DMU Research Symposium

December 3, 2015
Des Moines University
3200 Grand Avenue
Des Moines, IA

Des Moines University's Research Vision is to be…

A cultivator of distinctive faculty and student researchers who discover and disseminate new knowledge.

Welcome

Welcome to the sixth annual Des Moines University (DMU) Research Symposium! This year DMU is hosting over 450 attendees, showcasing an engaging and relevant keynote address, and presenting 57 multidisciplinary posters and research oral talks given by our research community.

One of DMU's four vision statements is to become "a cultivator of distinctive faculty and student researchers who discover and disseminate new knowledge." There is no event that captures this vision better than our Symposium where the entire DMU campus comes together to recognize the efforts of our students, faculty, and our colleagues from the health care and scientific community.

For some of the students it is their first step into the more formal world of research and academia. This Symposium is more than an opportunity to present research. It is an opportunity to discuss their work, receive constructive feedback from affiliated faculty and fellow students, and to establish relationships between future peers in the healthcare professions.

We celebrate their success by demonstrating the critical role research plays in the advancement of health care, providing a forum for the collaboration of ideas, and fostering the production of new hypotheses. The DMU Research Symposium highlights countless hours of effort over the past year and has real potential for impacting knowledge across disciplines.

We are excited to have Dr. J. Michael Oakes as our keynote speaker this year. Dr. Oakes is an active researcher on a wide variety of studies addressing social epidemiology and research ethics. He has chaired an institutional review board (IRB) for more than 15 years with five of those years serving as co-chair of the University of Minnesota's Human Research Protection Program and Conflict of Interest Committee. Dr. Oakes also serves on the National Bone Marrow Donor Program IRB and has been active in national training and discussion forums on protection of human research subjects. His keynote will address protecting vulnerable human subjects and conflict of interest in healthcare research. Dr. Oakes will, among other things, discuss the importance of protecting vulnerable populations as it relates to the findings of a recent IRB investigation at the University of Minnesota Department of Psychiatry on studies of schizophrenia and other mental health disorders.

DMU is striving to become a leader with our research culture and environment. This Symposium demonstrates the strong research that is occurring on the DMU campus and in our community. While attending the oral presentations and viewing the posters, I hope you will reflect on how the discoveries we are making in research today will impact the scientific and medical community and the future of our patients.

Please enjoy the Symposium and thank you for attending!

Jeffrey T. Gray, PhD
Vice President for Research, Des Moines University

Agenda

Time		Location
9 am	Informal Poster Viewing	SEC First Floor (Near the Bookstore)
12 pm	Lunch	SEC Auditorium
12:30 pm	Minnesota Nice? Some Perspective on Protecting Vulnerable Human Subjects and Conflict of Interest in Healthcare Research J. Michael Oakes, PhD *Associate Professor of Epidemiology and Community Health at the University of Minnesota* • Describe recent controversies in the protection of human research subjects, especially those with diminished cognitive capacity. • Describe recent controversies in conflict of interest policy and practice. • Recognize the potential impact of the proposed change in Federal human subject protection regulations.	
1:30 pm	Break	
1:45 pm	Poster Presentations (Odd Numbered Posters Will Be Judged)	SEC First Floor
2:45 pm	Poster Presentations (Even Numbered Posters Will Be Judged)	SEC First Floor
3:45 pm	Break	
4 pm	Oral Presentations	SEC Auditorium
5 pm	Awards Presentation	
5:15 pm	Adjourn	

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Purpose

The Research Symposium aims to recognize the research efforts of those at Des Moines University (DMU) and in the surrounding medical and scientific community by providing a forum for the collaboration of ideas, the production of new hypotheses, and to demonstrate to the attendees the critical role that research plays in the advancement of health care.

Mentored Research Program

DMU students

The mentored research program is a competitive program which encourages DMU students to work in one of the wide range of research projects. Funding for this program is provided by the research and grants committee in which participants are paid $10.75 per hour. The program began in 2002 and is a robust and active research opportunity at DMU. The eight week program also includes additional learning opportunities such as research presentations from our own DMU faculty, a closing program consisting of a guest speaker, poster and power point presentations. All applications are due by January 29, 2016. Additional information can be found at http://www.dmu.edu/research/student-research-opportunities/.

Undergraduate Students

The undergraduate mentored research program is committed to providing an array of research experiences to undergraduate students. Selection of applicants is based upon academic performance in the sciences, statement of career and academic goals and letter of recommendation from a biology or health science faculty member. Selected students will work with faculty researchers for an eight-week period usually in June and July, on projects including but not limited to microbiology, pharmacology, physiology, biochemistry, public health, and physical therapy. Students receive a stipend of $10.75 per hour, but no housing is provided. Students are required to work up to 40 hours per week. All applications are due by January 29, 2016. Additional information can be found at http://www.dmu.edu/research/student-research-opportunities/.

Continuing Education Credit

DO: Des Moines University is accredited by the American Osteopathic Association and approves this live activity for 4.0 AOA Category 2-A CME credit(s).

DPM: Des Moines University (DMU) is approved by the Council on Podiatric Medical Education as a provider of continuing education in podiatric medicine. DMU has approved this activity for a maximum of 4.0 continuing education contact hours.

MD: This activity has been planned and implement in accordance with the accreditation requirements and policies of the Iowa Medical Society (IMS). Des Moines University (DMU) is accredited by the IMS to provide continuing medical education for physicians. DMU designates this live activity for 4.0 *AMA PRA Category 1 Credit(s)*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Nurses: Des Moines University is Iowa Board of Nursing approved provider #112. This live activity has been reviewed and approved for 4.8 continuing education contact hour(s). No partial credit awarded.

Other Healthcare Professionals: This live activity is designated for 4.0 *AMA PRA Category 1 Credits*™.

Keynote Speaker

J. Michael Oakes, PhD

Dr. J. Michael Oakes is an Associate Professor in the Division of Epidemiology and Community Health at the University of Minnesota. He directs the Robert Wood Johnson Foundation's National Program Center for Interdisciplinary Research and is Co-Director of the University's Federal Statistics Research Data Center. Dr. Oakes's professional interests center on research methodology, social epidemiology, and research ethics. He is an active researcher and frequent principal investigator on a wide variety of studies addressing methodological, health, and ethical problems. Dr. Oakes has authored over 110 papers exploring problems at the intersection of the social and biomedical sciences. His first text *Methods In Social Epidemiology* was released in 2006 (second edition is forthcoming). He teaches several graduate-level courses in statistical methods and social epidemiology. Dr. Oakes has chaired an IRB panel for more than 15 years. For five years he served as Co-Chair of the University of Minnesota's Human Research Protection Program and its Conflict of Interest committee. Dr. Oakes also serves on the National Bone Marrow Donor Program IRB and has been active in national training and discussions on protection of human research subjects.

Michael Oakes received his Ph.D. in sociology from the University of Massachusetts. In 2007, Dr. Oakes was named a McKnight Presidential Fellow at the University of Minnesota, an award given to a select group of the University's most promising new associate professors. In 2010 he was awarded the Schuman award for excellence in graduate teaching, the School of Public Health's highest teaching honor. In 2011, he was awarded the school's highest award for his role in advising and mentoring.

Relevant to the content of this CME activity, Dr. Oakes indicated he has no relevant financial relationships to disclose.

How to Read a Poster Abstract

A common approach for evaluating posters involves considering the following factors in the technical, visual and presenter categories. This tool can be used when reviewing posters at this meeting and as a helpful guide for constructing your posters in the future.

Category	Notes
Technical	
Research topic clearly described with adequate introduction and a clear hypothesis.	
Good use of the space of the poster with sections on methods, results, and discussion as appropriate.	
Conclusion section which emphasizes the relevance of the research in the field of study.	
Visual	
Title, author(s), affiliations, and contact info included.	
Poster design logical and easy to follow with appropriate visuals (methods, results, etc.).	
Text easy to read, understand and free of errors.	
Graphics clearly contribute to the overall presentation.	
Presenter	
Able to communicate in-depth technical information in an easy-to-understand manner.	
Able to interpret the data properly, and clearly answer questions related to project.	
Recognize limitations of the project's procedures.	
Courteous and professional.	

♦ 1 G ♦

Walking Speed Effect on the Forefoot Metatarsal Arch Stiffness

Allen Kempf, DPM'18, David Stapleton, BS, James Mahoney, DPM, Vassilios Vardaxis, PhD

Des Moines University, Des Moines, IA

Purpose: Walking speed has been shown to affect lower extremity kinematics and should be taken into account when considering pathologies of the leg. However, the effect of walking speed on the kinematics of the foot has not been investigated despite of its significant role as the ground to body interface during locomotion. Considering the impairments related to multitude pathologies of the forefoot, this study was designed to describe and contrast forefoot function during the stance phase as related to walking speed.

Methodology: The typical forefoot function of 20 healthy males was measured using an 8-camera motion capture system (at 120Hz) tracking six retro-reflective markers attached to head and base of first, second, and fifth metatarsal bones.

Procedures: Forefoot function was assessed by proximal and distal transverse arch height index (AHI), angle, and width. Subjects performed ten walking trials per condition (self-selected and fast speed). Forefoot typical function during the stance phase of gait (sub-phases/rockers) was evaluated, bilaterally.

Results: The participants walked at average velocities of 1.27 (±0.11) m/s and 1.70 (±0.20) m/s. Regardless of walking speed, the distal and proximal transverse angle and AHI changed significantly with stance phase progression. Forefoot rigidity also increased with walking speed during the second and third rockers of stance phase.

Discussion: The more flexible/compliant forefoot conformation during first rocker changed into a more rigid (stiffer) arrangement as the forefoot was lowered to the ground and received load. When seeking to understand the effect of pathology on foot function, the walking speed cannot be ignored.

♦ 2 G ♦

Evaluation of Off-Loading Effects in Traditional TCC, Commercial Roll-On TCC System (TCC-EZ®), and Post-Op Surgical Shoe: A Biomechanical Analysis of Plantar Foot Pressure Reduction in Treatment of Diabetic Plantar Foot Ulcers

Dixon Xu, DPM'17, Jordan Vogt, DPM'17, John Bennett, DPM, Vassilios Vardaxis, PhD

Des Moines University, College of Podiatric Medicine and Surgery, Des Moines, IA

Lower extremity amputation is a common complication associated with patients who have diabetes mellitus (DM). Up to 85% of nontraumatic lower extremity amputations in diabetic patients are preceded by plantar foot ulcerations. Studies suggest a correlation between the development of plantar foot ulcers in diabetic patients with excessive plantar foot pressure.

The presence of ankle equinus is a significant predisposing factor for increased plantar foot pressure and resulted ulceration in patients with diabetes. Patients with ankle equinus are at risk three times greater for presenting with elevated plantar pressure.

Therefore, reduction of the plantar foot pressure by means of utilizing off-loading devices is critical in wound care of diabetic foot ulcers. The Total Contact Cast (TCC) has been shown in literature to be an effective method to provide adequate plantar off-loading and to facilitate healing of plantar ulcers. However, there is no uniformly accepted protocol in preparation of the TCC, and various prefabricated commercial TCC models are also available on the market, further complicates the selection of an appropriate off-loading device.

Therefore, in this study we aim to evaluate the off-loading effects of the traditional TCC, commercial roll-on TCC system (TCC-EZ®), and the post-op surgical shoe. A biomechanical analysis of plantar foot pressure reduction will compare and contrast these different off-loading devices. The devices will be tested on a pathological group with unilateral or bilateral ankle equinus deformity, and compared to a control group which lacks ankle equinus or any prominent foot and ankle pathologies.

♦ 3 G ♦

Objective Determination of the Effects of Foot Position on Clinical Measurement of Ankle Joint Dorsiflexion

Paul Dayton, DPM, Mindi J. Feilmeier, DPM, **Kalani A. Parker, DPM'17, Riane T. Otti, DPM'18**

Des Moines University, College of Podiatric Medicine and Surgery, Des Moines, IA

Equinus, or tightness of the gastrocnemius and soleus muscle complex, is a common anatomic abnormality. The literature has shown a clear association between equinus and pathological compensation in the foot and it has been identified as the cause of a variety of foot and ankle disorders. Ankle joint dorsiflexion is commonly measured in clinical settings to make the diagnosis of equinus; however, there are many identified sources of error associated with this clinical measurement. In an effort to improve accuracy and reproducibility of ankle dorsiflexion measurement, we are evaluating ways to standardize the method of measurement. We will be measuring ankle joint dorsiflexion with the foot in a supinated, neutral and pronated position to identify effects on the clinical measurements on fifty subjects. Experienced clinicians will take passive ankle dorsiflexion measurements with a goniometer in these positions. We will also analyze if there is an effect of supination and pronation of the foot on actual tibia-talar movement in the sagittal plane radiographically. To do this, we will use a method previously described in the literature with two lines drawn on each lateral radiograph. The first line will be the stable line (Line A), which will be drawn from the posterior to anterior lip of the distal tibia. The second line (Line B) will be drawn from the along the inferior aspect of the talus at the surface of the subtalar joint. Data will be analyzed using repeated measures ANOVA and a post hoc paired t-test.

♦ 4 G ♦

The Role of Patient Expectation on Plantar Heel Pain Treatment Outcomes

[1]**Ellen Barton, DPM'18** and [1]Shane McClinton,, DPT, OCS, FAAOMPT

[1]Des Moines University, College of Podiatric Medicine and Surgery, Des Moines, IA
[2]Doctor of Physical Therapy Program, Des Moines University, Des Moines, IA

Patient treatment expectations impact clinical treatment outcomes, but this has not been studied in individuals with plantar heel pain (PHP). This preliminary study assessed the effect of patient expectations on PHP treatment outcomes. Patient expectations were recorded as part of randomized clinical trial comparing usual podiatric care and early physical therapy intervention for PHP. Expectations for PHP outcomes at 6 weeks and 6 months were measured at baseline using a modified global rating of change scale. Changes in levels of pain and function at 6 weeks and 6 months following initial treatment were compared between patients with high versus low expectations in addition to patients who met and did not meet baseline expectations. In addition, the influence of depression status, educational level, and achievement of expected outcome on treatment success was analyzed. Analysis revealed no difference in 6 week and 6 month pain and function scores between patients with high and low expectations ($p = .08 - .75$) and both groups demonstrated clinically meaningful improvements. Individuals who met their 6 week and 6 month expectations were 6.3 times (95%CI 1.834, 21.527; $p = .002$) and 12.27 times (95% CI 1.282, 117.445; $p = .01$) more likely to achieve treatment success, respectively. Depression status and educational level did not have a significant impact on treatment success ($p = .13-.83$). Patients who met their expectations were more likely to achieve treatment success which suggests that reasonable expectations should be discussed in the management of patients with PHP to increase chances of success.

♦ 5 G ♦

Effect of Simulated Pregnancy on Gait Parameters

Muna Omar, DPT'17, **Brittany McCall, DPT'16,** Kari Smith, DPT, Catherine Stevermer, MPT, PhD, GCS

Des Moines University, Department of Physical Therapy, Des Moines, IA

Pregnancy impacts a woman's physical body in many ways. Walking is a common daily task which can be affected by the physical changes associated with pregnancy. Gait velocity, step length and time in single support are examples of gait parameters that may change during pregnancy. The GAITRite™ system is an instrumented walkway that quantifies temporal and spatial parameters of walking. This system may be used to detect fluctuating gait parameters and to monitor progress in various clinical populations.

The purpose of this study was to evaluate the effect of simulated pregnancy on gait parameters using the GAITRite™ system. Eighteen healthy females (23±1 years of age) participated in this project. Participants walked across the GAITRite walkway in a normal condition and in a simulated pregnancy condition involving a 10.5-kg pregnancy vest. Participants performed 5 trials in each condition and trials were averaged. Paired t-tests were used to compare conditions with an alpha level of 0.05 to detect significance.

Results indicated a significant difference in step length ($P<0.01$), cadence ($P<0.01$), and single support percentage between conditions ($P<0.01$). No differences in gait velocity were identified between conditions. Project results are consistent with published literature on pregnant women regarding step length and single support percentage. Previous authors have reported a reduced gait velocity during pregnancy, whereas our results suggest healthy females in a simulated pregnancy condition compensate to maintain a consistent gait velocity by increasing cadence.

♦ 6 G ♦

Are Pain Ratings Influenced by Patient BMI and Type of Anesthesia Used for TKA?

Cameron S. Piechota, DPT'17, Julie Ronnebaum, MPT, DPT, GCS, Cynthia Utley, MPT, DPT

Introduction: Total knee arthroplasty (TKA) is surgical orthopedic procedure performed to increase functional mobility and relieve pain due to arthritis and degenerative joint disease. There is a strong correlation between a patient's body mass index (BMI) and the need for TKA. Although more than 90% of people who receive this procedure show significant improvement, TKA remains one of the most painful orthopedic surgeries. To control pain after this procedure a number of surgical anesthetics, or techniques, have been introduced. The most common pain regimens are nerve blocks and general anesthesia. Pain continues to limit the patient's function. Pain ratings are a subjective measure of personal discomfort and can be affected by personal perception, comorbidities, BMI, age, etc. The purpose of this study was to determine for patients who have had a TKA, does BMI affect their pain ratings while controlling for regional anesthetic techniques compared to general anesthesia. For our study, we categorized the anesthetic techniques into 3 categories: general anesthetics, femoral nerve blocks, and a combination of both femoral and sciatic nerve blocks.

Subjects: One hundred and four electronic chart reviews of patients who received a TKA at an area hospital were completed.

Materials/Methods: For this retrospective study, 104 out of 500 electronic chart reviews were completed for patients who received a TKA from May 2012 to June 2013. The subjects were categorized by type of surgical anesthesia used: femoral nerve black (FNB), combined femoral nerve and sciatic nerve block (CNB), and general anesthesia (GA), and the BMI category they fit into: underweight (UW), normal (NW), overweight (OW), obese (O), and morbidly obese (MO). Data was collected on the following variables: surgical anesthetic, BMI, pain ratings, age, sex, length of stay, and functional outcomes. The current study focused on surgical anesthetic, BMI, and pain ratings. The data was analyzed with SPSS version 22.

Results: The data revealed that on Day 1 the OB group with CNB reported the highest average pain ratings = 5.43±.59 (MO with CNB 4.85±.72 and OW with CNB 3.18±.53). Day 2, the highest pain ratings were from the OB group with CNB 4.93±.59 (MO with CNB reported 4.70±.97 and OW with CNB reported 4.3±.72). Day 3, the highest pain ratings were from OB group with GA 5.12 ±1.16 (MO with GA =2.33±1.20 and OW with GA = 3.25±.59).

Conclusions: The results of this study indicate that although there are differences in the pain ratings of the different groups stratified by BMI and type of analgesia technique used, they are statistically not significant. A larger sample size could have provided more conclusive data for all the categories.

Clinical Relevance: The data gathered from this study can be used as a basis for promoting personal health and wellness to improve patient outcomes post TKA. It can also be utilized by practitioners and patients in determining a preferred drug regimen for TKA.

Key Words: Total knee arthroplasty, BMI, pain ratings, regional aesthetic, general anesthetic

♦ 7 G ♦

Validity of Pain Scales for Children with Reduced Function Cerebral Palsy: A Systematic Review

Alicia Ring, DPT'16 and Jason E. Cook, DPT, PCS

Des Moines University, Des Moines, IA

Purpose: Peer-reviewed articles were evaluated to identify the validity of pediatric pain scales used for children with severe forms of cerebral palsy.

Methods: Databases used include *PsychINFO*, *MEDLINE,* CINAHL, and the top 100 articles in *Google Scholar.* The search was conducted within the years 1984 and 2014 using the terms 'cerebral palsy' in combination with 'pain measurement', 'pain assessment', and 'pain scales'. Self-reporting measurement of pain were excluded. A total of 1,343 articles were reviewed. A preliminary review of the articles was performed by 2 independent reviewers utilizing the abstracts of the articles. The inclusion criteria included articles that indicated participants under the age of 21 with a GMFCS level of III to V. Articles with non-descriptors of cerebral palsy were flagged for review. Articles were excluded if neuromuscular disabilities or CP was not specified. 29 articles remained. These article were evaluated for pain scale type, GMFCS level of the participating subjects, and methodology of validation of the pain scale. 3 articles were identified as being studies that evaluated the validity of the pain measurement scales for children with cerebral palsy with a GMFCS level III-V.

Results: Within the 3 articles concurrent validity, extreme group validity, criterion validity, construct validity, divergent validity, and convergent validity were utilized to evaluate either the Pain Evaluation Scale or the Pediatric Pain Profile.

Conclusion: Evaluating validity in pain scales for children with Cerebral Palsy GMFCS level III-V can be challenging because of the limitations in communication, cognition and motor presentation of the children.

♦ 8 G ♦

Relationship Between Sports Specialization Age and Injury in Young Athletes

[1]**Jacqueline Pasulka, DO'19,** [2]Cynthia LaBella, MD, [3]Lara Dugas, PhD, MPH, [3,4]Neeru Jayanthi, MD

[1]Des Moines University College of Osteopathic Medicine, Des Moines, IA
[2]Northwestern University's Feinberg School of Medicine, Chicago, IL
[3]Loyola University Medical Center, Chicago IL
[4]Emory University School of Medicine, Atlanta, GA

Purpose: To determine whether the age at which a young athlete quits other sports to specialize in one primary sport affects their risk for injury and whether degree of sport specialization varies with sport type.

Methods: In this case-control study we recruited athletes (aged 8-18 years) from sports medicine clinics and primary care clinics. Participants completed a survey reporting sport type, degree of sports specialization, and if applicable, age at which they quit other sports to focus training on one primary sport (sports specialization age). Injured athletes completed an additional survey reporting injury type and sports limitations.

Results: Of the 1,190 athletes who completed the study, 51% (603) were male, and 38% (454) reported they had quit other sports to focus training in one primary sport. For these specialized athletes, the injured group contained a greater proportion whose sports specialization age was <12 years than the uninjured group (17.40% vs 14.13%, $p<0.01$). Participants whose primary sports were individual sports were more likely to be specialized (31.61% vs 23.44%, $p<0.01$), and more likely have overuse injuries (51.14% vs 47.14%, $p<0.05$) and serious overuse injuries (17.81% vs 13.43%, $p<0.05$) than those whose primary sport was a team sport.

Conclusion: Young athletes participating in individual sports report a higher degree of sports specialization, and develop a higher rate of serious overuse injuries than those participating in team sports.

♦ 9 R ♦

Creating a Cohesive Approach to Research

Kristin Gisselman, DO

Mercy Medical Center-Family Medicine Residency, Des Moines, IA

Problem Statement: Create a useful handbook and guide that can help Family Practice Residents better understand the requirements expected of them regarding research.

Background: In the past years, family practices residencies have been increasing their research requirements. The AAFBM has also instituted SAM modules and QI projects to help residents gain a better understanding of initiating, completing and analyzing research. In recent years, this requirement has grown. Previously family medicine residents have not had to complete research usually due to the time requirement. Family Medicine residents have unique schedules as they are pulled in multiple directions including Obstetrics, Pediatrics, Clinic and Inpatient medicine.

Incorporating research into a Family Medicine Residency can be challenging. Multiple variables must be weighed such as time commitment, financial restrictions, and access to materials. Many Residency programs provide clear guidelines as to what is expected of their residents. The AAFBM also requires residents to complete their requirements before registration of final boards.

Current State: Mercy Graduate Medical Education has now added an extra Quality Improvement Project for second year residents to complete. Much confusion has existed as there is not a clear and concise resource for residents to understand what is expected out of them from Mercy, ACGME, and AABFM.

Establishing Measures: An initial survey will be completed by all Mercy Family Medicine Residents to better gauge the resident's knowledge of what is expected of them regarding research. After the research handbook has been created, residents will be a given a post survey to see if the handbook has alleviated any misinformation about the requirements.

Selecting Changes: I will be looking at creating a guide that can be added up each year as requirements change. It will be geared toward the Mercy Family Medicine Residency. A Morning reports session will also be hosted to explain the handbook. Future suggestions will also exist to possibly try to incorporate a 2 week elective for residents to complete in second and third year to help with the research tasks.

♦ 10 G ♦

Investigation of Student Attitudes and Understanding in General Chemistry

Rachel E. Egdorf, DPM'19, Hannah M. Zidon, Roslyn M. Theisen, PhD

Department of Chemistry, University of Wisconsin – Eau Claire, Eau Claire, WI

Incorporating inquiry-based laboratory experiments in large introductory general chemistry courses is often challenging in terms of cost, institutional capacity, and grading time for the instructor. This project aims to test the hypothesis that there is a measureable difference in understanding of, and attitude toward chemistry when just one inquiry-based laboratory experiment is substituted for a traditional laboratory experiment in a semester-long sequence of ten total experiments. Participants were enrolled in first-semester General Chemistry at the University of Wisconsin-Eau Claire, a public, undergraduate-only institution. In this study, control- and inquiry-group students' attitudes and understanding were assessed by several quantitative measures. These included 1) a valid and reliable attitude survey administered before and after the treatment laboratory experiment, 2) a post-treatment conceptual quiz, and 3) calculation-based stoichiometry questions on a midterm exam and the cumulative final exam. All measures were evaluated and statistically analyzed. One significant finding was that attitude scores statistically increased from the beginning to the end of the semester for both groups, more so for the inquiry group. Other statistical analysis revealed no significant differences between the two groups in terms of comprehension or attitude.

♦ 11 G ♦

The Use of Clinical Training Student Self-Assessment as a Tool for Curriculum Evaluation

R. Tim Yoho, DPM, MS, FACFAS, Vassilios Vardaxis, PhD, **Kelsey Millonig, DPM'17**

Student self-assessment is a common practice in medical education. It is reported to offer a number of benefits including enhancement of student performance, critical awareness and reflection on learning. Little information exists as to the use of student self-assessment as a tool to evaluate curriculum. The purpose of this study was to examine the use of student self-assessment in evaluating curriculum.

Third-year podiatric students from the classes of 2012-2014 completed a self-assessment of their performance for each of five domains (Professionalism, Medicine, Radiology, Surgery and Biomechanics). The assessment was completed after students completed the first twelve weeks of their third-year clinical rotations (PRE) and again at the conclusion of the third-year (POST). Pooled data for each of the PRE and POST assessment domains was evaluated.

The PRE assessment results identified greater student confidence in the performance of the Professionalism and Podiatric Medicine domains compared to the other three domains. For the POST assessment, in all domains, students demonstrated a significant increase in their perception of performance compared to the PRE assessment results. The POST assessment results continued to demonstrate the greatest confidence in performing the Professionalism domain followed by the Podiatric Medicine, Radiology, Surgery and Biomechanics.

Self-assessment has been recognized as a necessary skill to lifelong learning and has been extensively integrated into health sciences education. This study expands the role of student self-assessment as a tool to evaluate curriculum. The results of this study may help to identify opportunities in the pre-clinical and clinical curriculum to enhance student clinical learning.

♦ 12 G ♦

Policy Framework for Supporting Intrinsic Capacity in the Ageing Population

[1]**Kelsey Millonig, DPM/MPH'17** and [2]Islene Araujo de Carvalho MD, MPH

[1]Des Moines University, Des Moines, IA
[2]World Health Organization Headquarters Department of Ageing and Life Course, Geneva, Switzerland

Background: Public health policy must re-evaluate how the health of the ageing population is measured. Rather than evaluating health by specific diseases, health should be evaluated by measuring an ageing person's ability to do what is of value to them termed functional ability. Both the environment and an individual's intrinsic capacity contribute to functional ability. Intrinsic capacity encompasses the composite of all the physical and mental capacities that an individual can draw on at any point in time. Healthy ageing demands a comprehensive restructuring of the health system with the goal to optimize trajectories for intrinsic capacity.

Methods: This review presents evidence for interventions aimed at enhancing intrinsic capacity among the ageing population, including studies and policy interventions from policy research conducted during an internship with the World Health Organization (WHO). Further evidence was obtained from the World Health Report on Ageing to be published by the WHO.

Results: Hallmarks of key public health policy interventions to maintain intrinsic capacity include creating clinical guidelines to optimize trajectories of intrinsic capacity and update existing guidelines to link to capacity, establishing performance monitoring rewards and financing mechanisms that encourage care that optimize capacity, and developing information systems to collect, analyze, and report data on intrinsic capacity.

Conclusions: Evidence suggests that focusing on optimizing trajectories for intrinsic capacity is more effective than prioritizing management of specific chronic disease. For example, by optimizing the trajectory for intrinsic capacity admission rates to the hospital and aged care institutions are reduced. These public health interventions will support the ageing population to reach maximal intrinsic capacity trajectories.

♦ 13 G ♦

Novel Predictors of Hospital Length of Stay and Number of Hospitalizations in the Elderly Population

Hannah Stonewall, PharmD'16 and Erin Ulrich, PhD

Drake University, Des Moines, IA

Background: Studies have shown there are significant costs related to a prolonged hospital stay. Past studies in this area have investigated common predictors of increased length of hospital stay. However, these predictors have not been investigated within a large, national data set.

Objective: The objective of this study is to determine novel predictors of hospital length of stay and number of hospitalizations in a large, nationally representative sample size.

Design: This study utilized an analysis of data from the 2012 Health and Retirement Study (HRS) survey data set. The subjects in the study are a representative sample of Americans over the age of 50.

Measurements: Number of times spent overnight in the hospital and number of nights spent in the hospital in the past two years.

Results: Number of times hospitalized in the past two years was significantly different between educational groups. Those who were current smokers, Medicare enrollees, or those who did not receive the flu or pneumonia vaccine were more likely to be have an increased number of hospitalizations. Number of conditions and children living within ten miles was also associated with increased length of stay.

Conclusion: Novel predictors determined from this study include: education level, insurance type, comorbid conditions, preventative vaccines, smoking status, and children within 10 miles of the patient. By further understanding what factors impact the need for increased hospital care, steps may be taken by healthcare providers to combat these factors to prevent avoidable hospitalizations or increased length of stay in the elderly.

♦ 14 G ♦

Long-Acting Reversible Contraceptive Healthcare Provider Pilot Study

Kristine Anderson, MPH'17 and Rachel Reimer, PhD

Des Moines University, College of Health Sciences, Master of Public Health Department, Des Moines, IA

When compared to other developed countries, the unintended pregnancy rate in the United States is significantly higher. A disproportional percentage of these unintended pregnancies are experienced by adolescents. In the United States, it is estimated that 80% of all pregnancies in 15-19 year-old women are unintended. The public cost associated with adolescent pregnancies is enormous. Adolescent childbearing in the United States cost taxpayers (federal, state, and local) at least $9.4 billion in 2010.

Long-acting reversible contraceptive (LARC) options have shown very low failure rates, but are some of the least commonly used methods of contraception. Access of LARCs for adolescents must come through healthcare provider identification, recommendation, and utilization. The focus of this research is to explore primary care healthcare providers' experiences, attitudes, and beliefs with recommending and providing LARCs to adolescents.

Primary care healthcare providers within a 150 mile radius of zip code 50312 (Des Moines, IA) completed a voluntary electronic survey to generate data on the ability to insert LARCs, perceived efficacy of LARCs, and assess knowledge of adolescent LARC recommendations. Validity of this pilot survey was conducted and data analysis for this research included demographic frequencies and between-group examinations to determine if provider-level variables impact adolescent LARC beliefs.

Through this research, barriers to access can be identified and interventions can be developed to increase the percentages of primary care healthcare providers who recommend and insert LARCs to this high risk population.

♦ 15 UG ♦

Analysis of Water Sources and Filtration Methods in Rural and Urban Uganda

[1]Hayley LeBlanc, **[1]Megan Lindmark,** [1]Ali Hassan, [2]Augusta Weide

[1]College of Arts and Sciences, Drake University, Des Moines, IA
[2]Drake University, College of Business and Public Administration, Des Moines, IA

Over 663 million people, worldwide, do not have access to clean water ("Global WASH Fast Facts" 2015). With this limitation comes disease, poverty, and loss of educational opportunities. Sub-Saharan Africa, *is a region of the world* that is particularly impacted by this water crisis, and more specifically Uganda continues to have ongoing issues with limited access to water. Following preliminary surveys of water filtration systems in Uganda, our team returned in August 2015 to conduct further water tests and surveys. Water tests were conducted in urban and rural setting including schools and a health centre. The aim of the project was to examine the perception of water cleanliness and safety throughout Uganda, while researching potential system solutions. To test purity of the water, Coliplate tests were used. The plate's wells changed color in response to presence of coliform bacteria and fluoresced if *Escherichia coli* was present. Additionally, interviews were conducted to determine the sources and any filtration systems. The water from the village borehole didn't show any evidence of coliform bacteria, while the sample from an urban secondary school showed the most contamination by high levels of coliform bacteria. Another urban secondary school noted that their water from the boreholes may be contaminated, and the water sample from this school showed the presence of coliform bacteria. The perception of how clean water was at each source was not always correlated to the coliform plate test of the water. Further research will be conducted to evaluate more specifically the bacteria found at these locations.

Global WASH Fast Facts. (2015, June 5). Retrieved November 9, 2015, from http://www.cdc.gov/healthywater/global/wash_statistics.html

♦ 16 HS ♦

Teen Tanning Study: Waukee High School Students' Understanding of the Benefits and Hazards of Tanning Practices

[1]Anna Shapiro, [1]Rachel Shapiro, [1]Faith Wilson, [1]Amy Patel, [2]Emilie Hulse, [2]Connor Littlefield, [2]Maddie Green, [2]Paul Akpan, [2]Holly Showalter, PhD, [3]Pramod Mahajan, PhD

[1]Waukee APEX, Waukee, IA
[2]Waukee High School, Waukee, IA
[3]Drake University, College of Pharmacy and Health Sciences, Des Moines, IA

Ultraviolet (UV) radiation from direct sunlight or from the tanning beds causes skin cancer in humans. Recent studies also indicate that exposure to UV rays in early life contributes to skin cancer in adulthood. Therefore, educating young adults about the ill effects of UV radiation on human health would help reduce the incidence of skin cancer. We seek to assess (1) knowledge of Des Moines metro area teenagers about the effects of UV radiation on human health and (2) their tanning practices. Such information would be useful in designing prevention practices and policies, which in turn will lead to better health outcomes. This poster describes results of the first phase of our study. An electronic survey of 143 Waukee School District students conducted during Fall of 2014 indicates a majority of the survey participants are aware of the effects of ultraviolet radiation on human skin. However, almost ~ 61 % of study participants think tanning makes them feel attractive, female respondents (~ 60%) outnumbering male respondents (~40%) in this category. Participants listed radio, television, social media and Internet as their major sources of advertisement promoting tanning. Of the respondents who reported using tanning beds, over 60 % said they were influenced by friends, ~ 20 % by their family members, and ~ 20% by their celebrity role models. These and other results will be used to guide future studies as we expand our project to other schools in the Des Moines Metro area.

♦ 17 G ♦

Age-Related Swallowing Deficits

[1,2]Ben Becker, DO'18, [2]John Russel, [2]Nadine Connor

[1,2]Des Moines University, Des Moines, IA
[2]Department of Surgery, Division of Otolaryngology-Head and Neck Surgery, University of Wisconsin, Madison, WI

Objective: Tongue strength, timing, and coordination deficits may underlie age-related swallowing function. Retrusive tongue actions are likely important in retrograde bolus transport. However, age-related changes in retrusive tongue muscle contractile properties have not been identified in animal studies. Because previous studies employed whole hypoglossal nerve stimulation that activated both protrusive and retrusive tongue muscles, co-contraction may have masked retrusive muscle force decrements. The hypotheses of this study were: (1) retrusive tongue muscle contraction forces would be diminished and temporal characteristics prolonged in old rats when lateral nerves were selectively activated, and (2) greater muscle contractile forces with selective lateral branch stimulation would be found relative to whole hypoglossal nerve stimulation.

Design: Nineteen Fischer 344/Brown Norway rats (9 old, 10 young adult) underwent tongue muscle contractile property recording elicited by: (1) bilateral whole hypoglossal nerve stimulation, and (2) selective lateral branch stimulation. Twitch contraction time (CT), half-decay time, maximal twitch and tetanic forces, and a fatigue index were measured.

Results: For whole nerve stimulation, CT was significantly longer in the old group. No significant age group differences were found with selective lateral nerve stimulation. Significantly reduced twitch forces (old group only), increased tetanic forces and significantly less fatigue were found with selective lateral nerve stimulation than with whole hypoglossal stimulation.

Conclusions: Retrusive tongue forces are not impaired in old rats. Deficits observed in swallowing with aging may be due to other factors such as inadequate bolus propulsive forces, mediated by protrusive tongue muscles, or timing/coordination of muscle actions.

♦ 18 UG ♦

Does Maternal Genistein Affect Non-Spatial Hippocampal-Dependent Memory Tasks?

Amber J. Amick, Cory B. Langreck, Sarah A. Lothspeich, Hayley R. LeBlanc, Craige C. Wrenn

Drake University, Harris Research Endowment, College of Pharmacy and Health Sciences, Des Moines, IA

Endocrine disruptors can impact brain functions such as memory and learning. One such endocrine disruptor, genistein, is a soy-derived phytoestrogen that binds estradiol receptors and therefore may alter brain development in a way that impacts behavior in adulthood. Previous work in our laboratory showed that maternal exposure to genistein in male rats resulted in impaired learning in a hippocampal-dependent spatial task, the Morris Water Maze. In the current study, we asked whether the effect of maternal exposure to genistein extends to non-spatial, hippocampal-dependent memory tasks such as the social transmission of food preference (STFP) and trace fear conditioning. STFP, an olfactory memory task, relies on a rat's ability to use memory for a socially cued scent to influence food choice. Male rats were exposed to genistein by placing pregnant dams on a diet of phytoestrogen-containing food (5mg/kg) throughout gestation and lactation. After weaning, male rats were placed on a phytoestrogen-free diet and were tested in STFP at approximately 2-3 months of age. Genistein-exposed rats showed no impairment in developing a socially transmitted food preference. At 5-6 months of age the rats were tested in trace fear conditioning, which requires learning the association between a tone and a temporally separated mild footshock. There was no effect on trace fear conditioning in the genistein-exposed males as indicated by freezing behavior during tone presentation. The present findings show that the behavioral effects of maternal exposure to genistein do not extend to non-spatial hippocampal tasks.

♦ 19 G ♦

Hemorrhagic Macules on the Palms and Soles

Emily E. Boes, DO'17, Hobart W. Walling, MD, PhD, Brian L. Swick, MD, Zijian Zheng, BS

The University of Iowa, Iowa City, IA

In its classic form, Darier's disease, otherwise known Darier-White disease or keratosis follicularis, is an inherited autosomal dominant disease that presents with red-brown, malodorous, warty keratotic papules in a seborrheic distribution on the trunk and scalp. Other characteristic findings include punctate keratoses of the palms and soles, keratotic warty papules on the dorsal hands (acrokeratosis verruciformis-like lesions), and nail changes consisting of thin brittle nails, V-shaped notching of the free edge of the nail, longitudinal alternating red and white lines, and subungual hyperkeratosis. These acral changes are quite common, present in 96% of patients. In contrast, hemorrhagic lesions in Darier's disease, first described in 1964 Jones et al., are uncommon, present in only 6% of patients. The pathognomonic hemorrhagic lesions of Darier's disease classically appear as jagged irregularly-shaped red-to-black macules that are 2-8 mm in diameter. These macules are typically preceded by trauma, arise on palmar and plantar surfaces, and usually appear without initial blistering. Early lesions are reddish, while older lesions take on a black coloration, resembling India ink or silver nitrate stains, before resolving in approximately three weeks. The pigmentation in these lesions is attributable to erythrocytes that reside within the epidermis. We report a case of Darier's disease, and compare its location, pathogenesis, histopathology, and associated systemic disease to that of its classic form.

♦ 20 G ♦

Efficacy of Silver Products on Diabetic Foot Ulcers: A Systematic Review

Audris Fan, DPM'17 and Katherine Frush, DPM

Des Moines University, College of Podiatric Medicine and Surgery, Des Moines, IA

Silver agents have gained popularity for treatment of diabetic ulcers to reduce bioburden and aid in wound healing. The aim of our study was to evaluate the efficacy of silver agents on diabetic foot ulcers. We underwent a systematic review of Pubmed, Scopus, and Cochrane Library Databases using the search term "silver" in combination with "diabetic OR diabetes" and "wound* OR ulcer*" to identify literature evaluating the efficacy of silver-impregnated dressings or topical silver creams on diabetic foot ulcers. Included studies evaluated the effectiveness of a silver agent using an objective measure of healing, determined here to be either complete wound closure or a reduction in surface area of the wound. Five studies were identified, 4 randomized and 1 observational study, with a total of 172 diabetic ulcers treated with a silver agent, and 133 diabetic ulcers treated with other products. The duration of the studies was between 4-14 weeks. Silver agents showed wound reduction of 54.7% - 89% and complete healing of 14.8%-52% compared to other wound treatment/control wound reduction of 23.9%-72.5% and complete healing of 16%-40% respectively. The results of this systematic review show that silver agents may aid in greater wound reduction and healing than other wound treatments.

♦ 21 UG ♦

Oral L-Tyrosine Supplementation Augments Vasoconstriction to Whole Body Cooling in Older Adults

[2]Kevin Smaller, [3]Raquel Relph, [1]James A. Lang, PhD

[1]Des Moines University, Department of Physical Therapy, Des Moines, IA
[2]Drake University, Department of Neuroscience, Des Moines, IA
[3]Grand View University, Department of Biology, Des Moines, IA

Healthy older adults consistently exhibit a blunted cutaneous adrenergic vasoconstriction (VC) response to cold exposure, which increases the susceptibility to rapid heat loss and hypothermia. We hypothesized that oral supplementation of L-tyrosine, the primary substrate for catecholamine biosynthesis, would augment reflex cutaneous VC to gradual whole-body cooling (T_{sk}=30.5ºC) in older adults. Eleven young (18-30 yrs) and twelve older (60-85 yrs) participants completed a randomized, double-blinded, placebo-controlled, cross-over experiment consisting of two visits separated by >3 days. Upon arrival to the lab, participants ingested either L-tyrosine (150 mg/kg) or

placebo. An hour post-consumption, whole-body cooling commenced, decreasing skin temperature from 34 to 30.5 ºC over a 30 minute period. Laser Doppler flux (LDF) was measured at the ventral forearm and cutaneous vascular conductance (CVC) was calculated as CVC= LDF/mean arterial pressure and expressed as a percent change from baseline (%ΔCVC). The VC response to whole body cooling was blunted in older adults (Placebo: Y = 27±1, O = 21±1 %ΔCVC), this was augmented with tyrosine supplementation (Tyrosine: Y = 40±2, O = 35±2 %ΔCVC; $P < 0.05$). Moreover, the increased VC response coincided with altered perception, assessed by a questionnaire using semantic differential scales, of the cold stress in some individuals. These results indicate that L-tyrosine supplementation restores the VC response to cooling in older adults and may improve tolerance to cold exposure. This suggests that L-tyrosine may be a limiting factor in vasoconstricting aged skin.

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♦ 22 G ♦

Contribution of Angiotensin II to Cutaneous Vasoconstriction is Dependent on Age and Sex

Kelsey E. Kolb, DPT'16 and James A. Lang, PhD

Des Moines University, Department of Physical Therapy

Angiotensin II type I receptor (AT_1R) stimulation elicits vasoconstriction (VC) that may be occurring through the activation of a pathogenic vascular pathway such as Rho kinase (ROCK). We hypothesize that the reflex cutaneous VC response to whole-body cooling (T_{sk}=30.5 ºC) is more reliant on AT_1R activation in older humans. Two microdialysis (MD) fibers were placed in the forearm skin of 10 young (Y) (24±1 years) and 10 older (O) (70±2 years) individuals for infusion of 1) lactated Ringer's solution (control) and 2) AT_1R blockade with 2 µg/L losartan. Laser Doppler flux (LDF) was measured over each microdialysis site and cutaneous vascular conductance (CVC) was calculated as CVC = LDF/mean arterial pressure and expressed as a percent change from baseline (%ΔCVC). In older individuals VC response to whole-body cooling was blunted (Y= -34 ± 2, O= -17 ± 3 %ΔCVC) and this was further attenuated at the losartan site (Y= -34 ± 3, O= -9 ± 3 %ΔCVC; $P < 0.05$). Unexpectedly, the VC response to an exogenous 10 µM dose of angiotensin II was augmented in older woman (43±5 %ΔCVC) compared to older men (24±5 %ΔCVC) and young (27±3 %ΔCVC, $P < 0.05$). This response was completely blocked in sites pretreated with losartan or with fasudil, a ROCK antagonist. These data indicate the angiotensin II contributes to the reflex VC response in aged but not young skin. Not only does this appear to be mediated by Rho kinase but the sensitivity of this response is uniquely elevated in older women.

Funding: DMU IOER Grant 05-13-05

♦ 23 G ♦

Functional Effect of Multi-Site Interactions between Calmodulin and the Human Angiotensin II Receptor Type 1A

Robert Clements, MBS'19, Kevin Ehlers, Mark VerMeer, Quang-Kim Tran, PhD, MD

Des Moines University, College of Osteopathic Medicine, Department of Physiology and Pharmacology, Des Moines, IA

The angiotensin II receptor type 1A ($AT_{1A}R$) plays an important role in regulating blood pressure and plasma volume. Calmodulin (CaM) is a ubiquitous transducer of intracellular Ca^{2+} signals. Our previous studies have identified CaM-binding to three distinct submembrane domains (SMDs) of $AT_{1A}R$, spanning a.a. 125-141, 215-242, and 309-327. However, the functional impact of these interactions remains unclear. We have generated new mutations on each of the three SMDs and introduced them into FRET biosensor format, $BSAT_{1A}R_{x\text{-}mut}$, where x denotes the a.a. numbering of a CaM-binding domain. Through titrating purified CaM under Ca^{2+} saturating conditions, we compared mutant and wild-type biosensor responses. Analysis of $BSAT_{1A}R_{125\text{-}141\text{-}mut}$, $BSAT_{1A}R_{215\text{-}242\text{-}mut}$, and $BSAT_{1A}R_{309\text{-}327\text{-}mut}$ revealed dramatic reductions in CaM binding affinities, K_d values increasing from 13.9 ± 0.39, 0.354 ± 0.05, 0.516 ± 0.01 µM to 318.11 ± 73.02, 4.52 ± 0.25, 6.60 ± 0.18 µM, respectively. The Ca^{2+} sensitivities of the mutant domains also decreased, with EC50 (Ca^{2+}) values increasing from 4.10 ± 0.11, 0.151 ± 0.006, and 1.26 ± 0.09 µM to 17.59 ± 0.78, 1.49 ± 0.03, and 2.34 ± 0.12 µM, respectively. Expression of full-length $AT_{1A}R_{125\text{-}141mut}$ in HEK 293 cells reduced AngII-induced MAPK activation, consistent with virtual abolition of AngII-induced MAPK activation in smooth muscle cells pretreated with the CaM antagonist W-7. On the other hand, $AT_{1A}R_{215\text{-}242mut}$ appeared to increase this response while $AT_{1A}R_{309\text{-}327mut}$ had no effect. This data indicates complex links between CaM-$AT_{1A}R$ interactions and the effects of AngII on various cardiovascular functions, which might hold significant therapeutic impact.

♦ 24 ♦

An Essential Role of Calmodulin Binding in the Function of the α-1A Adrenergic Receptor

Briana Gebert-Oberle, Quang-Kim Tran, PhD, MD, Sarah Clayton, PhD, Lara Terry, Mark VerMeer

Des Moines University, College of Osteopathic Medicine, Department of Physiology and Pharmacology, Des Moines, IA

The α_1 adrenergic receptor type 1A (α_{1A}-AR) plays crucial roles in the control of adrenergic functions. Calmodulin (CaM) is the ubiquitous transducer of intracellular Ca^{2+} signals. Here we show a novel physical and functional interaction between CaM and α_{1A}-AR. α_{1A}-AR and CaM coimmunoprecipitate in primary vascular smooth muscle cells and cardiac tissue in non-stimulated conditions. Hearts from ovariectomized rats showed increased interaction between α_{1A}-AR and CaM, changes that were reduced by post-ovariectomy estrogen administration. Novel FRET-based biosensors revealed direct interaction between CaM and the juxtamembranous segment of the fourth submembrane domain of α_{1A}-AR ($SMD4_{JM}$, a.a. 333-361), a domain that encompasses the nuclear localization signal of α_{1A}-AR (NLS, a.a. 333-351). Characterization of affinity and Ca^{2+} sensitivity for the interactions with CaM showed that the NLS itself interacts with CaM, but with significantly lower affinity and Ca^{2+} sensitivity compared to the $SMD4_{JM}$, suggesting that the entire $SMD4_{JM}$ is required for full interaction with CaM. K354Q and L357A substitutions in the non-NLS segment reduced CaM binding affinity of the $SMD4_{JM}$ by 3-fold, but completely converted α_{1A}-AR from a membrane targeted receptor to an intracellular receptor. These changes are also associated with reduced α_{1A}-AR-mediated ERK1/2 phosphorylation and total Ca^{2+} signals. Similar changes are observed with substitutions within the NLS, including F337A, R342Q, and R349Q. The results demonstrate an essential role for CaM binding to the $SMD4_{JM}$ in the subcellular localization and function of α_{1A}-AR and indicate a role for CaM in the control of adrenergic functions.

♦ 25 G ♦

Association Between the β -1 Adrenergic Receptor and the G Protein-Coupled Estrogen Receptor

Vahe Matnishian, MBS'16, Matt Boese, Briana Gebert-Oberle, Quang-Kim Tran, PhD, MD

Des Moines University, College of Osteopathic Medicine, Department of Physiology and Pharmacology, Des Moines, IA

Estrogen has been known to confer cardioprotection to women. The novel G protein-coupled estrogen receptor (GPER/GPR30) has been demonstrated to have numerous effects in the cardiovascular system; however, its role in cardioprotection is not fully understood. The beta1-adrenergic receptor (β1AR) is essential in adrenergic responses in the heart and other organ tissues. We have begun to examine possible physical and functional interactions between these two important receptors. A commercial antibody recognizing the C terminus of β_1AR was initially verified in cardiac tissue using a corresponding blocking peptide and species-matched non-immune IgG. Using this and previously verified antibody for GPER/GPR30, we observed reciprocal co-immunoprecipitation between GPER/GPR30 and β1AR in ventricular tissue. Rat H9C2 cardiomyocytes, verified to express cardiac troponin T, also demonstrated association of the two receptors. Heterologously expressed, fluorescent tagged β_1AR and GPER/GPR30 showed similar PM and intracellular distribution in HEK 293 cells. These results suggest potential physical interactions between β_1AR and GPER/GPR30.

♦ 26 G ♦

Adenosine Receptor Activation Blocks Dopamine-Induced Natriuresis

[1]Samuel L. Lampe, DO'18, [3]Angela Song, [1]Liran BenDor, DO'18, [1]John E. Norgaard, [1,2]Victor Babich, PhD, [1]Francesca Di Sole, PhD

[1]Department of Physiology and Pharmacology, Des Moines University, Des Moines, IA
[2]Department of Medicine, University of Maryland School of Medicine, Baltimore, MD
[3]Columbia University in the City of New York, New York, NY

The neurotransmitter dopamine is a potent natriuretic paracrine/autocrine hormone and its action is central for the maintenance of mammalian Na^+ and fluid homeostasis. Nephrogenic dopamine induces natriuresis mainly via inhibition of the activity of a major player in the regulation of renal Na^+ and fluid re-absorption, the Na^+/H^+ exchanger-3

(NHE3). Interestingly, locally produced adenosine increases renal Na^+ and fluid reabsorption via an action on NHE3 activity. Adenosine and dopamine receptors are known to crosstalk in the brain by receptor heteromerization. However, little is known regarding crosstalk of adenosine and dopamine receptors in the kidney to mediate the shift from a state where Na^+ and fluid are eliminated (natriuresis) to a Na^+ and fluid reclaiming state (antinatriuresis). This study investigates whether adenosine affects the ability of dopamine to act as a natriuretic hormone. NHE3 activity was determined in renal epithelial cells by spectrofluorometry. NHE3 activity was inhibited (-40%) by dopamine treatment (10^{-5} M, 30 minutes), while it was activated (+50%) by acute [N^6-cyclopentyladenosine (CPA), 10^{-9} M, 30 minutes] or not changed by chronic (CPA, 10^{-9} M, 24 hours) adenosine receptor activation. Dopamine inhibition of NHE3 activity was blocked by both acute and chronic activation of adenosine receptors. These findings suggest that adenosine and dopamine receptors cooperatively regulate renal Na^+ transport. Elucidating the intricacies of the interaction among these receptors will help understanding the regulation of renal Na^+ transport and will aid determining how aberrant control of these opposing systems might lead to salt retention and, subsequently, hypertension.

♦ 27 G ♦

Investigation of the Role of Complement Component C1q in the Engulfment of Cancer Cells

Emily M. Smith, MBS'18 and Suzanne S. Bohlson, PhD

Des Moines University, Department of Microbiology and Immunology, Des Moines, IA

Cancer is due, in part, to failure of the innate immune system to detect transformed cells. Cancer cells are unique and have acquired cell surface markers characteristic of live and apoptotic cells. C1q is an innate immune effector molecule that is required for engulfment of apoptotic cells, but its role in identification and clearance of cancer cells by phagocytes is unknown. Various models composed of macrophages and cancer cells were used to demonstrate that C1q enhances engulfment of cancer cells. Our lab previously demonstrated that C1q upregulated expression of Mer tyrosine kinase and its ligand Gas6 to facilitate clearance of apoptotic cells. Mer deficient mice failed to respond to C1q with enhanced engulfment of cancer cells, suggesting residual apoptotic cells in cancer cell preparations may contribute to C1q-dependent engulfment. Future experiments will investigate the contribution of apoptotic cells to the observed C1q-dependent engulfment of cancer cells.

♦ 28 G ♦

A Potential Role for Green Tea as a Radiation Sensitizer for Prostate Cancer

[1]**Andrew C. Schroeder, DO'18**, [2]Ziwen Zhu, [2]Qian Bai, [2]Tylor W. Ball, [2]Haiqing Yu, [1]Kristoffer T. Davidson, [2]Devon N. Cruzan, [2]Colin C. Dolan, [2]Jacob E. Lee, [2]Dylan R. Newcomer, [2]Kyla L. Szemplinski, [1]Jack W. Lin, [1]Adam Ebel, [1]Julianne Abrigo, [2]Mark R. Wakefield, [1, 2]Yujiang Fang, PhD

[1]Des Moines University College of Osteopathic Medicine, Department of Microbiology, Immunology, and Pathology, Des Moines, IA
[2]University of Missouri School of Medicine, Department of Surgery, Columbia, MO

Background: Prostate cancer (PCa) is the most common non-cutaneous cancer in the United States. It is often treated, in part, with radiation therapy (RT). We lack safe and effective radiosensitizers to enhance the effectiveness of RT in the treatment of PCa. Green tea extract (GT) has antitumor growth effects on many cancers including PCa. We previously showed that resveratrol enhances RT sensitivity in PCa. This study was designed to investigate if GT could be used as a radiosensitizer for PCa and its possible molecular mechanisms.

Methods: Clonogenic assay, PCNA staining, Quick Cell Proliferation assay, TUNEL staining and caspase-3 activity assay were used to assess proliferation and apoptosis in PCa DU145 cells. RT-PCR and IHC were used to investigate the possible molecular mechanisms.

Results: The percentage of colonies, PCNA staining intensity, and the optical density value of DU145 cells were decreased (RT/GT vs. RT). TUNEL + cells and the relative caspase-3 activity were increased (RT/GT vs. RT). Compared to RT, the anti-proliferative effect of RT/GT correlated with increased expression of anti-proliferative molecule p16. Compared to RT, the pro-apoptotic effect of RT/GT correlated with decreased expression of the anti-apoptotic molecule Bcl-2.

Conclusions: GT enhances RT sensitivity of DU145 by inhibiting proliferation and promoting apoptosis. These data extend our previous study on resveratrol as a radiosensitizer for PCa and, in addition to the literature supporting green tea localization to prostate tissue, highlight the potential role for green tea as a radiatiosensitizer for PCa.

♦ 29 R ♦

Impact of Resident Involvement in Whipple Procedures: An Analysis of 7,605 Cases

Krista L. Haines, DO, C. D. Goldman, J. Franko

Mercy Medical Center, Surgery, Des Moines, IA

Introduction: Recent decades have shown a substantial reduction in mortality and morbidity of Whipple procedures. Perioperative outcomes are thought to be volume-and surgeon-related. Therefore, using the NSQIP dataset, we examined effects of resident/trainee participation in Whipple procedures on mortality and morbidity.

Methods: The NSQIP database was queried for patients undergoing Whipple from 2008-2012. Data was categorized by resident participation (operation with resident versus attending only). Proportion of complications in each group was compared using chi-square test. Logistic regression model was built to analyze impact of multiple covariates on perioperative mortality within 30-days and first postoperative day. Data are presented as proportions and mean±SD.

Results: 12,104 Whipples were reported to NSQIP between 2008-2012. After excluding cases with missing data on resident participation, 7,605 were available for analysis. These cases were divided into two groups: attending alone (group A, n=1105) versus attending with resident (group B, n=6500). Patient comorbidities and demographics were the same between the groups. Operative time was increased with resident involvement (364±139 vs. 380±132 minutes, p<0.001). Length of stay was significantly decreased when residents were involved (13.7±15 vs. 12.7±12 days, p<0.0001). When comparing attending alone versus with resident, there was no significant difference in patient outcomes including incidence of renal failure (p<0.0001), septic shock (p<0.0001), reintubation (p<0.0001), death on operative day (p<0.0001), 30-day mortality (p<0.0001), and readmission rates (p<0.0001). Resident participation was not a significant 30-day mortality predictor in unadjusted (OR=0.73; CI 0.51-1.04, p=0.087) or risk-adjusted models (adjusted OR 0.79; CI 0.55-1.14, p=0.22).

Conclusion: Resident participation did not influence mortality and morbidity rates of Whipple procedure in this study. Resident participation is associated with longer operative time but shortened hospital stay.

♦ 30 G ♦

N-acetyl-leucine-amide (NALA), a Leucine Antagonist, Impacts the Energy Status and Growth of Osteosarcoma Cells

Shailer Brett Martin, DPM'18 and Elitsa Ananieva, PhD

Des Moines University, Des Moines, IA

Bone sarcomas have proven themselves a challenge to doctors and researchers with their unresponsiveness to traditional treatments and therapies. One novel solution to bone sarcoma resistance is to explore the role of branched chain amino acid metabolism of leucine, isoleucine, and valine. Leucine is a nutrient signal that regulates protein synthesis, and we hypothesized that the leucine antagonist, N-acetyl-leucine-amide (NALA), would produce an inhibitory effect on cell growth and protein synthesis in bone sarcoma cells.

For that purpose, we used a human osteosarcoma cell line (143B) donated by a 13 year old female. We treated this line with NALA (25 mM and 50 mM) for a twenty-four hour period. The impact of NALA on signaling pathways, (mammalian target of rapamycin [mTOR] and AMP-activated protein kinase [AMPK]), that regulate energy and nutrient status of cancer cells were examined by Western Blotting.

The lower concentration of NALA [25 mM] caused cell growth inhibition along with activation of AMPK. The higher concentration of NALA [50 mM] had a severe inhibitory effect on cell growth and protein expression of all proteins examined.

The activation of AMPK in leucine-compromised cells indicates that leucine and/or leucine metabolism may impact the energy status of osteosarcoma cells, and cause a reduction in growth. Thus, limited leucine availability may be one novel solution to treat bone cancer patients.

♦ 31 UG ♦

Rapamycin Inhibits the Protein Expression of the Cytosolic Branched Chain Aminotransferase (BCATc) in Lymphoma Cells

[1]Ashley Torres and [2]Elitsa Ananieva, PhD

[1]Mercy College of Health Sciences, Des Moines, IA
[2]Des Moines University, Department of Biochemistry and Nutrition, Des Moines, IA

The cytosolic branched chain aminotransferase (BCATc) is overexpressed in many cancers including lymphoma. BCATc catalyzes the first step in the degradation of leucine. Leucine is a known activator of the mammalian target of rapamycin (mTOR) pathway. mTOR pathway regulates cell proliferation, and is activated during cancer formation. An immunosuppressive drug, called rapamycin inhibits mTOR pathway.

The purpose of this study was to test the effect of rapamycin on BCATc protein expression and compare with the effect of other compounds such as cyclosporine A (CsA), which inhibits the Nuclear Factor of Activated T cells (NFAT) and 10058-F4, which inhibits the oncogene c-Myc. c-Myc controls the expression of more than 15% of human genes, BCATc included. NFAT regulates BCATc expression in immune cells.

A mouse lymphoma cell line (EL-4) treated with rapamycin, CsA, and 10058-F4 was used to look at the impact of these inhibitors on BCATc protein expression compared to the expression of other branched chain amino acid (BCAA) enzymes. Rapamycin inhibited BCATc protein expression by 46%, but increased the expression of another BCAA metabolic enzyme, E1α. CsA did not inhibit any of the enzymes studied, while 10058-F4 inhibited BCATc and E1α.

Suppression of BCATc by rapamycin demonstrates that mTOR pathway plays a role in the regulation of BCATc protein expression. Lack of response to CsA indicates that BCATc is regulated differently in cancer cells than in immune cells. Understanding the regulation of BCATc expression in cancer cells will help define BCATc function in cancer and potentially find new treatment options.

♦ 32 G ♦

Image Analysis of Ultrasound Images of Elastrography

[1]Brittany Duong, MS, DO'19, [2]Inder Makin, MD, PhD, [1]Vikram Kodibagkar, PhD

[1]Arizona State University, Tempe, AZ
[2]A. T. Still University, Mesa, AZ

Elastography is an ultrasound-based imaging technique that can be utilized to visualize and evaluate skeletal muscle stiffness parameters. These parameters can then be used to assist in patient management decision, increase diagnostic confidence, and lead to fewer invasive procedures. Specific to this project, ultrasound elastography images were obtained from phantom test objects using a GE LOGIQ P6 ultrasound system with high frequency probes. We wrote MATLAB algorithms to automatically segment out areas of different stiffness in the phantoms on both B-mode and elastography images.

♦ 33 G ♦

Diffusion Tensor Imaging of the Canid Brain and the Identification of White Matter Fiber Tracts in Six Canid Species

[1]George Zak, MSA,'20, [1]Seth Mommsen, MSA'20, [2]Edmund Wong, [3]Paul Manger, [4]Chet Sherwood, [5]Patrick Hof, [2]Cheuk Tang, [1]Muhammad Spocter, PhD

[1]Des Moines University, Department of Anatomy, Des Moines, IA
[2]Icahn School of Medicine, Departments of Radiology and Psychiatry, Mount Sinai New York, NY
[3]University of Witwatersrand, School of Anatomical Sciences
[4]George Washington University, Department of Anthropology
[5]Mount Sinai School of Medicine, Department of Neuroscience

There is an ever-growing interest in the canine brain as a model species for ongoing studies in translational neurology and neuroscience. Missing however from the current literature is a comparative canid white matter brain atlas, which would inform ongoing studies in veterinary medicine and aid our understanding of the evolutionary history of the canid brain. To address this need we used post-mortem magnetic resonance (MR) imaging and accompanying diffusion tensor imaging (DTI) to conduct a preliminary survey of the white matter in six closely related canid species, including the domestic dog (*Canis familiaris*), African Wild Dog (*Lycaon pictus*), coyote (*Canis latrans*), maned wolf (*Chrysocyon brachyurus*), fennec fox (*Vulpes zerda*) and red fox (*Vulpes vulpes*). Using an interactive interface, paired fractional anisotropic (FA) maps and vector files were loaded into the Freesurfer imaging software and common anatomical white matter tracts were identified in each species. These results are discussed in light of the existing literature on canid behavior and evolution.

♦ 34 G ♦

Ecomorphology of Modern and Fossil Carnivores Using 3D Surface Models

[1]Candice N. Cooper, DPM'17, [2]Julie A. Meachen, PhD, [2]Rachel H. Dunn, PhD

[1]Des Moines University, College of Podiatric Medicine and Surgery, Des Moines, IA
[2]Des Moines University, College of Osteopathic Medicine, Des Moines, IA

Previous studies on scapholunar bones of the wrists of modern carnivores have shown that the form of these bones reflects both shared ancestry (phylogeny) and function (ecology). Linear measurements have traditionally been used to quantify the morphology of the scapholunar together with qualitative observations. While these methods have yielded good results, they are limited in that qualitative observations are difficult to repeat, and linear measurements cannot accurately capture aspects of joint shape such as surface area, curvature, or angulation. New 3D surface methods enable the quantification of such complex morphologies and may add discriminative power to more traditional morphological methods. We used laser scanning to create surface models of the scapholunar of 6 species of modern carnivores in order to determine if surface areas and joint surface angles derived from the laser scans can successfully discriminate different phylogenetic groups of carnivores, and additionally whether these data can be used to infer forelimb function. We also created surface models of scapholunars of 3 species of fossil carnivores from Natural Trap Cave, Wyoming, to determine if surface area and angular measurements can effectively predict the phylogenetic position and locomotor category of fossil carnivores.

♦ 35 G ♦

Dogs Exhibit Increased Brain Gyrification Relative to Wild *Canids*

[1]Steven Rose, DO'18, [1]Chris Girardo, DO'18, [2]Geoffrey K. Aguirre, [2]Ritobrato Datta, [3,4]Clare Rusbridge, [4]Jelena Jovanovik, [5]Cheuk Tang, [6]Patrick Hof, [7]Chet Sherwood, [8]Paul R. Manger, [1,5]Muhammad A. Spocter, PhD

[1]Department of Anatomy, Des Moines University, Des Moines, IA
[2]Department of Neurology, University of Pennsylvania, Philadelphia, PA
[3]School of Veterinary Medicine, University of Surrey, Guildford, Surrey, UK
[4]Advanced Diagnostic Imaging, Fitzpatrick Referrals Ltd, Guildford, UK
[5]Departments of Radiology and Psychiatry, Icahn School of Medicine, Mount Sinai, NY
[6]Department of Neuroscience, Mount Sinai School of Medicine
[7]Department of Anthropology, George Washington University, Washington DC
[8]School of Anatomical Sciences, University of the Witwatersrand, Johannesburg, Republic of South Africa

Over the last 10 years research on dog cognition has revealed that dogs possess a surprising array of complex socio-cognitive skills, in many cases paralleling the behavioral abilities seen in relatively large brained mammals like great apes. Despite this, evidence in support of neuroanatomical restructuring of the dog brain has lagged behind and has left many wondering how dogs are able to perform these complex tasks with such diminutive brain sizes. One area not explored within the framework of canid domestication has been the degree of cortical folding (i.e., gyrification), a commonly used proxy for the functional complexity of the cerebral cortex and its information processing capacity. In the current study we used a quantitative magnetic resonance imaging (qMRI) approach to measure the gyrification index (whole brain, frontal and parietal-occipital) and associated white and grey matter volumes in the cerebral cortex of 17 carnivore species (including six wild canid varieties and five domestic dogs). Using allometric analyses we demonstrate that the cerebral cortex of the domestic dog is significantly ($P<0.05$) more folded than as predicted based on brain size and that dogs differ most markedly from wild canids in the degree of cortical folding observed in the parietal-occipital lobe, a region known to be involved in sensation, perception and the integration of visual information. These results provide the first evidence that the process of domestication may have inadvertently increased the complexity of the canine brain through expansion of the cortical surface area relative to brain size.

♦ 36 G ♦

Cadaveric Variations of Branching Pattern of the Axillary Artery

Tomasz Olejnik, DO'18 and Makhdoom Khan, PhD

Des Moines University, Des Moines, IA

The variations in the origins of the branches of the axillary artery were studied in 24 cadaver specimens. The axillary artery is an extension of the subclavian artery that begins at the lateral border of the first rib and terminates at the inferior border of teres major muscle. To better understand the branching pattern of the axillary artery, a brief description is given below.

The axillary artery is divided in three parts relative to the pectoralis minor. The first part gives off the superior thoracic artery. The second part gives off the lateral thoracic and thoracoacromial arteries. The third portion consists of the anterior and posterior circumflex humeral arteries as well as the subscapular artery—which is further divided into the circumflex scapular artery and the thoracodorsal artery.

During this study numerous variations were identified and studied. The first part of axillary artery was the least variant; only 4% of examined cadavers were missing the superior thoracic artery. Third part including subscapular artery was the most variant segment of axillary artery. In 24% of cases, the variant subscapular artery originated at the level of thoroco-acromial artery located in the second part. In 8% of the cases, the subscapular artery gave off extra branches—the posterior circumflex humeral in some cadavers or the anterior circumflex humeral in others. Identification of subscapular artery variation patterns is very important to be noticed during various surgical procedures. This is mostly because the subscapular artery supplies numerous structures in the shoulder region and posterior back.

♦ 37 UG ♦

The Brain of the Maned Wolf (*Chrysocyon brachyurus*)

[1,2]William Golden, [1,2]Sydney Bentley, [3]Muhammad Spocter, PhD

[1]Anatomy and Physiology, Central Campus, Des Moines Public Schools, Des Moines, IA
[2]Des Moines Area College, Des Moines, IA
[3]Department of Anatomy, Des Moines University, Des Moines, IA

The Maned wolf (*Chrysocyon brachyurus*) is an unusual South American canid possessing a unique mix of fox-like and wolf-like characteristics, described by some as a 'red-fox on stilts' (Clutton-Brock et al 1976). Despite some comparative data on their behavioral ecology, we know very little about the comparative anatomy of this reclusive species and how their anatomy compares with that of closely related canids. In light of this, we analyzed post-mortem magnetic resonance imaging scans of the brain of one adult maned wolf and compared this with that of a adult domestic dog (*Canis familiaris*). Using the ITK-Snap software, we generated 3D models of the brain for each species and used ImageJ to calculate the global gyrencephalic index (GI) and associated cortical thickness in the frontal lobe (anterior cingulate). This preliminary investigation provides some interesting data for the ongoing discussion of variation and evolution of enlarged cortical thickness in mammals and the potential affect this may have on the folding of the cerebral cortex.

♦ 38 G ♦

Cross-Sectional Area of the Corpus Callosum in Wild and Domestic Canids

[1]Ashraf Uddin, DO'18, [2,3]Clare Rusbridge, [3]Jelena Jovanovik, [4]Cheuk Tang, [5]Patrick Hof, [6]Chet C. Sherwood, [7]Paul R. Manger, [1,7]Muhammad A. Spocter, PhD

[1]Department of Anatomy, Des Moines University, Des Moines, IA
[2]School of Veterinary Medicine, University of Surrey, Guildford, Surrey, UK
[3]Advanced Diagnostic Imaging, Fitzpatrick Referrals Ltd, UK
[4]Departments of Radiology and Psychiatry, Icahn School of Medicine, Mount Sinai, NY
[5]Department of Neuroscience, Mount Sinai School of Medicine
[6]Department of Anthropology, George Washington University
[7]School of Anatomical Sciences, University of the Witwatersrand, Johannesburg, Republic of South Africa

Domestication marked a major turning point in human prehistory, enabling humans to artificially select for animal behaviors that favored the interests of early human communities, and dramatically affecting the behavior and morphology of these target species. While all domesticated varieties exhibit marked reductions in overall brain size, it is unknown whether the corpus callosum, an integral white matter fiber pathway for interhemispheric and intracortical communication, is affected by domestication in an allometric or a mosaic pattern. To answer this question we used a quantitative magnetic resonance imaging approach (qMRI) to compare the mid-sagittal cross-sectional areas of the corpus callosum, in 35 carnivore species including six wild canids and 12 domestic dogs. Using a standardized sectioning approach we also extracted Wittelson regions for the corpus callosum and evaluated potential correlations with cortical white matter volume. The results of this study indicate that under the influence of domestication, cortical white matter undergoes allometric reductions relative to brain size, emphasizing the role of architectural and energetic constraints on the evolution of enlarged fiber pathways. These results represent an early step towards a thorough investigation of the canid corpus callosum using complimentary tractography and electron microscopy to evaluate potential axonal caliber and fiber density across species.

♦ 39 UG ♦

The Corpus Callosum of the Coyote (*Canis latrans*)

[1]Liza Bering, [1]Alex Hilmes, [2]Muhammad Spocter, PhD

[1]Anatomy and Physiology, Central Campus, Des Moines Public Schools, Des Moines, IA
[2]Department of Anatomy, Des Moines University, Des Moines, IA

The mammalian brain like all aspects of species biology has been subject to evolutionary processes which continue to shape its structure and function. These changes affect not only the size of the brain and its subcomponents but also the size and distribution of the underlying white matter, which serve to connect parts of the brain and spinal cord. In this current study, we undertook a preliminary investigation of the extent and sub-components of the corpus callosum, a major white matter fiber bundle used to connect adjacent hemispheres. Using the much understudied coyote (*Canis latrans*) as a model animal, we identified and measured the seven Witelson regions coinciding with the functional sub-components of the corpus callosum. Using MRI scan data and processing in the Analyze 10.0 software we measured the corpus callosum and followed this up with diffusion tensor imaging (DTI) of this tract. This preliminary data is discussed in light of the existing description of the dog brain.

♦ 40 G ♦

Impact of GATA 4 and GATA 6 Transcription Factor on Adrenal Gland Development

[1]Tianyu Jiang, DO'19, [2]Elizabeth Jimenez, [2]Heather Hatch, [2]Shawna Fox, [3]Maria Padua, [2]Sergei Tevosian

[1]Des Moines University, Des Moines, IA
[2]Department of Physiological Sciences, College of Veterinary Medicine, University of Florida, Gainesville, FL
[3]Department of Surgery, School of Medicine, Indiana University, Indianapolis, IN

The adrenal gland is an endocrine gland located above the kidney and below the diaphragm. The adrenal cortex secrets different classes of steroid hormones while the inner medulla produces catecholamines. Dysfunctions with adrenal cortex can lead to rare disorders such as Cushing's syndrome and congenital adrenal hyperplasia. Delineating the mechanisms of adrenal cortex development in murine models may provide further insight into our understanding of adrenal diseases that deals with the cortical region, especially those of genetic in nature. GATA 4 and GATA 6 transcription factors are co-expressed in adrenal cortex. In order to delineate their role in the development of murine adrenal glands, we conditionally deleted GATA 4 and GATA 6 in adrenocortical cells with the aid of Sf1Cre recombinase methodology. The mice in middle to late embryonic stages with Sf1Cre mediated double deletion does not possess identifiable adrenal glands. Furthermore, the small clump of tissue in the suprarenal location in the mice with double GATA gene deletion does not show steroidogenic factor 1 nor steroidogenic gene expression. Postnatally, the female double deletion mutants die within two weeks of weaning. However, these female do survive if supplemented with artificial glucocorticoids, indicating that the lack of steroid hormone production from adrenal cortex may be the cause of death. On the other hand, the male mice with both GATA genes knocked out live their full lifespan. Our finding of adrenal cortex enzymes in the respective male murine testes may explain the survival of the male mice.

♦ 41 UG ♦

DNA Sequencing and Genetic Polymorphism Discovery in the Canine Monoamine Oxidase A (MAOA) Gene

Michael Ohman, Paul Skonieczny, Andrew Ruplin, James Sacco

Drake University, College of Pharmacy and Health Sciences, Des Moines, IA

Monoamine oxidase type A (MAOA) is an enzyme that degrades neurotransmitters. In humans, reduced activity of the MAOA enzyme due to genetic polymorphisms within the *MAOA* gene leads to increased neurotransmitter levels in the brain which may result in aggressive behavior. Aggression is the most frequent behavioral problem in dogs, and polymorphisms in other genes have been linked with aggressive/impulsive tendencies in certain breeds. However, genetic variation within the canine *MAOA* gene is unknown. The aim of this study was to identify and sequence functionally important regions of the *MAOA* gene in pure-breed dogs.

Genomic DNA was collected via cheek swabs from 26 pure-bred dogs. Following DNA purification, eight regions of the canine *MAOA* gene were amplified, sequenced, and screened for polymorphisms.

Eight novel genetic polymorphisms were found. Four were single nucleotide polymorphisms (SNPs) and four were deletion/insertion variations. One synonymous SNP, c.1517C>T, was discovered in the terminal exon 15. In one-third of the dogs, two highly polymorphic microsatellites, both TAAA deletions and/or insertions, were found in introns 1 and 10. The microsatellite region in intron 10 was represented by three alleles, representing variable numbers of TAAA repeats (10, 11, or 12). The polymorphism in intron 1 was a TAAA sequence inserted within a short interspersed nuclear element (SINE) that is unique to canids.

Additional dogs are being sequenced in order to study the genotype frequencies of these polymorphisms across breeds. Ultimately, these novel MAOA polymorphisms will provide useful information for behavioral genetic studies in dogs.

♦ 42 UG ♦

Evaluating the Effectiveness of FoldIt Software for Determining the Consequences of Point Mutations

Ryan Starkman, Mohammed Al Hussein, Miles Hackett, Kennedy Kiprop, Jerad Snyder, Corbin Zea, Bonnie Hall

Grand View University, Department of Chemistry and Physics, Des Moines, IA

Mutagenesis is an accepted method of changing the structure and thus the function of a protein. This is useful when engineering an enzyme to have a novel function. FoldIt is a computational software program that allows the user to make amino acid substitutions in a protein and calculates the effects on both the folding of the protein as well as interactions with the substrate. The goal of this study is to evaluate how effective FoldIt is at determining the effect of amino acid substitutions in the protein βglB. βglB was selected as it is an easily expressed protein with a simple spectrophotometric assay and an available crystal structure. A series of point mutations were made in the binding pocket of the βglB protein, including F418Y, W328S, Q22A, W410H, and W402C. These mutations should affect the polarity, charge, and pI of the binding pocket, which was evaluated *in silico* using FoldIt. These mutants were then generated and the activity of purified protein tested *in vitro*. Preliminary data will be presented on whether the predicted effects of each mutation correlate with the experimental data.

♦ 43 UG ♦

Mutational Analysis of the Polysaccharide Binding Site of Beta-Glucosidase B

Elizabeth A. Kras, Sean Giza, Kennedy Kiprop, Dr. Corbin Zea, Dr. Bonnie Hall

Grand View University, Department of Chemistry and Physics, Des Moines, IA

Beta-Glucosidase B (βgl-B) was originally found in *Paenbacillus polymyxa* and is able to break down disaccharides, oligosaccharides, and conjugated saccharides. These functions, along with a solved crystal structure and easy protein expression, make βgl-B an ideal enzyme to engineer to accept new substrates. E180 and H181 are amino acids found in the substrate binding pocket of βgl-B. H181 fixes the polysaccharide in place by linking via a water molecule to the sugar ring occupying subsites -1 and +1. E180 is part of the network of amino acids that hydrogen bond to the sugar unit in subsite +2 as well as linking to the proximal hydroxyl O3 and O6 of the sugar unit present in subsite +3. Changing of an amino acid that is responsible for binding with the substrate can result in changes in the catalytic efficiency of βgl-B.

In this study, E180 was mutated to aspartic acid (D), glutamine (Q), and tryptophan (W). These mutations result in changes in side chain size, shape, polarity, and acidity. H181 was mutated to arginine (R), changing the solubility and pI of the amino acid. Computational design of the mutants was done using FoldIt, a program that helps predict the effects of a mutation on the original enzyme. Oligonucleotides were created and outsourced to Transcriptic for mutant synthesis using Kunkel mutagenesis. Mutant proteins were over expressed, affinity purified, and enzymatic activity assayed. Preliminary catalytic efficiency data for the mutant βgl-B proteins will be presented. This information will be used to engineer βgl-B to have novel substrates.

♦ 44 UG ♦

Effects of CD73 Suppression on TGFβ-Mediated Migration and Invasion in Endometrial Cancer Cells

[1,3]Ashley Armantrout, [2]Russell R. Broaddus, [3]Carl Thurman, [4]Jessica L. Bowser

[1]The Cancer Prevention and Research Institute of Texas Summer Undergraduate Program
[2]Departments of Pathology, University of Texas MD Anderson Cancer Center, Houston, TX
[3]Summer Undergraduate Research Program, University of Northern Iowa, Cedar Falls, IA
[4]Translational Molecular Pathology, University of Texas MD Anderson Cancer Center, Houston, TX

Transforming growth factor-β (TGFβ) has been called the 'Dr. Jekyll and Mr. Hyde' of cancer for its paradoxical function as both a tumor suppressor and a pro-metastatic factor. In early stage disease, TGFβ suppresses tumor growth, inducing cell cycle arrest and apoptosis; in late stage disease, TGFβ promotes tumor progression, inducing epithelial-to-mesenchymal transition, invasion, and metastasis. TGFβ is a secreted cytokine that signals via receptor serine/threonine kinases and intracellular Smad effectors. Often, mutations or genomic alterations in the TGFβ signaling pathway shift the balance of TGFβ from tumor suppressive to tumor promoting. In endometrial cancer (EC), TGFβ-related mutations and genomic alterations are less common, which has indicated that other events, specifically the loss of function in downstream targets of TGFβ signaling, are involved. We sought to determine whether loss of CD73 (an important enzyme in adenosine biosynthesis) in EC shifts the balance of TGFβ from tumor suppressor to pro-metastatic factor. Our laboratory has shown that TGFβ induces CD73 in HEC-1-A cells, a model of early stage endometrial cancer, and that CD73 is down-regulated in late stage disease. HEC-1-A cells were treated with bovine serum albumin/hydrochloric acid (BSA/HCl; control) or 2.5ng/ml TGFβ. HEC-1-A cells were also treated with BSA/HCl or TGFβ + 100μM AoPCP, a CD73 inhibitor. Unmodified and modified Boyden chambers were used to assess HEC-1-A cell migration and invasion, respectively. TGFβ significantly decreased HEC-1-A cell migration and invasion compared to BSA/HCl ($P<0.005$). TGFβ-treated HEC-1-A cells treated with 100μM AoPCP (TGFβ + AoPCP) significantly increased cell migration and invasion compared to TGFβ ($P<0.005$). These findings suggest that the loss of CD73 in EC contributes to the shift in balance of TGFβ from tumor suppressor to pro-metastatic factor.

♦ 45 G ♦

Complement Component C1q Stimulates Engulfment of *Mycobacterium avium* While Limiting TNF-α Production

[1]Blair Tilkens, DO'18, [2]Emily Willmann, [2]Suzanne Bohlson, PhD

[1]Des Moines University, Des Moines, IA
[2]Des Moines University, Department of Microbiology and Immunology, Des Moines, IA

The intracellular pathogen mycobacterium evades the immune system by surviving within host macrophages. Defense collagens, such as C1q, enhance macrophage phagocytosis and inhibit the production of proinflammatory cytokines that are crucial for the host defense in eliminating the bacteria. This study tested the hypothesis that C1q facilitates macrophage engulfment of mycobacteria while dampening macrophage proinflammatory cytokine production. This mechanism may contribute to successful pathogenesis of mycobacteria within the host. To test this hypothesis, mouse bone marrow derived macrophages (BMDM) were harvested and activated with either a control protein (human serum albumin) or C1q. *M. avium* A5 was added to the macrophages and the percentage of macrophages associated with mycobacteria was quantified via fluorescence microscopy. Macrophages stimulated by C1q associated with 2.4 times as many mycobacteria compared to control macrophages ($n=4$, $p<0.05$). The production of the proinflammatory cytokines was quantified by measuring TNF-α from supernatants of macrophages associated with *M. avium* A5 using an ELISA. Activation by C1q resulted in a decrease in proinflammatory TNF-α production in response to *M. avium* A5 at multiple different macrophage to mycobacteria ratios. Following C1q-stimulation and subsequent activation with *M. avium*, western blot analysis of macrophages demonstrated a decrease in phosphorylated JNK and an increase in degradation of IκB over time indicating a dysregulation in pathways leading to proinflammatory cytokine production. These results suggest that *M. avium* utilizes C1q for engulfment into macrophages while down regulating the proinflammatory response allowing for successful pathogenesis within the human host.

♦ 46 ♦

An Investigation of C1q-Dependent Inflammatory Signaling and Efferocytosis in Macrophages

Holly Hulsebus, Sean O'Conner, Suzanne Bohlson, PhD

Des Moines University, Department of Microbiology and Immunology, Des Moines, IA

Complement protein C1q is important in clearing apoptotic cells (efferocytosis) and regulating inflammatory responses, and C1q deficiency results in autoimmunity. Our laboratory demonstrated that C1q enhances efferocytosis in mouse macrophages (BMDM) by upregulating expression of Mer tyrosine kinase (MerTK), a macrophage receptor important in efferocytosis and anti-inflammatory signaling. Here, we investigated MerTK's role in C1q-dependent inflammatory signaling, and explored shared and divergent pathways in BMDM and human monocyte derived macrophages (HMDM). C1q enhanced efferocytosis and dampened LPS-dependent TNF-α production in BMDM and HMDM. Protein synthesis was required for enhanced efferocytosis, as cycloheximide pre-treatment diminished the effect. MerTK was not required for C1q-dependent regulation of proinflammatory signaling in BMDM and was not upregulated in HMDM. Finally, full-length C1q was required for enhanced efferocytosis and decreased proinflammatory signaling since the collagen-like tails failed to mediate these activities. These data provide insight into the mechanisms by which C1q regulates inflammatory activity in macrophages.

♦ 47 ♦

Identification of Effector and Immunity Proteins in the Type VI Secretion System of *Acinetobacter nosocomialis* Strain M2

Holly Hulsebus and Michael Carruthers, PhD

Des Moines University, College of Osteopathic Medicine, Department of Microbiology and Immunology, Des Moines, IA

Type VI secretion systems (T6SS) are a class of bacterial secretion machinery by which bacteria can inject proteins into target cells to elicit responses such as cell death. We recently demonstrated that a clinical isolate of the pathogen *Acinetobacter nosocomialis* produces a functional T6SS that is utilized to kill neighbouring bacteria. Using Tn-Seq, we identified a gene cluster in the *A. nosocomialis* strain M2 genome that we hypothesize encodes a T6SS effector (Ase1) that is used to kill other bacteria, and a protein (Asi1) that confers immunity from T6SS killing. Herein, we present data that suggest Ase1 is a T6SS effector that is required for strain M2 T6SS-mediated bacterial killing and that Asi1 is required to be immune to this killing. Unmarked, in-frame mutations in both *ase1* and *asi1* were generated in strain M2. This double mutant was assessed for its ability to kill *Escherichia coli* and survive co-incubation with wild-type M2. The *ase1 asi1* double mutant was unable to kill *E. coli,* indicating that either *ase1* or *asi1* is a T6SS effector. In competition with wild-type strain M2, the *ase1 asi1* mutant was out-competed, suggesting that either Ase1 or Asi1 acts as an anti-toxin, protecting cells from T6SS killing. These data contribute to our knowledge of the proteins required for T6SS-mediated bacterial killing and self-immunity in *Acinetobacter*, and can prove useful for the development of targeted therapies for these infections.

♦ 48 G ♦

Influence of Boric Acid on Yeast Carbohydrate Metabolism and Ethanol Resistance

Dominic Tran-Nguyen, DO'18, Benjamin Pointer, Michael Boyer, Martin Schmidt, PhD

Des Moines University, Des Moines, IA

Boric acid (BA) increases cellular energy expenditure and causes weight loss. However, comprehensive metabolomic studies failed to identify a single target for BA toxicity that would explain increased energy consumption. Instead it has been found that BA has additive inhibitory effects on many separate cellular processes. A possible explanation for the broad spectrum of BA effects is a depletion of the electron acceptor NAD. BA forms complexes with NAD *in vitro*, suggesting that depletion of NAD inhibits NAD-dependent metabolic enzymes and NAD-dependent histone deacetylases that mediate the effects of energy charge on ageing. The present study examines the effects of BA on yeast energy homeostasis that might suggest synergistic improvements to antifungal therapies. Our enzyme assays show that BA does not significantly change the cellular concentrations of NAD and NADH. We also show that glucose consumption or ethanol production do not increase in the presence of BA, indicating that the rise in cellular ATP is not

due to increased carbohydrate metabolism – although a significant reduction in cellular glycogen stores suggests mobilization of reserve carbohydrates during BA stress. We further determined that BA reduces NAD-dependent alcohol dehydrogenase activity in permeabilized cells, suggesting somewhat contradictory - that the formation of BA-NAD complexes does occur *in situ*. A screening of a small library of bioactive compounds showed that BA has a specific synergistic effect with ethanol. The BA-Ethanol synergy suggests that both agents affect cell viability in similar ways and can be exploited to improve the efficacy of BA therapy for superficial candidiasis.

♦ 49 G ♦

Synergistic Effect of Aminoglycosides and Statins on Antibiotic Resistance *Enterococcus faecalis* Growth

Clint E. Jiroux, MBS'18 and Jeffrey T. Gray, PhD

Des Moines University, Department of Microbiology and Immunology, Des Moines, IA

Enterococci are a commensal bacterium that resides in the intestinal tract of many animal species, infection of this microbial can lead to sepsis and even death. This research investigates *Enterococcus faecail*s, measuring the possibility of synergism of statins and antimicrobials on inhibiting its growth. The antimicrobials include aminoglycosides, gentamicin and kanamycin and a beta-lactam, ampicillin. Observable differences between the strains and the effect of the treatment depended on the strain evaluated. *Enterococcus faecalis* (ATCC 29212) showed reduction of its growth when administered the treatment in growth curves, making it susceptible to combination treatment, its MIC in the susceptible range (<128 µg/ml). When it comes to the viability of the bacteria after treatment, we saw a noticeable difference between the drug concentration and whether it was combined with an aminoglycoside. When the drug simvastatin was increased to a higher concentration (70 µM) there was an increase in the amount of cells that resided in the living population after analysis with flow cytometry.

The importance of this research relative to the increasing prevalence of the antimicrobial resistant enterococci strains in nosocomial infections. Most of the combinations of antibiotics that have been used before are showing high level resistance. A new treatment option would be beneficial for these strains, with this treatment or the mechanism being further evaluated.

♦ 50 G ♦

EGCG and Telomerase Inhibitor MST-312 Inhibit HSV Infection in Vero Cells

Jesse Wilson, DO'18, Evan Beacom, DO'18, Prajakta Pradhan, Marie L. Nguyen, PhD

Des Moines University, Department of Microbiology and Immunology, Des Moines, IA

Approximately 90% of the world population has been exposed to herpes simplex virus (HSV). HSV infection often results in painful ulcerative lesions, with lifelong recurrent outbreaks. Antivirals for HSV exist, but drug resistance is an increasing concern, prompting the search for novel antivirals. Epigallocatechin gallate (EGCG) is a natural compound derived from green tea that can inhibit telomerase and has been investigated for anti-tumor properties. MST-312 is a synthetic analogue of EGCG. Here, antiviral properties of these compounds are assessed in Vero cells using microscopy and immunoblot assays. MST-312 and EGCG treatments failed to increase cell toxicity or decrease cell numbers compared to vehicle controls, demonstrating that they are neither cytotoxic nor cytostatic in this system. The presence of MST-312 during HSV infection reduced viral cytopathic effect (CPE) and caused a reduction in the accumulation of late viral proteins. Drug addition after viral attachment also decreased viral protein levels. Although EGCG treatment did not dramatically alter HSV CPE, treatment with 70 and 100µM EGCG inhibited the accumulation of the immediate early viral protein ICP4, and all late proteins tested. Subsequently, the virucidal activity of EGCG and MST-312 were assessed by quantifying the plaque forming ability of pre-treated virus. For MST-312, the minimum concentration required to significantly decrease plaques was 20 µM. For EGCG, 20 µM was a sufficient concentration to yield undetectable plaques. Thus, both compounds exhibited direct virucidal properties. Together, these results provide further insight into the antiviral properties of EGCG and its chemical analogue MST-312.

♦ 51 G ♦

Chronic Stress Alters the Murine Gut Microbiome

Aaron Shoskes, DO'18, Alexandra Proctor, Kathryn Battani, Vanja Duric, PhD, Gregory Phillips, LiLian Yuan, PhD

Background: Evidence supports communication between the brain, the gastrointestinal tract, and the gut microbiota. Stressors influence both the GI tract and its resident microbiota, and dysbiosis of GI tract colonization is associated with different diseases. We investigated the relationship between chronic stress and the murine gut microbiota by comparing the taxonomic composition before and after chronic stress.

Methods: Mice were subjected to chronic unpredictable stress (CUS) for six weeks. Bacterial DNA was extracted and sequenced from fecal samples before and after CUS. Taxonomic comparisons of the resultant sequences were made between the pre- and post- samples, and PICRUSt was used to predict functional metagenomic profiles based on organism abundance.

Results: We observed phylum level differences; mean abundance of *Bacteroidetes* increased and *Firmicutes* decreased over the chronic stress period. Decreases in *Bacilli* (a class within *Firmicutes*) and *Lactobacillus* (a genus in *Bacilli*) appeared to contribute to the phylum abundance decrease. No significant difference in alpha diversity was noted. PICRUST analysis revealed stress-induced significant differences in predicted amount of genes encoding for synthesis of short chain fatty acids and reuterin, molecules implicated in stress-related microbial signaling.

Conclusions: Our results support the hypothesis that CUS alters the murine gut microbiome resulting in changes in microbial signaling metabolites. Potential mechanisms for changes include stress-induced reductions in gastric acid or altered motility causing an altered environment for gut colonization Manipulation of the gut microbiome with medications could influence mental well-being. We currently await data addressing whether chronic pain results in similar microbiotic changes.

♦ 52 ♦

The Differential Impact of Donor-Specific Antibodies in Living vs. Deceased Donor Liver Transplantation

[1]**Chunfa Jie, PhD,** [2]Josh Levitsky, [2]Anat R. Tambur, [2]Hugo Kaneku, [2]Michael Abecassis

[1]Des Moines University, Des Moines, IA
[2]Northwestern University, Chicago, IL

Background: With less ischemia and improved donor selection, living donor liver transplantation (LDLT) may hypothetically lead to less donor-specific HLA antibody (DSA) formation or adverse outcomes compared to deceased donor liver transplantation (DDLT).

Methods: The A2ALL (Adult to Adult Living Donor Liver Transplantation) biorepository was probed for LDLT and DDLT recipients with available serum samples for DSA testing pre- and 3-12 month post-LT. We compared the prevalence of preformed/*de novo* DSA and its association with time-dependent outcomes in DDLT vs. LDLT.

Results: 129 LDLT and 66 DDLT recipients were identified. The prevalence of preformed and *de novo* DSA (p=0.93, Table) was not different in LDLT vs. DDLT. There was no association between patient survival and the timing, class and strength of DSA between the liver transplantation (LT) groups. However, preformed DSA was associated with higher graft failure only in DDLT (p=0.01). *De novo* DSA was associated with graft failure regardless of LT type (p=0.005) but with rejection only in DDLT (p=0.0001). By Cox Proportional Hazard modeling, DSA was found to be an independent risk factor for graft failure regardless of LT type (p=0.017 preformed DSA; p=0.002 *de novo* DSA).

Conclusion: Although similar in prevalence, DSA may have more impact on adverse graft outcomes in DDLT vs. LTLT.

Pyrrolopyrimidines are Immediate-Early Phase Inhibitors of Human Cytomegalovirus Replication

[1]Diana Schreier, PharmD'17, [2]Leroy Townsend, [2]John Drach, [1]Brian Gentry

[1]Drake University, Des Moines, IA
[2]University of Michigan, Ann Arbor, MI

Human cytomegalovirus (HCMV) can cause severe illness in immunocompromised and immunologically immature patients. Current pharmacotherapies for the treatment of systemic HCMV infections include ganciclovir (GCV), foscarnet, and cidofovir. However, long-term administration of these agents can result in serious adverse effects (myelosuppression, nephrotoxicity) and the development of viral strains with decreased drug susceptibility. Moreover and because all current pharmacotherapies have the same mechanism of action, the advent of cross-resistance (resistance to one drug resulting in decreased susceptibility to another) is a growing concern. Therefore, new compounds with increased therapeutic indexes and distinct mechanisms of action are warranted for HCMV treatment. The pyrrolopyrimidines elicit an anti-viral effect with EC_{50}'s ranging from 0.53 to 2.0 μM without any observable increase in cytotoxicity *in vitro*. Time-of-addition studies examining the mechanism of action revealed that the pyrrolopyrimidines exert their anti-viral effect early in the HCMV replication cycle losing efficacy starting at 12-24 hours post-infection. This is distinct from both GCV, an early-phase DNA polymerase inhibitor that loses efficacy between 48-72 hours post-infection, and BDCRB, a late-phase terminase inhibitor that loses efficacy between 84-96 hours post-infection. We therefore conclude that the pyrrolopyrimidines are immediate-early phase inhibitors of HCMV replication, a mechanism of action distinct from currently available drugs. In addition, their favorable toxicity profile makes them promising candidates for further investigation for the treatment of systemic HCMV infections.

Oral Presentation

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4 pm	Calcineurin Homologous Protein Genetic Variants Associated with an Increase in Blood Pressure **Liran BenDor, DO'18,** Samuel L. Lampe, DO'18, John E. Norgaard, Afshin Parsa, MD, MPH, Francesca Di Sole, PhD, Victor Babich, PhD	34
4:15 pm	Comparison of Transverse and Coronal Plane Stability at the First Tarsal-Metatarsal Joint with Multiple Screw Orientations **Andrea Cifaldi, DPM'18,** Britney Roberts, Mindi Feilmeier, DPM, FACFAS, Paul Dayton, DPM, MS, FACFAS, Merrell Kauwe, DPM, Hannah Johnk, DPM, Rachel Reimer, PhD	34
4:30 pm	Diffusion Kinetics of Ketamine in Brain Tissue: A Potential Roadblock to Understanding New Drug Mechanisms **Zachary S. Geiger, DO'18,** Jason S. Chen, Lori Semke, BS, Abdel K. Harrata, LiLian Yuan, PhD	35
4:45 pm	Scapulothoracic Muscle Strength in Individuals With and Without Neck Pain **Shannon Petersen, PT,** Nathan Domino, DPT, Chad Cook, PhD, PT	35

Presenting author(s) in bold.

Calcineurin Homologous Protein Genetic Variants Associated with an Increase in Blood Pressure

[1]Liran BenDor, DO'18, [1]Samuel L. Lampe, [1]John E Norgaard, [2]Afshin Parsa, MD, MPH, [1]Francesca Di Sole, PhD, [1,2]Victor Babich, PhD

[1]Des Moines University, Department of Physiology and Pharmacology, Des Moines, IA
[2]University of Maryland School of Medicine, Department of Medicine, Baltimore, MD

Hypertension affects ~80 million adults in the United States, making it a leading risk factor for cardiovascular disease, and a major burden for the health care system. Although genetic factors are known to play a role in an individual's risk for hypertension, specific genetic determinants of hypertension are poorly understood. The Calcineurin Homologous Protein (CHP) is a calcium-binding protein and binding partner of the Na^+/H^+ exchanger-3 (NHE3), a major regulator of body salt, fluid homeostasis, and blood pressure. In a genome-wide association study of 200,000 individuals (International Consortium for Blood Pressure), we identified CHP gene single nucleotide polymorphisms (SNPs) which were significantly associated with an increase in blood pressure. Using computational analysis, we mapped the SNPs located within putative transcription factor binding sites in non-coding regions of the CHP gene. Since CHP regulates NHE3 protein expression as well as activity, we hypothesized that these SNPs affect the regulation of CHP gene transcription, which could then change blood pressure via altering NHE3 transcription/activity. We investigated five SNPs for their influence on the binding of transcription factors using luciferase reporter gene assays; we cloned the SNPs in a luciferase reporter system, expressed the constructs in human renal cells and tested the luciferase activity. We found that major to minor allele replacements of four of the five SNPs revealed significant effects on promoter activity. Functional analysis of CHP genetic variants might aid the discovery of novel susceptibility loci that are responsible for genetic predisposition to develop hypertension.

Comparison of Transverse and Coronal Plane Stability at the First Tarsal-Metatarsal Joint with Multiple Screw Orientations

[1]Andrea Cifaldi, DPM '18, [1]Britney Roberts, [1]Mindi Feilmeier, DPM, FACFAS, [1,2]Paul Dayton, DPM, MS, FACFAS, [2]Merrell Kauwe, DPM, [2]Hannah Johnk, DPM, [3]Rachel Reimer, PhD

[1]Des Moines University, College of Podiatric Medicine and Surgery, Des Moines, IA
[2]Trinity Regional Medical Center, UnityPoint Clinic Foot and Ankle, Fort Dodge, IA
[3]Des Moines University, Master of Public Health Program, Des Moines, IA

Intercuneiform instability has been recognized as a potential cause of hallux valgus recurrence following tarsal metatarsal joint (TMTJ) fusion. Recommendations have been made for additional screw placement between the metatarsals and/or the cuneiforms to improve stability. The screw orientation that provides the best stability has not been documented. Twelve cadavers with the first TMTJ fixated were used for testing. Using a consistent force application of 15 pounds in both the transverse and coronal planes, we measured the change in IMA on radiographs. Force testing was repeated with screws deployed individually in the following orientations: first to second cuneiform (CC), first to second metatarsal (MM) and first metatarsal to middle cuneiform (MC). Our results indicate that stability of the first ray in the transverse and coronal planes is not improved with TMTJ fixation alone or with an additional CC screw. The MM screw consistently reduced first metatarsal instability in both planes. The MC screw had intermediate results. These findings strengthen the notion that first ray instability is complex and involves the tarsal and metatarsal articulations at multiple levels outside of the TMTJ alone.

Diffusion Kinetics of Ketamine in Brain Tissue: A Potential Roadblock to Understanding New Drug Mechanisms

[1]Zachary S. Geiger, DO '18, [2]Jason S. Chen, [1]Lori Semke, [2]Abdel K. Harrata, [1]LiLian Yuan, PhD

[1]Des Moines University, Department of Physiology and Pharmacology, Des Moines, IA
[2]Iowa State University, Department of Chemistry, Ames, IA

Introduction: Recent studies have demonstrated the efficacy of ketamine, at sub-anesthetic doses, in the treatment of major depressive disorder and in the reduction of chronic pain. Mechanistic studies *in vitro* have been utilized to determine and characterize the mechanism(s) underlying these effects. We examine the hypothesis that the diffusion properties of ketamine have a major impact on the effective drug dose achieved during *in vitro* studies.

Methods: Brain slices from adult mice were exposed to 17.7μM ketamine HCl in artificial cerebrospinal fluid (aCSF) for 0-120 minutes. Ketamine concentrations within the brain tissue were measured via tandem high performance liquid chromatography-mass spectrometry.

Results: The brain:aCSF partition coefficient for ketamine was 5.5 (95% confidence interval 4.1-6.8). A computational model was generated representing ketamine concentration as a function of time and depth within a slice of brain tissue. The diffusion coefficient for ketamine in brain tissue was approximately 0.12 $cm^{2} \cdot s^{-1}$.

Conclusions: The diffusion properties of ketamine have a significant effect on drug concentrations within brain tissue. Ketamine equilibrates quickly in brain tissue at a concentration 5.5 times higher than the surrounding aCSF. In previous *in vitro* mechanistic studies, reported concentrations of ketamine represent an 80% underestimate of the ketamine concentration within the brain tissue. Studies of drug actions *in vitro* are critical to understanding the mechanism(s) through which ketamine exerts its effects. Caution should be exercised when interpreting results derived from previous *in vitro* studies in which the concentrations of ketamine used greatly exceed those which produce specific effects *in vivo*.

Scapulothoracic Muscle Strength in Individuals With and Without Neck Pain

[1]Shannon Petersen, PT, [1]Nathan Domino, DPT, [2]Chad Cook, PhD, PT

[1]Des Moines University, Des Moines, IA
[2]Duke University, Durham, NC

The purpose of this study was to examine lower trapezius (LT), middle trapezius (MT) and serratus anterior (SA) muscle strength in individuals with and without neck pain. Impairments in scapulothoracic muscle performance have been associated with neck pain. Additionally, neck pain clinical guidelines have suggested coordination, strengthening, and endurance exercises for these muscles. It is not clear whether individuals with neck pain present with LT, MT, and SA muscle strength deficits when compared to asymptomatic individuals; and little evidence is available which compares scapulothoracic muscle strength between limbs in those with one-sided neck pain.

This descriptive cross sectional study examined 22 individuals with chronic neck pain and 17 asymptomatic individuals. Participants completed a screening questionnaire, Neck Disability Index, and underwent muscle testing for the LT, MT, and SA muscles bilaterally using a hand-held dynamometer. Data analyses included descriptive statistics in addition to paired and comparative independent t-tests.

For individuals with neck pain, significant differences in strength between limbs for the LT ($P<0.01$) and MT ($P<0.01$) were present, but not for the SA. In contrast, no strength difference between limbs for the asymptomatic group was found in any muscle. Individuals with neck pain were significantly weaker than asymptomatic individuals for the LT ($p= 0.04$), MT ($p= 0.02$), and SA ($p<0.01$).

Muscle weakness in the LT, MT, and SA muscles is present in individuals with neck pian. Strength of these muscles should be examined in patients who present with neck pain. Further investigation is warranted to determine the best management strategies and to determine if improvements in strength correspond to improvements in neck pain and function.

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