occlusion Protocols**

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Abstract: Background and Objective: Quantification of tissue metabolic rate of oxygen consumption (TMRO2) in leg muscles is important for the diagnosis of vascular diseases affecting walking/activity (e.g., peripheral arterial disease). This study was designed to compare near-infrared spectroscopy (NIRS) measurements of TMRO2 in calf muscles using arterial and venous occlusion (AO and VO) protocols. Methods: Nine young healthy subjects participated in this study. The subject lay supine with a pressure cuff wrapped on right thigh and a NIRS fiber-optic probe taped on top of the right calf for the measurements of oxy- and deoxy- hemoglobin concentrations (i.e., [HbO2] and [Hb]). Three 10-second VOs (55 mmHg) and one 3-minute AO (230 mmHg) separated by a 1-minute recovery each were performed after 3-minute baseline. TMRO2 was determined by averaging the [Hb] increase rate during VOs and as well as from the oxygen desaturation rate ([HbO2] – [Hb]) during the AO. Results: The mean values of TMRO2 were 0.033 ± 0.020 and 0.038 ± 0.020 ml/100ml/min from VO and AO, respectively. No significant differences in TMRO2 were found between the two protocols ($p = 0.362$). Linear regression suggested a marginally significant correlation [$R2 = 0.40$, $p = 0.067$, $Y(AO) = 0.61 \times X(VO) + 0.018$]. Discussion and Conclusions: The AO protocol is more accurate for TMRO2 measurement than the VO protocol which may be influenced by the variation of arterial oxygen saturation. In conclusion, the AO protocol is preferred when applying high pressure is tolerable; otherwise, the VO protocol can provide an approximate estimation.

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POSTER ABSTRACTS

#219 Abstract Title:	**Differences in Extramyocellular Lipid and Physical Function in Older Adults with Sufficient and Insufficient Vitamin D Status**
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Abstract: An inverse relationship between vitamin D deficiency (25(OH)D<20 ng/ml) and both extramyocellular lipid (EMCL) and physical function has been described previously in aged adults. The purpose of this study was to assess differences in muscle lipid and physical function in community dwelling elderly with vitamin D insufficiency (25(OH)D ≤ 30 ng/mL) compared to vitamin D levels that have been hypothesized to promote extra-skeletal health (25(OH)D ≥ 40 ng/mL). 25(OH)D and four square step test (FSST) were assessed in 21 adults, aged 65 to 83 years. Gastrocnemius muscle lipid (intramyocellular lipid (IMCL) and EMCL) were measured with magnetic resonance spectroscopy and fat ratio segmentation, respectively. Mean body mass index (BMI) was 26.9±0.9 kg/m2. Mean EMCL was 20.2±0.9% with a range of 11.8 to 25.9% and IMCL to water ratio was 0.5±0.06. Participants who were vitamin D insufficient (23.9±1.1 ng/mL) had higher levels of lateral gastrocnemius EMCL and slower FSST times compared to vitamin D replete (54.7±3 ng/mL) (p<0.05). IMCL, BMI, age, and reported physical activity levels were not significantly different between vitamin D groups. These data suggest that vitamin D insufficiency may also contribute to EMCL accumulation and impaired physical function independent of activity and body mass. Further study is required to validate the role of vitamin D repletion in minimizing EMCL accumulation and understanding the impact these variables have on muscle metabolic function in aging.

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POSTER ABSTRACTS

#220 Abstract Title: **Macrophage Coculture Inhibits PGC1-alpha and UCP-1 Expression in Human Adipocytes**

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Abstract: PGC1-□ is a transcriptional co-activator of PPAR□ that regulates mitochondrial biogenesis and uncoupling protein-1 (UCP-1) expression in brown adipocytes. Recent studies suggest that PGC-1□ plays a beneficial role in white adipose tissue (WAT). In humans, PGC-1□ is induced in WAT by pioglitazone, an insulin sensitizer, and PGC-1□ is decreased in WAT with increasing obesity. Since macrophages are increased in WAT with obesity, we sought to determine whether macrophages inhibit PGC-1□ expression in human adipocytes. Furthermore, recent studies suggest that PGC-1□ is inhibited by TGF-□, which is increased in adipose tissue with obesity; we previously reported that adipocytes increase TGF-□ signaling when cocultured with macrophages. We treated differentiated adult-derived human adipocyte stem cells (ADHASC) with a TGF-□ receptor blocker (SB505124) and found that the adipocytes expressed higher levels of PGC-1□ and UCP-1 (n=3; P<0.05). Next, we cocultured differentiated ADHASC cells with polarized macrophages, which were derived by treating THP-1 monocytes with LPS/□-interferon (M1), IL-4 (M2a), or IL-10 (M2c). Coculture with M1, M2a, or M2c macrophages potently (>90 %) inhibited adipocyte PGC-1□ mRNA and protein expression (n=3; P<0.05) and UCP-1 mRNA expression (n=3; P<0.05). However, inhibition of TGF-□ receptor signaling with SB505124 failed to protect against the reduction in PGC-1□ expression by macrophage coculture. We next evaluated other mechanisms of regulating PGC1-□ expression and found that macrophage coculture induced known inhibitors of PGC-1□ such as the pocket protein Rb and RIP140 2-fold (n=3; P<0.05). These data suggest that PGC-1□ and its targets such as UCP-1 are negatively regulated by macrophage infiltration into adipose that occurs with obesity. This may contribute to adipose dysfunction and inhibit the beiging process that may occur in WAT.

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POSTER ABSTRACTS

#221 Abstract Title: **RPE Cytotoxicity and Caspase Activation after Treatment with Valproic Acid**

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Abstract: Purpose: Age-related macular degeneration (AMD) is a progressive disease of the retina, retinal pigment epithelium (RPE) and choroid. Recent studies suggest that the HDAC inhibitor valproic acid (VPA) has neuroprotective properties and potential therapeutic efficacy in retinal degeneration. Here, we show that intravitreous delivery of VPA in a mouse model and treatment of human cell cultures induces RPE cytotoxicity. HDACs have become a novel target in aging and neurodegenerative diseases including AMD. An improved understanding of their regulation and pharmacologic inhibition in the eye is essential prior to translation to clinical studies. Methods: Primary human RPE (hRPE) isolates (n=6, individual single donors) were treated with VPA (1mM/4mM) or vehicle (PBS). Cell viability assays (SYTOX®, Invitrogen), caspase-3 fluorometric quantification (DEVD-AFC, Biovision) and targeted PCR arrays (Taqman®, Life) were performed. Wild-type C57BL/6J mice (n=6-8) were evaluated by fundus photography at baseline and 7 days after intravitreous injection of VPA (1/10mg). RPE/choroid flatmounts (n=4-6) were immuno-stained for the intercellular junction marker, zonula occludens-1 (ZO-1) and examined by fluorescent microscopy. RPE/choroid tissue (n=3) was harvested at 48 hours and analyzed by targeted PCR arrays. Results: Exposure of primary hRPE isolates to the HDAC inhibitor VPA led to a two fold increase in cell death (48 hours) and to a 4 fold upregulation of caspase 3 ($P<0.05$) at 12 hours compared to vehicle. Intravitreous injection of VPA induced frank RPE loss, deep hypo-pigmented lesions in the fundus image and severe disruption of ZO-1 staining on RPE flatmounts. Targeted PCR arrays revealed wide-spread disruption in pro-inflammatory cytokine gene expression in both human and mouse samples. Conclusion: Intravitreous injection in C57BL/6J mice or treatment of primary hRPE isolates with VPA induced cytotoxicity in a dose-dependent fashion with increased caspase-3 activation. Widely altered cytokine expression was observed with VPA and current studies in our laboratory have focused on the specific HDACs that are contributory to the inflammatory response.

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Classification / Health Topic Area: Basic Science / Ophthalmology

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POSTER ABSTRACTS

#222 Abstract Title: **Chronic Kidney Disease and Bone Microcrack Accumulation**

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Abstract: 26 million Americans suffer from Chronic Kidney Disease, a condition increasingly accompanied by the skeletal abnormalities of renal osteodrystrophy. The prevailing clinical indicator of fracture risk is bone mineral density; however, alternative parameters such as micro damage are being investigated as contributors to bone quality. Studies suggest that the inhibition of bone turnover in osteoporotic patients on long-term bisphosphonate therapy leads to the accumulation of micro damage and increased fracture risk. This study is being conducted to determine the relationship between bone turnover in patients with CKD and micro crack accumulation. Transiliac crest biopsies are stained with basic fuschin and examined using light microscopy. Samples selected from high turnover CKD, low turnover CKD, and normal bone categories are then evaluated for micro crack frequency and length using histomorphometry software. Preliminary results indicate that low turnover bone group contains over twice the mean number of cracks of the normal and high turnover groups when total bone area is accounted for. However, at this time only 18 total samples have been evaluated; therefore, we cannot reach a conclusion at this stage.

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Classification / Health Topic Area: Basic Science / Orthopedics

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9th Annual CCTS Spring Conference and 4th Annual ATRN Summit

Thursday, March 27, 2014 Lexington Convention Center

POSTER ABSTRACTS

#223 Abstract Title: **An Analysis of the Impact of Outreach Athletic Trainers on of ACL Surgical Referrals**

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Abstract: Context: The hiring of athletic trainers(ATs) by orthopaedic clinics to provide "outreach" coverage in the secondary school setting, has become common. However, the effect these programs can have on patient referrals has not been investigated. Hypothesis: That the number of anterior cruciate ligament(ACL) surgeries performed by a university-affiliated sports-medicine-practice would be greater for counties containing schools served by affiliated outreach athletic trainers(AO-ATs). Subjects: 722 Patients (0-22yr) residing in counties within a 50mile radius of the sports-medicine-practice who had undergone ACL surgery between 2009-2012. Procedures: Data from the Office of Health Policy, were utilized for the number of ACL surgeries performed on residents of each included county. For the sports-medicine-practice data, a retrospective chart review was conducted of patients who had undergone ACL surgery. Statistical Analysis: The operation rate performed by the sports-medicine-practice was normalized to ACL surgeries by county population for the included age range ((ACLs per county/county population, age 0-22) x10,000). Additionally, the percentage of total ACL surgeries from counties with and without AO-ATs performed by the sports-medicine-practice was calculated. Results: The ACLOR for counties with AO-ATs was 10.7per10,000 compared to 4.0per10,000 for counties without AO-ATs. Overall, out of all the ACL surgeries performed for the counties of interest the sports-medicine-practice performed 30.4% of ACL surgeries in counties with AO-ATs, versus 16.0% in counties where there were no AO-ATs present. The largest percentage of ACL surgeries performed by the sports-medicine-practice was in 14-18 year-olds for both AO-AT counties (68.3%) and non-affiliated counties (45.6%). Conclusions: The sports-medicine-practice performed 2x more ACL surgeries from counties with AO-ATs compared to counties with no AO-ATs. The impact of AO-ATs was most prominent among14-18 year-olds. This data supports that AO-ATs can impact a clinic's referral base, particularly regarding referral of high school age individuals.

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POSTER ABSTRACTS

#224 Abstract Title: **Diagnosis of Rotator Cuff Tear Using Radiographic Characteristics**

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Abstract: The purpose of this study is to determine the utility of radiography in diagnosis of Rotator Cuff (RTC) tears. As of now, the Gold Standard for RTC tear diagnosis is MRI. It would be useful if a cheaper, more rapid test such as a simple X-ray could offer diagnosis with comparable accuracy. Specifically, this study looks at five radiograph findings classically suggestive of RTC damage and correlates these findings with the presence of a tear (compared to MRI, 95% specificity). This goal is to determine which X-ray findings are most suggestive of a tear, and if any combinations of abnormalities could confer diagnosis with high statistical accuracy. 123 patients with a shoulder X-ray and MRI within 30 days were pulled from UK's database. The X-rays were transferred into an Excel spreadsheet. Each worksheet consisted of a patient's shoulder X-ray with five accompanying "Yes / No" questions, regarding X-ray abnormalities. Dr. Spicer, the MSK Radiologist has reviewer each patient's MRI and the presence of a tear is known only to the researchers. Currently, the test has only been reviewed as a pilot study. The preliminary data shows a general trend, that patients with more X-ray findings are more likely to have RTC tears. The study needs more reviewers to take to test in order to determine accuracy and reproducibility.

Supported by: There is no financial backing required fro this study

Classification / Health Topic Area: Clinical Science / Orthopedics

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POSTER ABSTRACTS

#225 Abstract Title: Biomimetic Oral Mucin Using Polymeric Filomicelle Networks

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Abstract: In the oral cavity, mucin networks are formed by the complexation of bottlebrush-like mucin glycoprotein with other small molecule glycoproteins. These glycoproteins create nanoscale strands that then arrange into a nano-porous mesh. These networks play an important role in ensuring oral surface hydration, lubricity and barrier protection. In order to understand the functional behavior in mucin networks, it is important to decouple their chemical and physical effects responsible for generating the fundamental property-function relationship. To achieve this goal, we propose to develop a synthetic biomimetic mucin using a layer-by-layer (LBL) deposition approach. In this work, we demonstrate generation of hierarchical 3-dimensional structures resembling natural oral mucin networks using affinity-based interactions on synthetic and biological surfaces. Unlike conventional polyelectrolyte-based LBL methods, we utilized biotin-functionalized filamentous (worm-like) micelles as the network building blocks, complimented by addition of streptavidin to generate mucin-like layers of the desired thickness. The biomimetic nature of the network was studied by evaluating its structural and bio-functional properties. The developed synthetic mucin possess excellent surface hydration property, where its network remained stable under harsh intra-oral environment for potential oral regenerative applications. Further its role as a drug delivery vehicle capable of providing localized and tunable release is explored and by incorporating antibacterial curcumin drug loading within synthetic networks, the bacterial growth was inhibited.

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POSTER ABSTRACTS

#226 Abstract Title: **Hematopoietic Stem Cell Expansion by Inactivation of Latexin**

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Abstract: Objective: Hematopoietic stem cells transplantation (HSCT) has been used as standard treatment for various hematological disorders. Even though HSCT has been applied in clinic for decades, regulation of HSC self-renewal and differentiation is still a major challenge. Better understanding of HSC regulation is critical to enhance the therapeutic efficiencies of transplantation. This study aims to investigate the novel role of latexin (Lxn) gene in the regulation of HSC self-renewal and expansion and to determine its translational potential in HSCT. Methods: Latexin knockout mice (Lxn-/-) are generated and the hematopoietic phenotypes in the peripheral blood (PB) and bone marrow (BM) are characterized in Lxn-/- mice. The number and function of HSCs and progenitor cells (HPCs) are analyzed by in vitro (colony forming assay and flow cytometric immunophenotypic analysis) and in vivo transplantation experiments. Gene expression profile in Lxn-/- HSC is defined by microarray analysis. The correlation between Lxn expression and HSC number in human samples is investigated. Results: PB cell counts and lineage staining show that the numbers of both myeloid cells and lymphocytes are significantly increased by 50% to 100% in Lxn-/- mice ($p<0.05$). Lxn-/- BM has 2-fold more HSCs and HPCs than WT marrow ($p<0.01$). When both Lxn-/- and WT HSCs are subject to transplantation, Lxn-/- cells demonstrate nearly two-fold higher reconstitution capacity than WT cells. These data suggest that loss of Lxn enhances HSC self-renewal leading to the stem cell expansion. At the mechanistic level, genes involved in cell-matrix interaction, cell-cell communication and cell cycling are dysregulated in Lxn-/- HSCs. In the preliminary study of the role of Lxn in human HSCs, a negative correlation is identified between Lxn protein level and the HSC number ($R = -0.95$), indicating that Lxn is a potential molecular target for the expansion of human stem cells. Discussion/Significance: Future study will direct to the translational potential of antagonism of Lxn activity for HSC expansion and HSCT efficiency in clinic.

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POSTER ABSTRACTS

#227 Abstract Title: **Antioxidant Poly (β-Amino Esters) Nanogels for the Control Cellular Oxidative Stress**

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Abstract: Poly (β-Amino Esters) (PBAE) are pH sensitive, hydrolytically degradable polymers systems, which have a readily tunable degradation and release profile. As such, they have gained much interest as a loading matrix for drug delivery. Using PBAE itself as a produrg carrier by covalently incorporating therapeutically active phenolic drugs into the polymer backbone of the hydrogel can enhance the drug loading efficiency, structurally stabilize and control the release of labile drugs wherein chemical cleavage/ester hydrolysis essentially determines the drug release rate. In our previous work, antioxidants, such as curcumin and quercetin, have been conjugated into PBAE bulk gel systems and the therapeutically active form was released over time. However, formulating these polymeric systems into nanoparticles would allow the carrier system to be administered through various routes, including intravenous injections, oral administration. In this work, a single-phase reaction-precipitation was developed to formulate quercetin conjugated PBAE nanogels. The nanogels were synthesized using quercetin multiacrylate and a secondary diamine, which was stabilized in acetonitrile medium during the particle formation. PEGylation of these nanogels further enhanced their stability and stealth characteristics. The nanogel size was controlled by varying feed reactant concentrations, confirmed by analyzing the hydrodynamic radius via DLS. The spherical shape of these nanogels was confirmed by scanning electron microscopy. Upon hydrolysis in physiological conditions, continuous release of active quercetin was observed for 48 hours. These nanogels were capable of suppressing cellular oxidative stress induced using hydrogen peroxide over 48 hours in contrast to pure quercetin and showed concentration dependent cellular toxicity similar to pure quercetin.

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POSTER ABSTRACTS

#228 Abstract Title: **Urinary NT-proBNP as a Marker of Patent Ductus Arteriosus in Preterm Infants**

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Abstract: Background: About one-third of preterm infants develop a hemodynamically-significant patent ductus arteriosus (PDA) during the first few days after birth. Augmentation of the left-to-right shunt through the ductus may increase pulmonary blood flow that results in pulmonary edema and increased cardiac preload. Although echocardiography is the gold standard for diagnosis, there are no universally accepted criteria for grading the hemodynamic significance. B type natriuretic peptide (BNP) is synthesized in the ventricles and released in response to volume and pressure overload. Objective: To determine the correlation of urinary NT-proBNP with echocardiographic findings in preterm infants with PDA. Study design: Preterm infants with birth weight less than 1000 grams were enrolled prospectively. Infants were divided into two groups. Group 1 included infants with hemodynamically significant PDA who required pharmacological treatment; group 2 consisted of infants with no PDA. Urinary NT-proBNP and creatinine ratios were compared between the 2 groups. Results: 29 preterm infants were enrolled. There was no significant difference in mean gestational age (GA) or birth weight (BW) between the 2 groups, GA: (25.6 ± 0.5 vs 26 ± 1.2 weeks), BW: (833.3 ± 194.2 vs 860.4 ± 94.6 grams). Urinary NT-proBNP/creatinine ratios were significantly higher in babies with large PDA compared to those with no PDA (2541±1670 vs 389 ± 176 pg/ml p=.02). Conclusion: Preliminary data shows that urinary NT-proBNP may be used as a marker of the presence of a hemodynamically significant PDA. It is a non-invasive and simple method and may be a useful adjunct to echocardiography.

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POSTER ABSTRACTS

#229 Abstract Title: **Effect of Prenatal Exposure to Buprenorphine or Other Opiates on Incidence and Severity of Neonatal Abstinence Syndrome in a Poly-Drug User Population**

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Abstract: Purpose: Methadone, a full opioid agonist, is the standard treatment of opioid dependence in pregnant women. Infants born to mothers who are using opioids during pregnancy are at risk of developing Neonatal Abstinence Syndrome (NAS), which is often treated with morphine. Data from the Maternal Opioid Treatment: Human Experimental Research (MOTHER) project suggest that pregnant women treated with buprenorphine, a partial opioid agonist, will deliver infants less likely to have severe NAS symptoms. In Kentucky, many pregnant women are poly-drug users. The purpose of this study is to examine the effect of methadone and/or buprenorphine and/or other opioids on neonates born to these mothers. Methods: A medical record review of all opioid-exposed neonates, > 35 weeks gestation, admitted to Kentucky Children's Hospital during 2010 was performed. Eighty neonates were divided into four groups depending on opioid exposure: (1) opioids other than methadone and buprenorphine, (2) methadone, (3) buprenorphine, and (4) both methadone and buprenorphine. Presence of NAS was assessed using the Finnegan Neonatal Abstinence Score Sheet. Fisher's exact test and the Kruskal-Wallis test compared the groups. Results: The overall incidence of NAS was 62.5% (n=50), with a mean NAS score of 16.8; 92.0% (n=46) of the neonates with NAS received treatment. Paired analyses by group found no significant difference in NAS incidence between Groups (2) and (3) (p=0.62). Treatment with more than one medication, number of dose increases, and treatment duration served as indicators of NAS severity; none of these indicators was significantly different when comparing Groups (2) and (3) (p=1.0, p=0.12, p=0.62, p=0.78, p=0.65). Conclusion: In our Kentucky population, there is insufficient evidence to predict incidence and severity of NAS based on methadone or buprenorphine exposure during pregnancy.

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POSTER ABSTRACTS

#230 Abstract Title: **Indices to predict successful discontinuation of mechanical ventilation in neonates: Spontaneous breathing trials**

Author(s): F.O. Odago, College of Medicine, U of Kentucky
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Abstract: Optimal ventilation support is essential for survival of sick premature infants (=/<32 weeks of gestation). Often their respiratory system is not sufficiently developed to support spontaneous breathing and these infants require mechanical ventilation for life support. Ultimately they must be weaned from mechanical ventilation as their pulmonary function improves. Unfortunately, some neonates following discontinuation of mechanical ventilation fail and must be re-intubated due to an inability to sustain spontaneous breathing. However, It is well known that many neonates are continued on mechanical ventilation beyond an optimal time for discontinuation. Clearly defined clinical indicators for discontinuation of mechanical ventilation, based upon pulmonary function indices, remain to be determined. Prolonged mechanical ventilation and supplemental oxygen exposure are known to cause injury to developing lung tissues, thus the need to minimize the duration of mechanical ventilation is compelling. We are evaluating the applicability of spontaneous breathing tests, based on recently recognized newborn pulmonary indices, for the determination of an optimal time for successful discontinuation of mechanical ventilation. These pulmonary indices include ; CROP (Compliance, Resistance, Oxygenation and Pressure), RSBI (Rapid shallow breathing), SF (SpO_2/FiO_2), SF/MV (minute ventilation) and PF (PaO_2/FiO_2).

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POSTER ABSTRACTS

#231 Abstract Title: **Pathologic Outcomes Following Adrenalectomy**

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Abstract: Introduction: Adrenalectomy is indicated for removal of functional adrenal masses and nonfunctional adrenal masses suspicious for malignancy. Imaging characteristics on CT and MRI are used to help determine likelihood of malignancy based on factors such as size at presentation, rate of growth, washout, and fat content. Methods: We retrospectively reviewed data on all adrenalectomies performed from 2/1/2006 to 4/30/2013 at the University of Kentucky. We included all patients with available preoperative imaging and data. We examined variables including age, gender, indications for adrenalectomy, and final pathology. Results: 71 patients met inclusion criteria, including 47 (66%) women and 24 (34%) men. Twenty−three (32%) masses were removed based on functionality. Twenty (28%) masses were removed based on size at presentation, of which one (5%) was consistent with malignancy. Fourteen (20%) masses were suspicious for metastasis, of which nine (64%) were metastases. Twelve (17%) masses were removed based on rate of growth, but none were malignant. Seven (10%) masses appeared inconsistent with adenoma on imaging, of which two (29%) were malignant. Eight (11%) masses met more than one criterion, of which one (1%) was malignant. Four (6%) masses were taken out for other reasons, but none were malignant. Conclusions: These results highlight the challenges faced in appropriate selection of patients for adrenalectomy. Of the 71 adrenalectomies performed, only 13 (18%) were malignant and 23 (32%) were functional masses. Therefore, 35 (49%) adrenal masses were benign non−functional tumors which may not have needed treatment. Better imaging and clinical criteria are needed to optimize our management of adrenal masses.

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POSTER ABSTRACTS

#232 Abstract Title:	**Risk Factors for 30-day Readmission after Hepatectomy: Analysis of 2,444 Patients from the ACS-NSQIP Database**
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Abstract: Objective: To identify risk factors associated with unplanned readmissions after hepatectomies. Background: With optimization of surgical technique and perioperative care, the mortality rate from hepatectomy has declined substantially over the last two decades. In addition to traditional measures, readmission rate has been proposed as a primary endpoint for quality assurance. Method: Patients who underwent hepatectomies between January-December 2011 were identified using the ACS-NSQIP procedure-specific database. A multivariable logistic regression analysis was performed to determine predictors of unplanned readmissions related to the procedure (UPRR) within 30 days. Result: Unplanned readmissions occurred in 10.5% of patients undergoing hepatectomy in this national cohort. On multivariate analysis, transfusion within 72 hours after surgery (odds ratio [OR] 1.74, p<0.001), complexity of procedure (extended, OR 1.84, p=0.004; right hepatectomy, OR 1.66, p=0.003), and longer operative time (>median 320 min, OR 2.43, p<0.001) were independent perioperative predictors of UPRR. Independent preoperative risk factors included elevated alkaline phosphatase (OR 1.45, p=0.017), bleeding disorders (OR 1.72, p=0.051), and hypoalbuminemia (OR 1.30, p=0.036). Conclusion: Transfusion, complexity of procedure, and duration of operation were the strongest predictors of unplanned readmissions after liver resection.

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Classification / Health Topic Area: Clinical Science / Surgery

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POSTER ABSTRACTS

#233 Abstract Title:	**Increased Inflammatory and Thrombotic Gene Expression in Visceral Adipose Tissue of Patients with Sepsis**
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Abstract: Background: Sepsis is an infection-initiated clinical condition characterized by systemic inflammation, intravascular coagulation, and multi-organ failure. Our previous studies using mice demonstrated that visceral adipose tissue is a major source of inflammatory cytokines and thrombotic factors during experimental sepsis. Objective: To verify whether patients with intra-abdominal sepsis exhibit increased inflammatory and thrombotic gene expression in visceral adipose tissue and to evaluate the differences in inflammatory profiles among various fat depots. Methods: Patients with intra-abdominal sepsis and patients undergoing elective abdominal procedures for non-inflammatory conditions (controls) were enrolled in this study. Adipose tissues (mesenteric, epiploic, and omentum) were collected during surgery. Histological analysis was performed on formalin-fixed tissues. qRT-PCR was utilized to determine the expression level of inflammatory and thrombotic factors. Results: Adipose tissues from septic patients exhibited signs of leukocyte margination and migration along with reactive mesothelial cells. In patients with sepsis, compared to control, all adipose depots expressed higher levels of inflammatory cytokines interleukin (IL)-1α, IL-1β, IL-6 and TNFα, and procoagulant factors thrombospondin-1, and plasminogen activator inhibitors (PAI)-1 and -2. Among these genes, IL-1α and PAI-1 showed particularly strong expression in the mesentery. While similar expression was observed for most genes across the depots, omentum from patients with severe sepsis expressed higher levels of IL-1α (4-6 fold) and PAI-2 (8-17 fold). Conclusion: Inflammatory and thrombotic gene expression is strongly induced in visceral adipose tissues of patients with intra-abdominal sepsis, validating our mouse models. Further studies will elucidate whether these responses are an inciting event or sequela of intra-abdominal sepsis.

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Classification / Health Topic Area:	Clinical Science / Surgery
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POSTER ABSTRACTS

#234 Abstract Title: **Epidemiological Evaluation of Multiplicity in Patients with Intracranial Aneurysms**

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Abstract: Introduction: An estimated 15 million Americans unknowingly live with unruptured, intracranial aneurysms. Furthermore, as many as 1/3 of patients who present with subarachnoid hemorrhage have multiple aneurysms. Purpose: The published literature on treatment of patients with multiple intracranial aneurysms provides some guidance on previous cases, but is inadequate to develop a uniform treatment paradigm. However, the experience at UK since July 1, 2011, provides a good retrospective data set for evaluating patients with multiple aneurysms. This analysis will provide the most specific examination of multiple intracranial aneurysms yet published in the literature. Furthermore, by analyzing these results, we hypothesize that using the University of Kentucky Protocol for treating patients with multiple aneurysms will lead to favorable patient outcome and contribute a standard method to the literature. Methodology: A retrospective chart review was conducted of 111 patients who were treated with surgery or embolization from June 2011-June 2013 at our center. We evaluated these patients to determine the incidents of multiple intracranial aneurysms, the propensity to rupture relative to patients with single aneurysm, their demographics, their outcomes, and the treatment paradigm used. Most importantly, we typically treat patients with multiple aneurysms in a staged fashion, addressing one aneurysm per treatment, regardless of incidental versus hemorrhagic presentation. Results: Analysis demonstrated a trend toward an association between smoking and multiplicity. History of smoking was more common in patients with multiple aneurysms (77%) than those with a single aneurysm (58%, p=0.08). Patient outcome, as measured on the Glasgow Outcome Scale at 3 months, showed multiple aneurysm patients had better outcomes (means GOS = 4.8± 0.4) than single aneurysms (4.6± 0.6, P = 0.05). Conclusion: Despite the small denominator of patients, we detected a trend toward higher risk of aneurysm multiplicity in smokers. This is consistent with the published literature on smoking; smoking is known to increase aneurysm growth and rupture. Patients with multiple aneurysms had better outcome scores. This may be due to more aggressive treatment of patients with multiplicity or possibly more opportunities of detection of incidental aneurysms; this clearly requires further study. Most importantly, patients with multiple aneurysms did not have higher rates of hemorrhage. Using a staged treatment protocol for multiple aneurysms did not result in any interval hemorrhages of aneurysms during the latency period between treatments.

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POSTER ABSTRACTS

#235 Abstract Title: **Gabapentin Management of Autonomic Dysreflexia after Spinal Cord Injury**

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Abstract: Autonomic dysreflexia (AD) is a potentially life-threatening condition occurring after spinal cord injury at or above spinal level T6, characterized by an uncontrolled sympathetic increase in blood pressure and reflexive parasympathetic decrease in heart rate; colon and bladder distension are common triggers. To understand maladaptive responses accompanying AD, our goals were: first, to assess the impact of colorectal distension (CRD)-induced AD on gene expression in rats following complete T4 transection (T4Tx), and second, to determine whether gabapentin (GBP, a GABA analog for treating neuropathic pain) attenuates this expression. Genes evaluated included the inflammatory cytokine IL-1B and transcription factor ATF-3 in dorsal root ganglia (DRG), spinal cord (SC) and visceral tissues. Results by qRT-PCR show that in all populations of DRG examined (T7/8, T13/L1, L6/S1), ATF3 and IL-1B increased after CRD but decreased with GBP treatment. This was not seen in the SC. In the colon, bladder, and spleen, IL-1B expression after T4Tx and CRD increased markedly compared to naïve, which was reversed by GBP. ELISA on peripheral tissues confirmed changes in IL-1B protein levels paralleled mRNA expression. These results support our hypothesis that CRD increases ATF3 and IL-1B expression in DRGs, but we also found IL-1B increased in peripheral tissues as well. Furthermore, GBP partially reversed this up-regulation. The SC lacked similar trends, suggesting that changes mediating AD and the mechanism for GBP action target the DRG. This study suggests ATF3 (implicated in axonal sprouting) after CRD may elicit undesired DRG sprouting underlying AD, while GBP decreases this maladaptive plasticity.

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Classification / Health Topic Area: Basic Science / Trauma/Injury/Rehabilitation

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POSTER ABSTRACTS

#237 Abstract Title:	**Stay Healthy U - A multiple health behavior change intervention program**
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Abstract: Background: The residents of Appalachian counties are at higher risk for chronic diseases. Hart County, Kentucky—an Appalachian county— has a high incidence of obesity and smoking rates (33.3% and 26%, respectively). Both obesity and smoking increase the probability of developing type 2 diabetes, cardiovascular disease and cancer. Weight gain associated with smoking cessation can undermine health benefits of quitting and may lead to smoking relapse. Aim: This program is designed to test the potential benefits of combining Cooper Clayton Method to Stop Smoking and the National Diabetes Prevention Program (DPP). Method: A multiple health behavioral change (MHBC) intervention program will be administered at Hart County Health Department, Munfordville, KY. Participants will be men and non-pregnant women aged 18 or older who are current smokers at risk for diabetes or pre-diabetic. Baseline assessments will consist of measures like height, weight, waist circumference, breath CO level, lipid profile and HbA1C. Approximately one week after baseline assessment, participants will attend weekly classes. During the initial 3 weeks participants receive the Cooper-Clayton curriculum, and then at week 4 of Cooper-Clayton, they will begin the modified 12-week DPP. Posttest assessment will include program evaluation. Outcomes will be summarized by visit, as change from baseline, and percent change from baseline. SAS v9.3 will be used for analyses at a significance level of 0.05 for all statistical tests. This MHBC program could be used to improve existing smoking cessation approaches by preventing smoking relapse due to weight gain.

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Classification / Health Topic Area: Community Science / Behavior - Seed

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POSTER ABSTRACTS

#238 Abstract Title: **Using Telemedicine to Deliver a Smoking Cessation Intervention: Is it Feasible and Effective?**

Author(s): D. A. Gross, St. Claire Regional Medical Center, Morehead, KY

Abstract: Background: Kentucky has the nation's highest rates of smoking and lung cancer mortality. Unfortunately, many smoking cessation resources are unavailable to residents of rural Kentucky. While a recent Canadian study found telemedicine to be an effective mechanism for offering smoking cessation to small groups of patients in rural locations, to our knowledge no such assessments have been conducted in Appalachian Kentucky. Methods: We are delivering the 13-week Cooper/Clayton Method to Stop Smoking to groups in northeastern Kentucky. Those who attend meetings at the Center for Health Education and Research in Morehead receive the intervention in-person, while attendees at the St. Claire Family Medicine Clinic in Olive Hill and Maysville Community & Technical College's Morehead campus participate non-concurrently via telemedicine. Variables of interest between the groups include cessation rates and participant satisfaction. Results: To date, 48 smokers have participated in the study (36 in-person and 12 via telemedicine). Fifteen participants have "graduated," or completed the intervention (14 in-person and one via telemedicine, with an eight-person telemedicine group in process). Pre- and post-study breath samples found lower carbon monoxide levels in each of the 15 graduates and nearly all of those participants (including the telemedicine participant) expressed satisfaction with the intervention delivery method. Conclusions: Due to the small sample sizes (and the fact that a telemedicine group remains in process), we are not yet able to make meaningful comparisons between the two groups. We anticipate finding in this and subsequent studies that telemedicine is an effective way to deliver a smoking cessation intervention, thus validating its use in larger venues (e.g., schools, work places).

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POSTER ABSTRACTS

#239 Abstract Title: **Enhancing Services for the Fragile Elders in Eastern KY and Southern WV**

Author(s): S. Swinford, Hospice of the Bluegrass

Abstract: Kentucky Appalachian Transition Services (KATS) has a single purpose – to decrease the number of 30 day hospital readmissions of frail elderly Medicare recipients. The root cause analysis conducted for the CCTP to analyze why patients in our community are readmitting to the hospital within 30 days found poverty, health literacy, illiteracy, and non-compliance with discharge instructions on medication management as key drivers. With an estimate of 72,282 beneficiaries, the likelihood of a hospitalization for 25,000 elders is possible, especially given the chronic illnesses the patients encounter. The task is immense and requires the participation of four partner hospitals in the ARH system – Hazard, Harlan, Whitesburg, and South Williamson. Acquiring community services is another aspect to maximum service delivery. KATS is based upon the Transition Care Model of post hospitalization practice which has been developed and perfected by Mary Naylor, PhD, RN at the University of Pennsylvania. With approximately 40 community based collaborators and downstream providers, KATS is well positioned to affect health care change in Eastern Kentucky and Southern West Virginia. The primary disease trajectories addressed by KATS are heart failure, heart attack, COPD, pneumonia, and end stage renal disease. The TCM model adopted by KATS affords participants access to a home visiting nurse who assists with teaching self-management and strategies for optimal health maintenance and medication compliance. KATS nurses may accompany patients to initial post hospitalization physician visits to assure that compliance issues are addressed and understood. 1500 frail elders have been served during the first year of KATS.

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Classification / Health Topic Area: Community Science / Other - seed

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POSTER ABSTRACTS

#240 Abstract Title: **Using D-Cycloserine to Enhance Exposure Treatment of Dental Phobia: From Bench to 'Chairside'**

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Abstract: Dental phobia is a widespread, significant public health problem resulting in 5-10% of adults avoiding necessary care. Often, these fearful adults fall into a “cycle of avoidance,” wherein they seek dental care only on an emergent basis. Exposure-based psychological therapies represent a standard of psychosocial care for such phobias. Nevertheless, this therapy is largely unavailable in the dental setting; avoidant patients are introduced to dentistry through emergency care, which may lead to sensitization, disallowing them from proceeding further with treatment. Nonetheless, if naturalistic exposures could be made more effective, fear and avoidance could be reduced. D-Cycloserine (DCS) has promise for such acceleration of the treatment process in exposure. DCS-augmented naturalistic exposure may be particularly applicable within the dental setting, at the time of dental treatment. A double-blind, placebo-controlled preliminary clinical trial was conducted with outpatients with dental avoidance of at least one year, in comparison to age- and sex-matched healthy controls. Trait measures of dental fear were collected across treatment. There were two exposure sessions, both “chairside” in the dental setting. The first exposure session included display of films of dental procedures on an iPad. The second exposure involved a dental cleaning with a hygienist and exam by a dentist. In comparison to controls, dental phobia patients indeed had higher levels of dental fear and avoidance. Ratings of dental fear decreased after the second exposure; ratings of treatment acceptability were quite high. These findings suggest the utility and treatment acceptability of DCS-enhanced exposure “chairside,” in the dental setting.

Supported by: IDeA CTR support - National Institute of General Medical Sciences/NIH #U54GM104942 and pilot funding from the West Virginia Clinical and Translational Science Institute and the Indiana University Clinical and Translational Science Institute NIH/NIDCR award: R01 DE014899, Center for Oral Health Research in Appalachia (COHRA) The content of this presentation is solely the responsibility of the authors and does not necessarily represent the official views of the NIH

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POSTER ABSTRACTS

#241 Abstract Title: **Enhancing Lives of Appalachian Youth: The Results of 3 -Year Assertive Adolescent and Family Treatment Program**

Author(s): B. Kellersberger, BA, Evaluation Center Research Assistant, U of Kentucky
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E. Stevenson, PhD, MSW, Evaluation Center Director, U of Kentucky

Abstract: In 2010, the Substance Abuse and Mental Health Services Administration awarded Mountain Comprehensive Care Center (MCCC) federal funds to develop an Assertive Adolescent and Family Treatment (AAFT) Program. The project goal was to expand behavioral health services for adolescents ages 12-17 with substance use or co-occurring mental health problems in Kentucky's Central Appalachian communities of Floyd, Magoffin, and Pike counties. Adolescent Community Reinforcement Approach (A-CRA) was the intervention model. Case planning and outcomes were monitored with Global Assessment of Individual Needs (GAIN) at intake and 12-months. Data was examined for 71 participants who completed an intake and 12-month follow-up interview using GAIN's low, moderate and high problem severity scales. Significant reductions were found in the percentage of youth meeting criteria for moderate levels of substance use problems; 82% of youth showed an 18% reduction in moderate levels of health problems; and 100% of youth showed significant reductions in high emotional problems. In addition, a high level of participation in illegal activities was reduced by 21%. Interviews with stakeholders revealed that AAFT teaches youth and their family new coping skills. Stakeholders expressed optimism regarding the lifelong benefits of coping skills training for participants, as well as strengthening the community around the youth in the process. Understanding the patterns of behavioral health problems and successful programs like AAFT can help emphasize the need for prevention, treatment, and recovery service for youth.

Supported by: The Substance Abuse and Mental Health Services Administration (SAMHSA) awarded Mountain Comprehensive Care Center (MCCC) federal funds to develop an Assertive Adolescent and Family Treatment (AAFT) Program. Staff at UK Evaluation Center serve as the outside program evaluator for the project.

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POSTER ABSTRACTS

#242 Abstract Title: **Barriers to Medication Adherence for Neurologic Disorders in Appalachian Kentucky**

Author(s): S. Gutti, Pikeville Neurology Clinic, Pikeville, KY
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Abstract: Appalachian Kentucky is a region with pronounced health disparities. Although there have been extensive investigations of chronic disease in this population, little research has been carried out on neurologic conditions and barriers to adherence with medication regimens for serious neurological conditions such as Multiple Sclerosis (MS) and seizure disorders (SD). Management of these conditions usually requires a complex regimen of costly medications. The cost of medications for MS or SD is very high, a situation that is likely to present substantial barriers to the Appalachian population. This pilot investigation was designed to document and quantify factors associated with adherence to medication regimens for patients with MS or SD in Appalachian Kentucky. Participants for this pilot study were recruited from a large community neurology practice in Appalachian Kentucky. Patients age 21 to 99, any race/ethnicity or gender, with a diagnosis of MS or SD were eligible to participate. Data were collected using participant interviews and medical record review. A total of 35 individuals were enrolled in the study, 18 with MS and 17 with SD. A majority of the patients were female; 13 (72%) of the MS patients and 12 (71%) of the SD patients. The cost for medications ranged from $67-1200/mo for medications for SD patients and $3300-4000/mo for MS patients. In addition to cost, complexity of the regimen and limited availability of some medications in rural pharmacies were found to be barriers for patients. Future research is planned to increase understanding of barriers and to identify opportunities for interventions.

Supported by: UK Center for Prevention Research

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POSTER ABSTRACTS

#243 Abstract Title: **Medical Care and Treatment for Hepatitis C Virus among Rural Appalachian Drug Users**

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Abstract: Objective: Despite high risk of contracting hepatitis C virus (HCV), people who inject drugs (PWID) often lack access to screening and healthcare services. HCV treatment is rapidly evolving and can be cost-effective as both primary and secondary disease prevention among PWID. However, at-risk populations tend to experience many barriers to HCV medical care—especially in underserved areas like Central Appalachia, where high HCV prevalence has been reported among PWID. Therefore, this study examined medical follow-up and treatment uptake among HCV-seropositive drug users in rural Eastern Kentucky. Methods: 503 recent drug users in Eastern Kentucky were recruited using respondent-driven sampling. Participants were serotested for HCV, and computer-assisted interviews were used to collect sociodemographic and behavioral characteristics. Individuals receiving a seropositive test and CDC-recommended counseling (n=193) were assessed for receiving medical follow-up, seeking treatment, and receiving treatment within 6 months. Multivariate logistic regression was used to determine correlates of receiving follow-up. Results: 56 (29.0%) participants reported prior HCV+ status awareness. 91 (47.2%) followed up with a clinician, 19 (9.8%) sought HCV treatment, and 10 (5.2%) reported receiving treatment. Prior HCV+ awareness (adjusted OR=2.1, 95% CI: 1.1-4.2), lack of health insurance (aOR=0.5, 95% CI: 0.2-1.0), and meeting DSM-IV criteria for generalized anxiety disorder (OR=2.2, 95% CI: 1.1-4.3) were independently associated with obtaining medical follow-up after status disclosure. Conclusions: Widespread HCV and low healthcare uptake underscore a growing public health problem in this underserved region, particularly among individuals lacking health insurance or screening services. Future HCV-related burden will likely be severe in Central Appalachia without significant intervention. Better characterizing healthcare barriers among HCV+ PWID is vital to public health efforts in the context of expanded access to healthcare under the Affordable Care Act.

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POSTER ABSTRACTS

#244 Abstract Title: HIV and HCV intervention among female Appalachian drug users

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Abstract: Rates of injection drug use are increasing in Appalachia, creating an impending and significant public health concern. Rural women offenders are at especially high risk for HIV and HCV exposure due to the limited resources for drug treatment and health care. Considering this, there is significant need to implement evidence based practices in this area. The current study examines implementation of an evidence-based brief intervention on rural female inmates. This presentation will describe the intervention and discuss the innovative adaptations used to target rural women. The study recruits women from three Appalachian jails by using screening and random selection. Women participating in the study are self-reported drug users and are scheduled for release into the community within two to twelve weeks. The women participate in a brief intervention in jail that uses motivational interviewing to address their motivation to change injection drug use, other drug use, and risky sex behaviors. This presentation will describe the client population participating in intervention sessions, as well as provide an overview of the brief intervention. Implications include the delivery of evidence-based practices in real-world settings where drug users are accessible. Criminal justice venues such as jails provide an opportune setting for intervention. Due to the limited services available in rural communities, it is critically important to establish and provide an evidence based intervention to this population in order to combat the injection drug use and the spread of HIV and HCV.

Supported by: Acknowledgment: Research reported in this manuscript was supported by the National Institute on Drug Abuse of the National Institutes of Health under Awards R01DA033866, K02DA35116, and T21DA035200. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. We would also like to recognize the cooperation and partnership with the Kentucky Department of Corrections and the local jails including the Laurel County Detention Center, Kentucky River Regional Jail, and the Leslie County Detention Center.

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POSTER ABSTRACTS

#245 Abstract Title: **Health Education for Prenatal Providers in Appalachia: Program Evaluation in West Virginia**

Author(s): I.R. A. Chertok, School of Nursing, West Virginia U
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Abstract: Background: West Virginia faces health disparities and limited prenatal health resources, especially in at-risk areas. In an effort to augment prenatal smoking cessation resources in at-risk areas of the state, the "Health Education for Prenatal Providers in Appalachia" (HEPPA) based on the ACOG 5As prenatal smoking cessation intervention was developed. Method: Evaluation of the HEPPA program that was delivered to 140 healthcare and social service providers working in four contiguous counties in West Virginia. A modified version of the Smoking Cessation Counseling (SCC) scale was used to measure the change in smoking cessation counseling behaviors among the providers. Results: There were significant increases among the overall group in the frequency of six items on the modified SCC regarding specific smoking cessation counseling behaviors. Comparing pretest and posttest, the frequency with which the overall group of providers engaged their pregnant clients in the Advise and Assist steps of the 5As smoking cessation program significantly increased ($z=-2.434$, $p=0.015$ and $z=-2.707$, $p=0.007$, respectively). Conclusions: The program evaluation indicated effectiveness in increasing the incorporation of prenatal smoking cessation into the care by different types of prenatal providers. By including both healthcare and social service providers in the training, a consistent message by interprofessional providers is promoted. Continued and expanded efforts to facilitate access to health resources among various providers working in rural areas of the state are necessary to support pregnant women and their families in decreasing smoking exposure.

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POSTER ABSTRACTS

#246 Abstract Title:	**Adolescent Tobacco Use and Social Influences in Rural, Appalachian, and Urban Communities**
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Abstract: Purpose: Rural adolescents experience higher rates of smoking, smokeless tobacco use and secondhand smoke exposure than urban youth. This disparity perpetuates the burden of tobacco-related deaths and disease in rural communities. There is limited research on the predictors of rural adolescent tobacco use, particularly in Appalachia. This study examines differences in family and social influences related to adolescent tobacco use and exposure in rural Appalachia, rural non-Appalachia, and urban communities. Methods: A secondary data analysis of four existing data sets will provide a unique opportunity to examine adolescent tobacco exposure and rural/urban status. Two datasets comprise Appalachian and non-Appalachian adolescents from Ohio (N = 161). A third dataset includes rural non-Appalachian adolescents from Indiana (N = 147); the remaining dataset has urban adolescents from Columbus, Ohio (N = 138). Results: A preliminary study with the rural, non-Appalachian data set (N = 147) comprising adolescents from two Indiana high schools was completed. Nearly one-fourth (22%) had elevated salivary cotinine indicative of tobacco use and secondhand smoke exposure; 10% reported smoking. Nearly half (47.6%) stated their family members (i.e., parents, siblings) smoked cigarettes. Salivary cotinine levels were significantly associated with smoking by family members ($X^2 = 10.81$, $p = .001$) but not by peers ($X^2 = 1.21$, $p = .271$). Conclusions: Understanding the family and social influences of tobacco exposure among rural and Appalachian adolescents is critical in developing and testing effective solutions to reduce tobacco use and, ultimately, lower the chronic disease and premature death experienced by rural and Appalachian communities.

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POSTER ABSTRACTS

#247 Abstract Title: **Are Health Care Providers a Barrier to the Health of Rural Sexual Minorities?**

Author(s): K. Bennett, Dept of Family and Community Medicine, U of Kentucky

Abstract: Objectives: Sexual minorities experience a number of health disparities, and studies suggest that delayed contact with health care providers (HCPs) may play a role. There is a paucity of research on the provider side of this equation, especially in rural areas. The aim of this study was to describe factors relating to care of sexual minority patients in the practices of rural HCPs. Methods/study population: online or paper survey administered to HCPs and patient care staff in rural Kentucky counties. Participants were recruited using personal invitations, tabling at physician events, links on social media, and snowball sampling. Results: 64 eligible HCP's from 21 counties completed the survey. 92% reported serving lesbian, gay, or bisexual (LGB) and 56% serving transgender (T) patients; 35% did not know whether they served T patients. 70% reported a nondiscrimination policy including sexual orientation and 47% believed their policy included gender identity. 86% agreed or strongly agreed that they provide quality care for LGB patients but only28% agreed that they would display symbols or materials specifically welcoming of sexual minorities and only 35% would advertise in LGBT media. Discussion: This study adds to knowledge about the policies, practices, and attitudes of rural providers that relate to their interactions with sexual minority patients. The data indicate a disconnect between provider beliefs about their quality of care for LGBT patients and their willingness to actively change their practice. Interventions including and linking HCPs and the LGBT community are needed to improve care and reduce health disparities.

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POSTER ABSTRACTS

#248 Abstract Title: **Stable Knockdown of Tumor-NQO1 Levels Causes a Significant Decrease in ALDH-HIGH Cancer Stem Cell Populations.**

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Abstract: Despite recent advances in cancer treatment such as targeted and personalized medicines, lung cancer has sustained its unenviable position as the leading cause of cancer related deaths in the U.S. Thus, new ideas leading to early diagnosis and more potent therapeutics are desperately needed. In recent years cancer stem cells (CSC) have become a topic of great interest due to their purported ability to evade standard chemotherapeutics and promote the progression of metastatic disease. In an attempt to increase the effectiveness of chemotherapeutics and prolong survival in the clinic, many investigations have been conducted to identify CSC markers, such as Aldehyde Dehydrogenase, which is purportedly a CSC marker that is differentially expressed in a subset of cancer cells within the heterogeneous tumor population. Previous investigations have shown that Isolation and destruction of these ALDHhigh tumor cell populations leads to a loss in primary tumor burden and inhibition of metastatic disease. In the present study we show that stable knockdown of the Phase II detoxifying enzyme NQO1, which is highly expressed in various solid tumors including non-small cell lung cancer (NSCLC), significantly decreases ALDHhigh populations in NSCLC as well as other cancer cell models. Furthermore, we show that stable NQO1 knockdown leads to inhibition of growth in soft agar, increased sensitivity to detachment induced cell death (anoikis) and decreased tumor invasion. In summary these data suggest a unique role for NQO1 in tumor progression and survival and a potential novel target for cancer stem cell chemotherapeutics.

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POSTER ABSTRACTS

#249 Abstract Title:	**Pre-clinical studies to determine efficacy of Aurora A kinase inhibitors in prevention and treatment of breast cancer metastasis using patient-derived tumors.**
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Abstract: Although advances in treating early stage breast cancer have increased the overall survival rate, once the disease has metastasized treatment options become severely limited. About 94% of breast cancers have an abnormally high level of Aurora A kinase (AURKA). AURKA stimulates cell division and is normally present in the cell for only a short period of time. Several AURKA inhibitors are currently in clinical trials for cancer treatment. Unfortunately, these inhibitors were found not efficient for treatment of solid tumors and particularly breast tumors. Our work on mouse models of breast cancer indicates that inhibition of AURKA does not limit primary tumor growth but dramatically decrease metastasis thus providing us with an efficient means to formulate new treatment strategies for advanced breast cancer patients. In our current study we evaluate our previous findings of anti-metastatic activity of AURKA inhibitors in xenograft models of transplanted patient-derived breast tumors procured at the MBR Cancer Center. We successfully collected and established several patient-derived tumor xenografts and assessed expression of AURKA. We also defined the efficacy of AURKA inhibitors against metastasis in this model. Based on our findings we plan to develop new clinically relevant guidelines for the application of AURKA inhibitory compounds as new anti-metastatic agents in Phase I/II clinical trials with AURKA inhibitors and use AURKA expression as prognostic metastasis biomarker in breast cancer patients.

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POSTER ABSTRACTS

#250 Abstract Title: **Attitudes Toward Cancer Clinical Trials Among Rural Individuals with Lung Cancer**

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Abstract: Lung cancer (LuCa) remains the leading cause of cancer mortality, with only 16% of those diagnosed expected to achieve 5-year survival. Participation in clinical trials is necessary to advance LuCa care, but residents in rural areas likely experience personal and systemic barriers to participation. This study examined decisions to participate in clinical trials among LuCa survivors residing in the Central Appalachian region of Kentucky. Individuals recently diagnosed with LuCa were identified through the Kentucky Cancer Registry, and home health coordinators collected data. Survey items assessed preferred treatment decision role, history of trial accrual, subjective knowledge and attitudes toward cancer clinical trials. Participants were predominantly white (98%), with men/women equally represented (mean age=62.2±11.4; 51% female). Most preferred a shared decision making role (62%), yet nearly 25% wanted the oncologist to lead the decision process. While few had participated in a clinical trial (6%), the majority had not been offered participation (83%). Willingness to participate in a trial varied greatly (3.4±2.2; 1-7 scale) with most respondents endorsing the extreme response options (37% extremely unlikely; 14% extremely likely). Trial knowledge was suboptimal (2.9±1.2, 1-5 scale) with only 30% reporting a moderate amount of knowledge or more. Rural LuCa survivors preferred a shared role in decision making. However, trial access was limited and there were highly divergent perspectives on willingness to participate. To advance care, efforts are needed to reduce barriers to trial accrual among this underserved population, and targeted decision support tools may be one approach to promote accurate information about cancer clinical trials.

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POSTER ABSTRACTS

#251 Abstract Title: **Differences in Cancer Outcomes among Women Diagnosed with Breast Cancer Living in Appalachia and non-Appalachian Kentucky**

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Abstract: In this large population-based cohort study of women diagnosed with breast cancer and included in the Kentucky Cancer Registry, we hypothesized that residents in Appalachian Kentucky would experience poorer cancer outcomes relative to those living in non-Appalachian Kentucky. Consenting women were interviewed by phone (n=1057) approximately 12 months after diagnosis. Multivariate analysis of covariance was used to determine associations between Appalachian (27%; n=283) or non-Appalachian residence (73%; n=774) and the range of correlated cancer outcomes adjusting for socio-demographic differences. Results: Relative to women diagnosed with breast cancer and living in non-Appalachian Kentucky, those living in Appalachia were diagnosed at a later stage (p=.03), with more comorbid physical conditions (p=.002), more symptoms of stress (p=.002) yet not depression, and lower Functional Assessment of Cancer Therapy scores indicating poorer physical status (p<.0001). There were no differences in survival by geographic region. After adjusting for significant regional difference in education, income, private insurance coverage, race, age, rurality, and current smoking status, Appalachian residence was no longer associated with stage, number of comorbid conditions, or stress. When additionally adjusting for stage at diagnosis, Appalachian residence was associated with less frequent use of chemotherapy (46.2% vs 50.3%; p=.01) and radiation (48.4% vs 60.0%; p=.007). Conclusions: Socioeconomic factors explain the majority of noted differences in breast cancer outcomes between Appalachian and non-Appalachian regions with the noted exception of treatment received.

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POSTER ABSTRACTS

#252 Abstract Title: **Marty Driesler Lung Cancer Project (MDLCP): Demographic Comparison with the National Lung Screening Trial (NLST) Population**

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Abstract: Background: Kentucky has the highest incidence rates of lung cancer in the United States. The MDLCP screened high risk individuals within Appalachian Kentucky with low-dose CT screening annually for 3 years, using the same entry criteria as the NLST with the exception of a requirement for significant airways obstruction (FEV1/FVC <70%). Objective: This post-hoc analysis compared the baseline demographics and characteristics of the screened populations of the MDLCP and the NLST. Methods: Eligible subjects were between 55 to 75 years of age, current or former smokers with a >30 pack-years smoking history and an FEV1/FVC<70%. All MDLCP research participants completed a study questionnaire used in the present analysis and NLST baseline characteristics were previously reported by the NLST. Results: In the MDLCP, a total of 955 individuals were screened for eligibility and 626 (65%) were eligible. Of those 531 had PFTs, 254 of these subjects had FEV1/FVC<70% and 227 matched the criteria of the NLST. MDLCP participant characteristics were as follows: 222 (97.8%) were Caucasian (reflecting the demographics of the region), 114 (50.2%) were men, 154 (67.8%) were younger than 65 years, and 156 (68.7%) were overweight or obese. 142(62.6%) were current smokers; median cigarette exposure was 65 pack-years (range 35-216). 31 (13.7%) had a college or higher degree, 46 (20.3%) had not completed high school. 95 (41.9%) reported household incomes < $25,000, including 41 (18.1%) < $15,000 below the poverty level. Conclusion: When compared to the NLST participants, MDLCP participants had higher smoking rates, lower income, lower education level and older age. In contrast to the NLST participants, who were younger, better educated and more often former smokers, the MDCP participants more closely resembled the demographics of Appalachian Kentucky and represent a higher risk screened population than the NLST.

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Classification / Health Topic Area: Community Science / Cancer

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POSTER ABSTRACTS

#253 Abstract Title: **Appalachian Mountaintop Mining Particulate Matter Promotes Human Lung Carcinoma Tumor Formation**

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Abstract: Lung cancer is the leading cause of cancer death, and after smoking, environmental and occupational exposure is the major cause. West Virginia (WV), one of the top two coal mining states in Appalachia, ranks the third highest rate of lung cancer incidence in the United States. Our epidemiological studies suggest that living near WV mountaintop coal mining (MTM) activities is a contributing factor of the high lung cancer risk. The purpose of this study was to investigate the long-term carcinogenic effects of MTM particle exposure on human lung epithelial cells. Air particulate matter (PM) collected within one mile of active MTM site in Edwight, WV (PMMTM), consisting mainly of silica (Si, 48%) and molybdenum (Mo, 29%), was used for cell exposure studies. As control, PM collected from the neighboring areas that do not have coal mining in Green Bank, WV (PMCON) was used. Chronic exposure (3 months) of non-tumorigenic human lung epithelial BEAS-2B cells to sub-cytotoxic concentration (1 μg/mL) of PMMTM, but not PMCON, was found to induce accelerated cell proliferation and malignant transformation. Subcutaneous injection of the PMMTM-transformed cells along with human lung carcinoma H460 cells in a xenograft mouse model resulted in a high rate of tumor formation compared with the coinjection of PMCON-treated cells and H460 cells, indicating the tumor-promoting effect of PMMTM. Exposure to Mo, and to a lesser extent Si, strongly promoted the human lung carcinoma tumor formation in mice, suggesting that Mo may be a key contributing factor of the PMMTM tumor-promoting effect.

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Classification / Health Topic Area: Community Science / Cancer

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POSTER ABSTRACTS

#254 Abstract Title: **Complete Life Tables and Life Expectancy by Region and Socioeconomic Status in KY, OH and WV**

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Abstract: Background: the Appalachian region in the three states KY, OH and WV has experienced higher rates of poverty and lower levels of education than the rest of the United States. The burden of cancer is higher for residents of Appalachia than for the United States as a whole. This project is to develop complete smoothed life tables by region and socio-economic status, then subsequently to examine cancer survival disparities in relative survival by Appalachian and socioeconomic status. Aim: Develop specific life tables for this region for years 2000-2010 and examine life expectancies at birth by region and socioeconomic status. Methods: The populations and mortality data were acquired from the US NCHS for each of the calendar years 2000-2010. Appalachian counties were defined based on the Appalachian Region Commission. County-level obesity, poverty and education data for years 2000-2010 were calculated from the state BRFSS data or the US Census. Flexible Spline Poisson regression models were applied to smooth the raw mortality rates. Simulations were conducted to identify the best models by varying combinations of numbers and locations of knots. The complete, smoothed life tables will be based on a set of variables including state, race, Appalachian region, and socioeconomic status. Results/Discussions: In general, higher life expectancies were found in non-Appalachian, urban, more affluent regions compared to Appalachian, rural and less affluent regions. However, the results were not consistent across gender, race and regions. The specific life tables generated in this study are essential for estimating population-based relative cancer survival and providing better understanding of cancer survival in this region.

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Classification / Health Topic Area: Community Science / Cancer

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POSTER ABSTRACTS

#255 Abstract Title: The Epidemiology of Pediatric Brain Tumors in Appalachia

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Abstract: Although a great deal is known about which types of cancer are increased in Kentucky (KY) adults, very little is known about whether KY children have a higher risk of any cancers, especially in Appalachia. We therefore compared the incidence of various pediatric cancers in KY, including Appalachia, with 17 other Surveillance, Epidemiology, and End Results (SEER) Programs across the United States. The age-adjusted incidence rate of pediatric central nervous system (CNS) neoplasms in KY was 18% higher compared to the SEER average (3.48 per 100,000 person-years vs. 2.94, $P < 0.05$). This difference was mostly attributable to the astrocytoma subset of CNS neoplasms, which was 28% higher in KY children (1.86 vs. 1.45, $P < 0.05$). In contrast, hematopoietic neoplasms (e.g. leukemias and lymphomas) were actually 13% lower in KY children (3.96 vs 4.56, $P < 0.05$), with no other major cancer category showing a significant difference between the two cohorts. Within KY, children from Appalachia had a 14% higher incidence rate of CNS cancers compared to non-Appalachian children (3.83 vs 3.35), again being mostly attributable to the astrocytoma subset (2.13 vs. 1.76), although none of the differences quite reached significance. These data suggest that the risk of CNS cancer is higher in KY children, especially in Appalachia. Additional data is being retrieved to see if this extends to other Appalachian regions. If so, then this will provide the foundation for a unique large-scale molecular and environmental epidemiologic study to determine the cause(s) of this risk in Appalachian children.

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POSTER ABSTRACTS

#256 Abstract Title: **Cancer Health Disparities in Appalachia: Addressing Barriers and Building Bridges with Cancer Navigation**

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Abstract: While intravenous and intra-arterial thrombolysis are mainstays in acute ischemic stroke therapy, clinical outcomes lag significantly behind improving rates of revascularization. In this setting, we explore adjunctive, targeted pharmacotherapy for reducing ischemic injury. Previous neuroprotective studies failed due to long intervals between symptom onset and drug administration, lack of concordant thrombolytic revascularization, and lack of targeted administration to the affected vessel. Despite known neuroprotective properties, verapamil, a calcium channel blocker (CCB) that is already safely injected intra-arterially (IA) for vasospasm, has never been rigorously investigated as a stroke therapy. To determine whether verapamil might be an effective stroke therapy when administered in this fashion, we have developed a novel method to mimic the clinical condition of superselective IA pharmacotherapy administration after vessel recanalization in rodent models after experimental ischemic stroke (transient middle cerebral artery occlusion, MCAO). Specifically, after 1 hour MCAO in three month old male C57/Bl6 mice, we examined the potential neuroprotective effects of verapamil administered via the external carotid artery (10mg/kg) to the internal carotid artery or intraperitoneal injection (IP, 15mg/kg). On post stroke day three (3), Tetrazolium chloride (TTC) staining of sectioned brains and subsequent infarct volume measurement with NIH Image J software demonstrated a significant reduction in infarct volume with IP verapamil that was even further reduced with IA administration, both as compared to controls injected IA or IP with 0.9% saline. These results suggest that IA administration of verapamil following recanalization after acute large vessel occlusion, may be an effective neuroprotective stroke therapy that could be readily employed in human ischemic stroke patients.

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Classification / Health Topic Area: Community Science / Other

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POSTER ABSTRACTS

#257 Abstract Title: **To TPA or Not to TPA**

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Abstract: Capsular warning syndrome is a form of crescendo TIAs that occur in the lenticulostriate artery (Lee, Jun MD, et al.). Risk of completed stroke with TIA is 9.5% to 20%; however the risk greatly increases with capsular warning syndrome to 40% (Lee, Jun MD, et al.). Resistance to therapy such as thrombolytic agents, anticoagulants or hemodiluting is common with capsular warning syndrome (Donnon, GA, et al.). An 81-year-old female presents to the ED as a stroke call with drooling, dysarthria, and right sided facial droop. Patient was unable to raise arms, legs, grip with right hand, or make vocal sound. Initial National Institute of Health Stroke Scale (NIHSS) was 18. She was immediately taken to CT scan which was negative for acute intercranial pathology. Her symptoms started to resolve with a NIHSS of 3; however, within minutes patient returned to her stroke like state. Dr. K. John examined patient in the ED with resolution of symptoms. Patient was diagnosed with capsular warning syndrome because of the recurrence and subsequent resolution of symptoms. Dr. John discussed with the patient that if symptoms lasted greater than 90 minutes than she had the option of TPA, but patient declined. Patient was placed in NSICU and had recurrent episodes the next two days of admission that lasted 30-45 minutes. Patient's stroke work up was negative except elevated LDL 159. She was placed on aspirin, Plavix and discharged home. First described in 1993 by D.A. Donnan, Capsular warning syndrome is significant for increased risk of complete CVA and is typically refractory to conventional therapies. High dose clopidogril and aspirin have been reported as beneficial in several cases (Teng, Hao and Hong, Chi). Early recognition of capsular warning syndrome is important to the treatment and prevention of complete stroke.

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Classification / Health Topic Area: Clinical Science / Cardiovascular

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POSTER ABSTRACTS

#258 Abstract Title:	GPSM3 as a Potential Biomarker and Drug Discovery Target in Rheumatoid Arthritis

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Abstract: Successful therapeutics targeting G protein-coupled receptors (GPCRs) have had a large impact on the treatment of human disease. Chemokine receptors are GPCR family members that regulate cellular migration, survival, and angiogenesis in inflammatory conditions, but neutralization strategies have had mixed results in autoimmunity and even less efficacy in rheumatoid arthritis (RA). This has been partially attributed to chemokine receptor/ligand redundancy in inflammation, and it has been proposed that a regulator of GPCR signaling should be targeted rather than neutralization of singular chemokines or their receptors. One such GPCR signaling regulator, GPSM3, inhibits nucleotide release by G-alpha-i subunits of the chemokine receptor signaling pathway. We have found that GPSM3 expression is uniquely restricted to leukocytes with the highest in monocytes – cells critical to RA disease. In a collagen antibody-induced arthritis (CAIA) mouse model of inflammatory arthritis, we recently found that GPSM3-deficient mice have reduced expression of proinflammatory monocyte cytokines IL-6 and IL-1beta and chemokine receptors in the joints, which we attribute to mechanisms of reduced monocyte chemotaxis toward CCL2, CX3CL1, and chemerin. Compelling genome-wide association studies (GWAS) have identified protective alleles in the GPSM3 gene locus in healthy individuals, which are significantly less prevalent in patients with autoimmune disease including RA; our exciting new preliminary data show human GPSM3 transcript levels correlate with these protective alleles. Although the role of GPSM3 polymorphisms in autoimmunity and the immunologic function of its gene products are not yet known, GPSM3 blockade could be a novel clinical approach for RA treatment with significant advantages over current cytokine or receptor neutralization strategies.

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POSTER ABSTRACTS

#259 Abstract Title: **Association of Gallbladder and Irritable Bowel Syndrome in an Appalachian Population**

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Abstract: Purpose: The purpose of the study was to assess the relationship between gallbladder dysfunction and irritable bowel syndrome by gender and age in rural Appalachian population. Methods: We recorded the age, height, weight, the IBS diagnosis, and results from the HIDA- scan, from patients in the ARH Hospital in Hazard, KY, from June 2011- May 2013. CCK-HIDA scan were defined as abnormal if the ejection fraction was less than 35%. Results: The 220 patient ranged in from 8-90 years of age (Mean= 42; Standard of Deviation (SD)= 18.8) and included 145 (66.2%) females. The mean BMI was 29.7 (SD=8.6) overall; 29.9 and 29.6 for males and females, respectively. There was no association between BMI and abnormal HIDA scan or the diagnosis of IBS. Overall, 9 (12.2%) males and 34 (23.4%) females had IBS and abnormal CCK-HIDA scan (Chi Square= 13.9; p= .000). Using age quartiles (≤ age 28, 29-41, 42-55, >55 years), a significant association was found between IBS and HIDA <35% for females aged 29-41 years (Chi Square= 6.9; p= .008) and for males and females aged 42-55 years (Males Chi Square= 6.9; p= .009; Females Chi Square= 4.6; p= .033). Conclusion: The prevalence of gallbladder dysfunction in IBS patients is increased in this rural Appalachian population. Although this was true for males and females, the age distribution of this association was broader for females. This finding suggests that smooth muscle motility disturbance in IBS maybe pervasive. Further study will evaluate the association of potential confounders.

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Classification / Health Topic Area: Clinical Science / Inflamation

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POSTER ABSTRACTS

#260 Abstract Title: **Chronic pancreatitis - are high risk dietary choices to blame?**

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Abstract: While previously considered chiefly a diagnosis in males, in University of Kentucky (UK) hospitals patient records indicate women are equally at risk for developing pancreatitis, and women have a disproportionately high risk for developing associated abdominal pain. A high incidence of pancreatitis is particularly prominent in young female patients (ages 20-40), suggesting an unrecognized emerging health issue. Our initial findings are from the retrospective chart review of 4098 de-identified patient records at the UK Hospitals which serve a catchment area of 3.5 million people in Central and Eastern Kentucky, including 55 counties of Appalachia. Complete records for patients diagnosed and treated for pancreatitis are available for 9 years (January 2005 - December 2013). The preliminary analysis indicates patients diagnosed with pancreatitis were 48.3% female and 51.7% male. This equal percentage of women among patients is at variance with numerous national and international averages indicating great need for further study. In the North American Pancreatitis Study-2 from 2000 to 2006 at 20 US referral centers, alcoholic pancreatitis is more frequently diagnosed in men (59.4% men vs 28.1% women), but nonalcoholic (18% men vs 36.7% women) and idiopathic etiologies (22.6% men vs 35.2% women) are reported more often in women ($P<0.01$ for all comparisons). Our Preliminary Data concur that risk factors associated with pancreatitis are multifactorial but are different for women and for men. Striking comorbidities higher among female patients in our UK data set are abdominal pain and obesity. While pancreatitis has been considered an older men's disease (age >50), the equal incidence in women identifies pancreatitis as an emerging health problem that predicts higher future risk for abuse of alcohol and opioid therapy for pain, and increasing long-term health care costs that potentially extend beyond Kentucky.

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Classification / Health Topic Area: Clinical Science / Inflamation

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POSTER ABSTRACTS

#261 Abstract Title: **Rural Healthcare Provider Knowledge and Practice Patterns Regarding Infant Hearing Loss**

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Abstract: Objective: Diagnosis and intervention for infant hearing loss is often delayed in areas of healthcare disparity, such as rural Appalachia. Primary care providers play a key role in timely hearing healthcare. The purpose of this study is to assess the knowledge and practice patterns of rural primary care providers regarding early hearing diagnosis and intervention (EHDI). Study Design: Cross sectional questionnaire study. Methods: Primary care practitioners in a large rural region of Appalachia were surveyed on practice types, patterns, and knowledge on congenital hearing loss diagnosis and treatment. Results: 94 practitioners responded and 84.9% believe newborn hearing screening is very valuable for pediatric health. General practitioners predominate the region but are less likely to receive infant hearing screening results than exclusive pediatric practices (54.5% versus 95.2%, $p < 0.01$). Providers' knowledge of EHDI standards was assessed and they reported a goal diagnosis age of 7.8 months and a goal hearing aid use age of 9 months. Participants estimated the earliest age for cochlear implantation to be 18.6 months after birth. Over 50% were lacking confidence in counseling families and directing the care through the EHDI process, and 46% of providers felt their training in infant hearing was inadequate. 43% of participants stated that they did not use any in-office hearing testing. Conclusions: Delays in diagnosis and treatment of infant hearing loss in rural regions of healthcare are due to multiple factors. Lack of practitioner knowledge and confidence in managing infant hearing loss may impede timely care in rural areas.

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Classification / Health Topic Area: Community Science / Opthamology

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POSTER ABSTRACTS

#262 Abstract Title: Rural Barriers to Early Diagnosis of Infant Hearing Loss

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Abstract: Objective: In spite of Early Hearing Detection and Intervention (EHDI) programs, the diagnosis of congenital hearing loss is often delayed. Rural residents, from areas of healthcare disparity such as Appalachia, may face multiple barriers to timely care. The purpose of this study is to assess regional barriers in the diagnostic and therapeutic process following abnormal newborn hearing screening testing. Study Design: Cross sectional questionnaire study. Setting: Tertiary referral center. Patients: Parents of infants who failed newborn hearing screening from 2009-2011. Intervention and Main Outcome Measures: In collaboration with state EHDI agencies, subjects were identified and mailed a questionnaire assessing demographic information, county of origin, and perceived barriers to infant hearing screening. Results: Of the 410 participants, 28% of parents were from a rural Appalachian region. Of the non-Appalachian subjects, 72.5% were from metro regions. 30% of Appalachian parents considered the diagnostic process difficult, compared with 16.7% of non-Appalachian parents. A higher percentage of Appalachian parents were lacking a high school diploma (OR 1.69, p=0.028). Medicaid insurance was more common in Appalachians (51.3% versus 29.6%) (p<0.001). Distance from the diagnostic/therapeutic center represented was a significant barrier for Appalachian parents (OR 3.00, p=0.001). Appalachian parents expressed a strong interest in telemedicine (56.8% versus 34.1%) (p<0.001). Of those children diagnosed with hearing loss, 52.6% of Appalachian children were diagnosed after 3 months of age compared with 39.5% of non-Appalachian children. Conclusions: Multiple barriers can affect timely diagnosis and treatment of congenital hearing loss. Educational and telemedicine programs may benefit parents in rural regions.

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Classification / Health Topic Area: Clinical Science / Opthomology

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POSTER ABSTRACTS

#263 Abstract Title: **The Art of Analytics: Leveraging Electronic Health Record Data for Practice Based Research and Population Health**

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Abstract: Electronic health records (EHRs) provide foundation for surveillance, data sharing, reporting of complex metrics, and collaboration essential for practice based research. Each of these extensions support data-driven public health efforts and the national effort in achieving the Triple Aim. The analytics potential of EHRs is especially promising given the complexities of medical care and need for timely clinical decision support. What is not receiving sufficient attention, however, is the need for a heightened level of data maturity and ability to demonstrate value in the data collected. Health analytics is often equated with “big data,” “data warehouses,” and enterprise systems automating the handling and synthesis of health care data. This focus on software detracts from the need to meaningfully apply data to population health. The West Virginia Practice Based Research Network, comprised of primary care centers, academic institutions, state government, local health, and public health partners, helps advance the use of data in primary care and fosters an enhanced level of data maturity. This complements the Network mission to conduct practice based research addressing priority health disparities. Efforts span EHR data quality, data management, selecting targets for change, measuring change over time, identifying measures that are meaningful to the provider while contributing to an understanding of the population, and asking research questions aimed at improving outcomes. Attending to these fundamental notions of data adds value to health analytics and supports data-driven collaborations to improve patient care and outcomes.

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POSTER ABSTRACTS

#264 Abstract Title:	**Effective Approaches for Recruiting Rural Appalachian Religious Congregations for a Fall-Prevention Exercise Program**
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Abstract: Community-based health promotion activities have previously found captive audiences within religious congregational settings. Despite the cultural value placed upon religion in Appalachian communities, limited congregational outreach has been undertaken in this region. This study compared two approaches for recruiting 20 rural, Appalachian religious congregations for a fall-prevention exercise program (Tai Ji Quan: Moving For Better Balance). A traditional scientific approach using mixed sampling methods, mailings, and press releases was initiated but quickly abandoned due to community feedback, limited success, and literacy concerns. In its place, a snowball sampling strategy was implemented that emphasized face-to-face contact and message personalization for each congregation. To date, two congregations have been recruited using the traditional approach, 15 via the snowball approach. Although more effective, the snowball approach created a need for additional resources to support the increased travel that was required. Additionally, logistical and Appalachian religio-cultural factors posed challenges to effective congregational recruitment. For example, the cultural tendency to distrust outsiders forced the recruitment phase to run longer than originally estimated since researchers had to take the time to integrate into the communities being served (e.g., attend prayer services, volunteer at events). Acknowledging and addressing these challenges gradually led to increased efficiency at congregation recruitment. These lessons can be employed during future attempts at implementing health promotion activities into rural, Appalachian congregations. Researchers can also use these results to better plan recruitment strategies and budget resource needs, when recruiting religious congregations in Appalachian communities.

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Classification / Health Topic Area: Community Science / Trauma/Injury/Rehabilitation

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