DMU MENTORED STUDENT RESEARCH PROGRAM

July 22, 2013

Des Moines University
Olsen Medical Education Center
Des Moines, IA 50312

RESEARCH IS VITAL AND AT DMU STUDENTS ARE VITAL TO RESEARCH.

DES MOINES UNIVERSITY

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Agenda

9:30 a.m. **Registration and Poster Presentations**

10 a.m. **Welcome**

Jeffrey Gray, Ph.D., Vice President for Research, Director of Master of Science in Biomedical Sciences, and Professor of Microbiology and Immunology, Des Moines University

Rachel Reimer, Ph.D., Assistant Professor of Master of Public Health, Chair of the Research and Grants Committee, Des Moines University

10:15 a.m. **Keynote Address: The Biopsychosocial Model and the Prevention of Chronic Pain**

Robert J. Gatchel, Ph.D., ABPP, Chair and Distinguished Professor of the Department of Psychology, College of Science at The University of Texas at Arlington

Objectives

- Describe the heuristic value of the biopsychosocial model of chronic pain.
- Appraise the treatment and cost benefits of early intervention in order to avoid the development of chronic problems.
- Assess the major components of an early intervention program.

11:15 a.m. **Presentation of Certificates and Recognition of Scholarship Recipients**

11:30 a.m. **Lunch and Poster Presentations**

1 p.m. **Oral Presentations**

- Movement Science and Public Health – Ryan Hall 181
- Biomedical Sciences – Ryan Hall 281

Keynote Speaker

Robert J. Gatchel, Ph.D., ABPP

Robert J. Gatchel received his BA in Psychology, Summa Cum Laude, in 1969 from the State University of New York at Stony Brook, and his Ph.D. in Clinical Psychology in 1973 from the University of Wisconsin. He is also a Diplomate of the American Board of Professional Psychology (ABPP). Dr. Gatchel is currently the Chair and Distinguished Professor of the Department of Psychology, College of Science, at The University of Texas at Arlington, as well as the Nancy P. & John G. Penson Endowed Professor of Clinical Health Psychology. In addition, he is a Clinical Professor at The Eugene McDermott Center for Pain Management, Department of Anesthesiology & Pain Management, at The University of Texas Southwestern Medical Center at Dallas, as well as the Director of Biopsychosocial Research at the University of North Texas Health Sciences Center, Ft. Worth.

Dr. Gatchel has always been involved in new “cutting edge” areas of science and medicine. He has conducted extensive evidence-based clinical research, much of it continuously funded for the past 30 years by grants from the National Institutes of Health (NIH). He was also the recipient of consecutive Research Scientist Development Awards from NIH, and a prestigious Senior Scientist Award from NIH. His major areas of clinical and research expertise involve the biopsychosocial approach to the etiology, assessment, treatment and prevention of chronic stress and pain behavior, and the comorbidity of physical and mental health disorders; and clinical health psychology. He has published over 240 journal articles, 100 book chapters and has authored or edited 23 books

Dr. Gatchel’s research has strengthened the biopsychosocial approach to physical and mental health disorders and made possible the early identification and successful treatment of patients at risk for the development of chronic pain. He has led many in the medical profession to carefully consider salient psychological and social factors. His tireless leadership in the area of health psychology has inspired his colleagues in the field of psychology and numerous medical specialties.

Dr. Gatchel has been a major participant in science and pain management education. To date, he has trained and mentored 65 Ph.D. graduate students, 6 postdoctoral Fellows, 32 Masters level students, and numerous junior faculty members. Many of these have gone onto prestigious careers in academia and pain management.

The Biopsychosocial Model and the Prevention of Chronic Pain

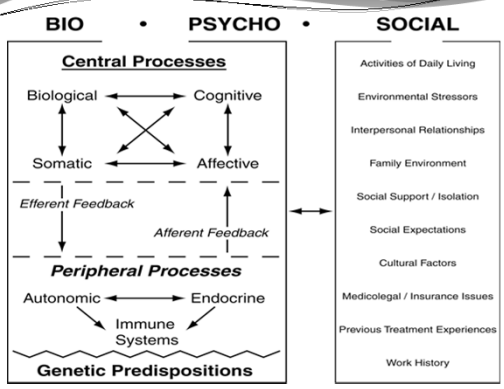
Robert J. Gatchel, Ph.D., ABPP
Chair and Distinguished Professor of the Department of Psychology, College of Science at The University of Texas at Arlington

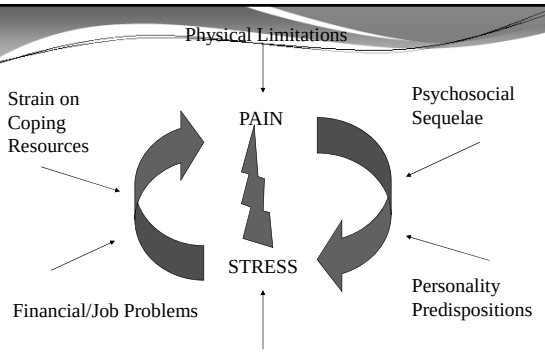
THE BIOPSYCHOSOCIAL MODEL AND THE PREVENTION OF CHRONIC PAIN

Robert J. Gatchel, Ph.D., ABPP
Nancy P. and John G. Penson Endowed Professor of Clinical Health Psychology
Distinguished Professor, Department of Psychology, College of Science, The University of Texas at Arlington
Director of Center of Excellence For the Study of Health and Chronic Illnesses

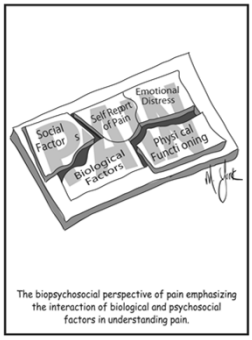
BIOPSYCHOSOCIAL MODEL

Complex and Dynamic Interaction among Physiologic, Psychologic and Social Factors, which Perpetuates and May Worsen the Clinical Presentation

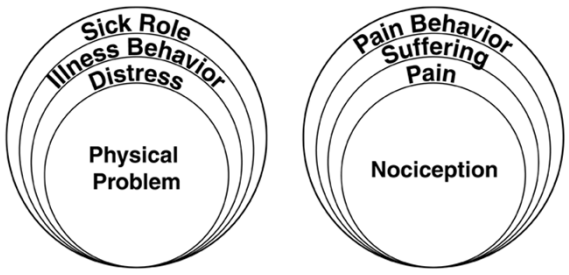




The pain-stress cycle, emphasizing the interaction of stress-related issues and the actual pain. It is helpful to draw patients' attention to this cycle



The biopsychosocial perspective of pain emphasizing the interaction of biological and psychosocial factors in understanding pain.



BIOPSYCHOSOCIAL MODEL FOCUSES ON ILLNESS

- The interrelationships among biological changes, psychosocial status, and the sociocultural context all need to be considered
- This helps to explain the diversity of pain or illness expression, including its severity, duration and psychosocial consequences.

DISEASE versus ILLNESS

"MANAGEMENT" vs. "CURE" PHILOSOPHY

PATIENT HETEROGENEITY AND RESPONSE TO TREAMENT

TAILORING TREATMENT FOR EACH PATIENT

- Physical modalities, including ultrasound, exercise, transcutaneous nerve stimulation, and hot/cold packs
- Cognitive-behavioral strategies, including coping skills, positive imagery, distraction, and so on
- Stress management, including relaxation and biofeedback

- Hypnosis
- Acupuncture
- Operant treatment strategies
- Interdisciplinary pain management
- Individual, group and family therapies
- Modeling and social support
- Pharmacotherapy
- Interventional injections

BIOPSYCHOSOCIAL, INTERDISCIPLINARY TREATMENT

THE ASSESSMENT-MANAGEMENT PROCESS: PUTTING IT ALL TOGETHER

Biopsychosocial Assessment
then
Biopsychosocial Treatment

TREATMENT- AND COST-EFFECTIVENESS

The Journal of Pain, Vol 7, No 11 (November), 2006: pp 779-793
Available online at www.sciencedirect.com

ELSEVIER

FOCUS ARTICLE

Evidence-Based Scientific Data Documenting the Treatment and Cost-Effectiveness of Comprehensive Pain Programs for Chronic Nonmalignant Pain

Robert J. Gatchel* and Akiko Okifuji†
*Department of Psychology, College of Science, The University of Texas at Arlington, Arlington, Texas.
†Pain Research Center, Department of Anesthesiology, University of Utah, Salt Lake City, Utah.
Written for the American Pain Society Task Force on Comprehensive Pain Rehabilitation, Glenview, Illinois.

Abstract: Chronic pain is one of the most prevalent and costly problems in the United States today. Traditional medical treatments for it, though, have not been consistently efficacious or cost-effective. In contrast, more recent comprehensive pain programs (CPPs) have been shown to be both therapeutically efficacious and cost-effective. The present study reviews available evidence demonstrating the therapeutic efficacy and cost-effectiveness of CPPs, relative to conventional medical treatment. Searches of the chronic pain treatment literature during the past decade were conducted for this purpose, using MEDLINE and PSYCINFO. Studies reporting treatment-outcome results for patients with chronic pain were selected, and data on the major outcome variables of self-reported pain, function, healthcare utilization and cost, medication use, work factors, and insurance claims were evaluated. When available, conventional medical treatments were used as the benchmark against which CPPs were evaluated. This review clearly demonstrates that CPPs offer the most efficacious and cost-effective, evidence-based treatment for persons with chronic pain. Unfortunately, such programs are not being taken advantage of because of short-sighted cost-containment policies of third-party payers.

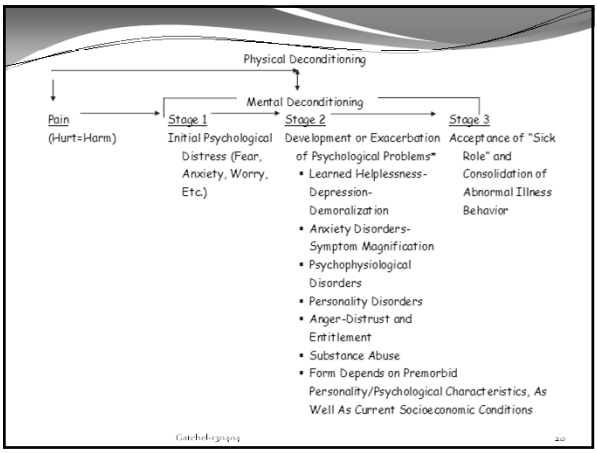
Perspective: A comprehensive review was conducted of all studies in the scientific literature reporting treatment outcomes for patients with chronic pain. This review clearly revealed that CPPs offer the most efficacious and cost-effective treatment for persons with chronic pain, relative to a host of widely used conventional medical treatment.

Key words: Chronic pain, comprehensive pain programs, biopsychosocial, interdisciplinary treatment, cost-effectiveness, treatment efficacy

IDEALLY: PREVENTION OF CHRONIC MUSCULOSKELETAL PAIN AND DISABILITY

TRANSITION FROM ACUTE TO CHRONIC PAIN

GATCHEL MODEL



EARLY INTERVENTION WITH HIGH-RISK PATIENTS

NATIONAL INSTITUTES OF HEALTH (NIH)-SUPPORTED CLINICAL RESEARCH ON THE EARLY IDENTIFICATION AND FR INTERVENTION OF "HIGH RISK" ACUTE LOW BACK PAIN (ALBP) PATIENTS

PROJECT 1

- Large-scale prospective study of over 500 ALBP patients, referred to an occupational medicine clinic, who underwent a comprehensive biopsychosocial evaluation within 6 weeks of the injury.
- Carefully followed this cohort for the next year to determine return-to-work (RTW) status.
- At the end of one-year, approximately 20% cohort did not RTW.

- Used a receiver-operator curve (ROC) analysis, based on the probabilities estimated from a logistic regression model, differentiating RTW and non-RTW patients.
- Statistical algorithm developed that successfully identified (overall accuracy rate=89.2%) RTW (low risk) patients versus non-RTW (high risk) patients.
- Construct validity of the algorithm subsequently demonstrated in two additional NIH-funded projects.

PROJECT 2: EFFICACY STUDY

- A large cohort of ALBP patients were screened to determine their high-low risk status based upon the earlier developed algorithm.
- HR patients were then randomly assigned to: (1) an early intervention FR program group; or (2) a treatment as usual group.
- During the next year, 3-month follow-up evaluations were conducted to assess important socioeconomic outcomes (RTW, healthcare utilization, medication use, etc), as well self-reported pain and disability.

- The early intervention FR program significantly reduced the prevalence of chronic pain and disability on a wide range of work, healthcare utilization, medication use and self-reported variables, relative to the treatment as usual group.
- More likely to have ↑RTW (OR=4.55); less likely to be taking narcotic analgesics (OR=0.44); less likely to be taking psychotropic medication (OR=0.24).
- Treatment as usual group also displayed more symptoms of chronic pain and disability, relative to the initial low-risk patients.

- There were also significant cost-savings over the one-year period: the early intervention FR program cost one-half of what the treatment as usual group cost.

PROJECT 3: EFFECTIVENESS STUDY

- Early FR intervention & Workplace Transition vs. Early FR intervention only vs. Workplace Transition Only.
- Results revealed Early FR intervention was just as efficacious as the combined treatment.
- Cost-effectiveness of the approach was also again demonstrated.

TEMPOROMANDIBULAR JOINT AND MUSCLE DISORDER (TMJMD) is a prevalent musculoskeletal problem in the U.S., and ranks second only to low back pain. Treatment costs average $4 billion annually.

NIDCR- SUPPORTED CLINICAL RESEARCH ON THE EARLY IDENTIFICATION AND INTERVENTION OF "HIGH RISK" TMD PATIENTS

PROJECT 1

- Epker, Gatchel and Ellis (1999) created a statistical algorithm, based on a logistic regression model, which used certain components of the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD).
- Algorithm successfully categorized the risk status (high-risk vs. low-risk) of 91% of acute TMD patients for developing chronic TMJMD problems at one-year follow-up.

PROJECT 2

- Evaluation of whether early biobehavioral intervention with HR patients would produce lower levels of pain one-year follow-up, relative to HR patients not receiving such early intervention (Gatchel, Stowell, Riggs & Ellis, 2006).
- The outcome data showed significant differences between the HR early intervention and the HR non-intervention groups at one-year post-intervention follow-up.

Long-Term Outcome Results at One-Year Follow-up

OUTCOME MEASURES

•Self-reported pain as measured by the Characteristic Pain Intensity (CPI); effect size=.872 ("large")
• Self-reported symptoms of depression as measured by the BDI; effect size=.44 ("medium")
• Adaptive and maladaptive coping styles; effect size for "Self Blame"=.40 ("medium")
• Psychopathology (Affective Disorders, Anxiety Disorders and Somatoform Disorders)
• Health care utilization related to jaw pain (e.g., dentists, orthodontists, oral surgeons, chiropractors, etc.) outside of the study.

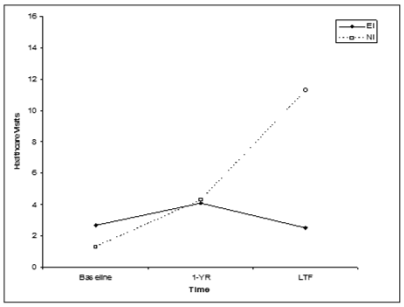
- Stowell, Gatchel, and Wildenstein (2007) examined the cost-effectiveness between the intervention group and the non-intervention group. Health-care costs related to jaw pain were collected for all patients throughout the duration of the study, from initial complaints of pain to the one-year milestone of the study.
- Examples of types of expenses patients might incur included: costs for health-care visits; treatments that require appliances/splints; travel distance and time to visits; medicine; etc.

- The cost analysis showed significantly larger overall costs connected with the non-intervention group, compared to the intervention group. For example, the non-intervention group spent an average of $422.91, while the early intervention only spent an average of a mere $131.84. This is a statistically significant difference of almost $300. This does not include averages at the initial intake as there were no differences.

- Also completed an initial investigation of even longer-term follow-up results of patients used in the above two studies by Gatchel and colleagues.
- In this analysis by Gatchel (2010), longer-term follow-up post-treatment results (from an estimated two to six years since initial intake) were assessed in order to establish if the benefits achieved at one-year were maintainable.
  - Results plainly showed this sustainability, with the early intervention group exhibiting lower pain and indicators of depression at long-term follow-up, compared to the non-intervention group.

- Furthermore, the patients who received early intervention reported a continuation of the use of skills and techniques at the long-term period, and they regarded the intervention as very helpful, with 96% very likely or likely to recommend the intervention to others.
- Also, the patients who received early intervention had a significantly smaller amount visits to health care professional for jaw-related pain, compared to patients who received no intervention (Gatchel, 2010).

Statistically Significant Linear Trend for Jaw-Pain Related Health Care Visits



EI=Early Intervention

NI=Non-Intervention

LTF=Long-term Follow-up (2-6 Years Post Treatment)

PROJECT 2
AN IMPLEMENTATION AND BIOBEHAVIORAL STUDY OF TMD

- To both replicate and implement the results of our just-completed randomized controlled trial in community-based clinics. It is hypothesized that our early biopsychosocial intervention will be both more therapeutically- and cost-effective in these community settings, relative to an attention-control group, at post-intervention, one-year and two-year follow-ups.

- To more comprehensively evaluate biobehavioral patterns in TMJMD, at both the acute and chronic stages, as well as for both high-risk and low-risk acute TMJMD patients. For example, it is hypothesized that, at both post-intervention and the one- and two-year follow-ups, there will be significant differences in functional chewing performance between the high-risk, early intervention and high-risk attention-control groups.

- 675 acute TMJMD patients are being recruited from a variety of community dental clinics in the Dallas-Ft. Worth area. Based upon our "risk" screening algorithm, those patients who meet the criteria for high risk of developing chronicity are being randomly assigned to one of two groups: (1) an early biopsychosocial intervention group; or (2) an attention/education control group. We are also including a sample of acute low-risk TMJMD patients as an observational control group.

- Patients with acute onset (≤ 6 mos.) of TMJMD are considered at "high-risk" for developing chronic pain symptoms if they endorse moderate to severe levels of pain on the Characteristic Pain Intensity Scale (CPI; a portion of the RDC/TMD History Exam).
- Some patients are also being included within the "high risk" parameters who identify 3 or more physical points of facial/jaw pain during the physical examination portion of the RDC/TMD that uses palpation.

- Patients who are identified as "high-risk" during this baseline evaluation are being randomized into one of two treatment groups:
  - Biobehavioral Treatment: Includes training in Biofeedback, Cognitive-Behavioral Coping Skills, Progressive Muscle Relaxation, and other risk reduction strategies.
  - Self-Care Treatment: Involves an educational didactic format that guides the participant through understanding how to reduce and prevent further pain symptoms.

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Poster Presentations: Schedule and Abstracts

Poster Presentations: Schedule and Abstracts

1

Preliminary Findings from an Asynchronous IPE Activity: A Qualitative Study of Health Professions Students' Interprofessional Education Experience in a Virtual Environment

Theresa V. White[1]*, Pamela A. Duffy, PT, Ph.D.[2], Teri Stumbo, PT, Ph.D.[2], Kari N. Smith, D.P.T.[2], Julie Ronnebaum, D.P.T.[2]

[1]Des Moines University, College of Osteopathic Medicine, Des Moines, IA
[2]Des Moines University, College of Health Sciences, Des Moines, IA

The purpose of this research project was to examine the use of a case-based, asynchronous, virtual IPE learning activity on students' self-assessment of their own learning outcomes. Participants (N=314) were health professions students from eight clinical and non-clinical graduate programs at DMU, who were randomly assigned to an interdisciplinary team. This qualitative project used narrative reflection papers as the data collection method for data analysis. These data were coded for major themes and sub-themes. Preliminary findings indicate that the participants were able to identify key knowledge and affective domain learning outcomes which corresponded to desired IPE core competencies. Conclusions support the use of a virtual learning environment and patient case study as an innovative and effective IPE teaching strategy to enhance learning outcomes.

2

The Impact of Relationship Status on HPV Vaccination and Beliefs

Emily Sibigtroth[1]* and Rachel Reimer, Ph.D.[2]

[1]Des Moines University, College of Osteopathic Medicine, Des Moines, IA
[2]Des Moines University, College of Health Sciences, Des Moines, IA

The purpose of this study was to examine the impact of gender and relationship status on HPV vaccination and beliefs related to vaccination among White and Hispanic men and women. Differences in vaccination status, anticipated impact of HPV infection and the HPV vaccine were examined. A community sample was recruited from local health care clinics in Des Moines, IA between May 2010 and December 2011. Participants (N=507) were White (n=243) and Hispanic males (n=202) and females between the ages of 14-30. Results indicate that participants' relationship status may influence likelihood of receipt of an HPV vaccine recommendation from a healthcare provider. Additionally, gender appears to affect participants' perceptions of the potential impact of HPV and the vaccine on their romantic relationships and physical health. Several relationship status by gender interactions emerged. Overall, it appears as though relationship status does not impact the beliefs and attitudes for females as much as it does for males. These results suggest patients and practitioners' beliefs and behaviors may be influenced by the gender and relationship status of their patients.

3

Predictors of Health Information Avoidance

Sivan Ben-David[1]*, Kathleen Stover[1], Rachel Reimer Ph.D.[2]

[1]Des Moines University, College of Osteopathic Medicine, Des Moines, IA
[2]Des Moines University, College of Health Sciences, Des Moines, IA

Information avoidance (IA) is the choice to either temporarily or permanently avoid unwanted information relevant to the self or others central to the self. Research on health information avoidance is important as

there are at times potential benefits associated with increased knowledge (e.g. early detection). Yet there are still many gaps in the literature, such as few comparisons on the differences in IA between pertinent health issues, and many individual differences that have not yet been empirically examined in connection with IA. 609 participants were presented with information regarding genetic mutations associated with AIDS, Hereditary Hemochromatosis, Alzheimer's, Breast/Prostate Cancer, and Amyotrophic Lateral Sclerosis. Participants were asked a series of questions about their perceptions of the medical conditions and whether they would like to know whether they had the genetic variation for each disease (IA). Perceived benefit and importance of the genetic test and anticipated regret were strong predictors of IA for all medical conditions. Perceived severity and susceptibility, and anticipated change in self-concept, change of future plans, negative emotions, and impact were predictors of IA only for certain diseases. Individual difference such as age, income, dispositional optimism, experiential/rational inventory (REI), and subjective health were also all predictors of information avoidance for certain medical conditions. These results are the first to test patterns of information avoidance among a large diverse sample for multiple health conditions and the first to show trends for IA and individual differences such as REI. Implications for past and future research are discussed.

4

Gender and Ethnic Differences in Social and Behavioral Factors Related to Human Papillomavirus Vaccination Rates Among a Community Sample

Julie Schommer[1]*, Tara Blalock Hughes[2], Rachel Reimer, Ph.D. [2]

[1]Des Moines University, College of Osteopathic Medicine, Des Moines, IA
[2]Des Moines University, College of Health Sciences, Des Moines, IA

The purpose of this study was to examine factors associated with HPV vaccination among White and Hispanic men and women. Differences in HPV knowledge, sources of information, vaccine awareness, vaccination status, and interest in vaccination were examined. A community sample was recruited from local health care clinics in a medium sized Midwestern city between May 2010 and December 2011. Participants (N=507) were White (n=243) and Hispanic males (n=202) and females between the ages of 14-30. Results indicate that Whites and women were significantly more likely to have heard of HPV, have higher levels of HPV knowledge, have been diagnosed with HPV, to be aware of the HPV vaccine for women. Whites and Women were also more likely to have heard of HPV from their physicians. Hispanic and female participants were significantly more interested in receiving the HPV vaccine in the future. There was no effect of ethnicity on interest in the vaccine per a doctor's recommendation, however. Findings suggest that Whites and females have greater levels of HPV awareness and knowledge and that while Hispanic participants are less likely than Whites to be told about the HPV vaccine from their provider; they may be equally receptive to such a recommendation.

5

Middle Trapezius Muscle Strength in People With and Without Chronic Neck Pain

Aimee Dahlhauser[1]* and Shannon Petersen, P.T.[2]

[1]Iowa State University, Department of Biology, Ames, IA
[2]Des Moines University, Doctor of Physical Therapy Program, Des Moines, IA

Objective: To compare middle trapezius strength between people with and without chronic neck pain.

Background: Strength and endurance deficits of the middle trapezius muscle are a component of the neck pain clinical practice guidelines for patients with movement coordination impairments. Previous research has found significant side-to-side differences in lower and middle trapezius strength in people with unilateral

neck pain and suggests pain can be associated with imbalances of the trapezius muscle. No studies to date have compared middle trapezius strength between people with neck pain and healthy individuals.

Methods: Thirty-four individuals with and without neck pain participated in the study. Middle trapezius muscle strength was assessed bilaterally in each group using a handheld dynamometer. Paired t-tests were used to determine within-subject differences and independent t-tests were used to determine between group differences.

Results: Significant differences were found bilaterally in people with neck pain ($p < 0.001$), between the ipsilateral to pain side and the control's right side ($p < 0.001$), and between the contralateral to pain side and the control's left side ($p = 0.052$). No significant difference was found bilaterally in the control group.

Conclusion: The results of this study demonstrate that people with unilateral neck pain have weaker middle trapezius muscles than individuals without pain. It is also confirmed that within painful subjects, the side with pain is significantly weaker than the opposite. This study suggests that neck pain and a weak middle trapezius muscle may be correlated.

6

First Metatarsophalangeal Joint Fusion and its Effects on Function and Gait

David Burt*, Nathan Shumway, Mindi J. Feilmeier, D.P.M., FACFAS

Des Moines University, Des Moines, IA

Hallux abducto valgus (bunion) and hallux limitus are two common pathologies of the foot. A hallux abducto valgus deformity is known as a lateral deviation of the great toe and can cause pain and difficulty with gait. A hallux limitus deformity is stiffness of the great toe which limits its range of motion. Both of these conditions once severe enough can cause pain and difficulty with gait and it is at this point that patients start seeking medical help. A first metatarsophalangeal joint (MPJ) fusion is a fusion between the head of the first metatarsal and the base of the first proximal phalanx. Some alternative methods for patients are cheilectomy, osteotomy, and arthroplasty. We believe that first MPJ fusion yields equal to or better results and allows for a quick recovery time without the need for revision later. This procedure causes the patient no functional limitation, only the inability to wear a high heeled shoe. The literature shows that normal range of motion of the MPJ is 65 degrees of dorsiflexion but that does not necessarily mean that 65 degrees is required for gait [1]. Current knowledge is that a first MPJ fusion only be used in severe cases of the previously mentioned pathologies as well as cases of severe arthritis and as a recovery procedure for other failed surgeries [2]. Surgeons who currently think this are concerned that the patient will have functional gait derangement with this procedure. It has been Dr. Feilmeier's experience that this is not the case and patients are very pleased with the results. Dr. Feilmeier has also seen no gait derangement in her patients and noticed with video gait analysis that it is nearly impossible to differentiate which side the person has had the procedure on.

References

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7

Fusions Between Nuclear Estrogen Receptors and Red Fluorescent Protein

Tanner Davis*, Mark VerMeer, Quang-Kim Tran, M.D., Ph.D.

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

The reduction in circulating estrogen concentration in post-menopausal women is associated with a substantial increase in risk and incidence of cardiovascular disease. Hormone replacement therapy is expected to restore the cardiovascular protection conferred by estrogen but has not shown to provide the desired effects. Our central hypothesis is that specific targeting of estrogen receptor subtypes could produce better outcomes and prevent undesirable effects. We have previously observed that chronic estrogen treatment substantially upregulates the expression of total cellular calmodulin, a ubiquitous yet limiting signaling molecule, in the vasculature. This project is part of the studies identifying the estrogen receptor(s) (ER-α, ER-β, or the novel G protein-coupled estrogen receptor (GPER)), responsible for the effect of 17β-estradiol to upregulate cellular CaM. ER-α and ER-β were PCR amplified from existing plasmids encoding the respective human sequences. The red fluorescent protein $DsRed_2$ was then fused to the C-terminus of each receptor. Next, the fusion DNAs were introduced into a mammalian plasmid. These plasmids were then transiently transfected into human embryonic kidney HEK 293 cells. Intracellular imaging contrasting $DsRed_2$ and loaded fura-2/AM fluorescence revealed nuclear expression for ERα-$DsRed_2$ and ERβ-$DsRed_2$ fusions, consistent with the functional role of ER-α and ER-β as nuclear receptors. The successful heterologous expression of these fusion proteins allows for subsequent evaluation of total CaM expression following chronic treatment with 17β-estradiol.

8

Regulation of Store-Operated Ca^{2+} Entry in the Vascular Endothelium by the G Protein-Coupled Estrogen Receptor GPER/GPR30

Lara Terry[1]*, Mark Ver Meer[2], Jennifer Giles[2], Quang-Kim Tran, M.D., Ph.D.[2]

[1]Drake University, Des Moines, IA
[2]Des Moines University, College of Osteopathic Medicine, Department of Physiology and Pharmacology, Des Moines, IA

The novel G protein-coupled estrogen receptor (GPER/GPR30) has been found to participate in numerous cardiovascular functions. Store-operated Ca^{2+} entry (SOCE) is an essential mechanism that is required for many endothelial cell functions. We found that activation of GPER using the GPER specific agonist G1 is associated with a dose-dependent inhibition of SOCE in primary vascular endothelial cells. Interestingly, the GPER specific antagonist G15 increases SOCE in cells unstimulated by GPER intrinsic or exogenous ligand. Overexpression of GPER in HEK 293 cells is associated with a 40% decrease in the rate of SOCE, while knockdown of GPER in endothelial cells using antisense oligomer directed against GPER increases SOCE by approximately 50%. In addition, coimmunoprecipitation revealed that GPER exists in endothelial cells as a glycosylated protein and forms a complex with the stromal interaction molecule 1 (Stim1). These data suggest that GPER may be an important regulatory input of store-operated Ca^{2+} entry via its interaction with Stim1.

9

Statins and Aminoglycosides in Combination have Synergistic Antimicrobial Effects

Kelsey M. Randel*, Holly Hulsebus, Matthew K. Henry, Ph.D., Jeffrey T. Gray, Ph.D.

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Sepsis is the 10th leading cause of death in the United States. The emergence of antimicrobial resistant strains has limited treatment options. Studies have shown that HMG-CoA reductase inhibitors, or statins, have pleotropic effects beyond their intended cholesterol lowering capabilities. This study examined the potential synergistic effects of statins and antimicrobials on *Staphylococcus aureus*. Thirteen *S. aureus* strains, five MSSA and eight MRSA, were utilized in this study. Bacterial growth was measured by optical density (OD_{600nm}) comparing controls to treatment combinations of five statins and ten class representative antimicrobials. Subtherapeutic concentrations of aminoglycosides (gentamicin; 0.125µg/mL, amikacin; 1.0µg/mL, kanamycin; 1.0µg/mL) had a significant synergistic effect on *S. aureus*, when combined with inactive simvastatin (15µM). Synergism was not observed with any other antimicrobial class. Statins induced a dose-dependent decrease in bacterial cell growth, as they increased in concentration (7.5µM-60µM), when gentamicin concentration was held constant (0.125µg/mL). There was no significant difference between MSSA and MRSA. In combination, aminoglycosides and statins have a synergistic antimicrobial effect on *S. aureus*. This effect was limited to aminoglycosides and was not observed with any other antimicrobial class. While all statins show a synergistic antimicrobial effect, generally fungal derived statins (simvastatin and lovastatin) are more potent than synthetic statins (atorvastatin and fluvastatin). Inactive simvastatin was the most potent and efficacious statin tested. Of clinical relevance, this antimicrobial effect is independent of methicillin resistance. Therefore, as statins enhance the antimicrobial action of aminoglycosides at subtherapeutic concentrations, they should be explored further as a possible aid in sepsis treatment.

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Screening of *C. Albicans* Libraries for Mutants with Abnormal Resistance to Boric Acid

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In this study, two *C. Albicans* deletion libraries were screened for abnormal boric acid resistance. *C. albicans*, which is naturally found in the microbiome of many people, is an opportunistic pathogen and the most frequent cause of fungal infection in the United States (Noble, 2010). As the prevalence of drug resistant yeast strains is increasing clinically, it is becoming more vital to develop new antifungal treatments. It has been shown that boric acid (BA) is toxic to yeast, however the mode of action is still unknown (Schmidt, 2011). Before further development of a BA-based topical treatment can be made, the exact molecular action must be identified. In this study, 735 different homozygous null mutants of *C. albicans* from both the Homann and Noble deletion libraries were screened for BA resistance. Values of the minimum inhibitory concentration (MIC) for each mutant were observed and recorded. The data from each collection was cross-referenced for duplicates, and a list of sensitive or resistant mutants was produced. It is the intent of further study to examine the function of the genes deleted from these selected mutants in order to generate hypotheses into what mechanism BA may target in a growing yeast colony.

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Regulation of Brain MAPK Protein Activity after Exposure to Chronic Restraint Stress

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Major depressive disorder (MDD) is one of the most debilitating psychiatric illnesses that has been linked to changes in function and activity of the hippocampus and prefrontal cortex (PFC), central limbic regions involved in regulation of emotions and mood. However, the specific neural events underlying the wide range of clinical symptoms and altered responses to stress are still poorly characterized. Our previous findings have shown enhanced activation of mitogen-activated protein kinase (MAPK) phosphatase-1 (MKP-1), a negative regulator of MAPK pathway, in brains of depressed human subjects and chronically stressed animals, which further implicates attenuated activity of the MAPK signaling in depression pathophysiology. In this study, we examined changes in activation of individual MAPK proteins that may underlie pro-depressive actions of MKP-1 in the limbic brain regions. Using western blot analysis we assessed the phosphorylation state of c-Jun N-terminal kinase (JNK) and extracellular signal-regulated kinase (ERK) proteins within the hippocampus and PFC of rats exposed to chronic restraint stress (CRS) paradigm. CRS consisted of exposing animals to 60 min of restraint twice daily for 21 consecutive days. Development of depressive-like behaviors in CRS animals was assessed in sucrose preference and novelty suppressed feeding tests. Together these studies will improve our understanding of the role that MKP-1 and MAPK signaling play in development of depression and may further help identify novel targets for treatment and diagnosis of this neurological disorder.

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Molecular Analysis of Isogenic Salmonella Typhimurium Strains Carrying Different Inc Plasmids

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In *Salmonella* increased antibiotic resistance is often due to multiple plasmids. Previous work from our lab has shown the presence of several plasmids in clinical *Salmonella* isolates that confer multiple antibiotic resistance. One of the genes that these plasmids carry is bla_{cmy2} that confers resistance to second generation cephalosporins. Some of these plasmids were transferred into an antibiotic sensitive *Salmonella* Typhimurium background. In this study, we compared six plasmid positive *Salmonella* strains with their isogenic plasmid-negative parent in order to determine their role in antibiotic resistance as well as stress response of *Salmonella*. We performed multiplex and simplex PCR to ascertain how many plasmids were transferred from the donor to the recipient strain. We also used PCR to determine if bla_{cmy2} gene was successfully transferred. Our data show that strains SA430 and SA437, which carried two Inc plasmids, were only able to transfer the Inc A/C plasmid to the recipient *Salmonella* strain SA321. The bla_{cmy2} gene was found to be associated with the Inc A/C plasmid because our newly formed strains were both positive for the bla_{cmy2} gene. SA439 strain carrying the I1 plasmid successfully transferred its plasmid into the recipient strain. Our growth and stress response analyses do not reveal any significant difference between the strains suggesting no significant fitness cost on the host due to the presence of these large plasmids. With this study, we hope to increase the understanding of the role of these plasmids in both fitness and stress response of *Salmonella* Typhimurium isolates.

Effects of Pan-Caspase Inhibitor on Herpes Simplex Virus Type 1 Gene Expression

Bridget Conlon*, Prajakta Pradhan, Marie Nguyen, Ph.D.

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

Herpes simplex virus 1 (HSV-1) can cause disease as mild as oral lesions or as a severe as a potentially fatal disseminated infection in neonates. A principal response of cells infected with a foreign agent is apoptosis, a form of programmed cell death. Apoptosis involves the activation of a cascade of key proteins known as caspases, which are a family of cysteinyl aspartate-specific proteases. Caspases degrade essential proteins within the cell and are ultimately responsible for the morphological changes characteristic of cells dying through apoptosis. Prior research in Dr. Nguyen's laboratory illustrated that blocking caspase activity significantly decreased the viral yield of HSV-1. Thus, activation of the apoptotic pathway enhances replication of HSV-1. However, the specific point in viral replication that is blocked by apoptosis inhibition has not yet been determined. We investigated the impact of apoptosis on HSV-1 gene expression of two immediate-early genes, ICP0 and ICP27, and one early gene, Pol, in the presence and absence of a pan-caspase inhibitor, zVAD-fmk. Pre-treated and untreated human carcinoma, HEp-2, cells were mock infected or infected with the wild type HSV-1 in the presence or absence of the pan-caspase inhibitor. RNA was isolated from infected cells at 3 and 6 hours post infection and was reverse transcribed. The cDNA was used for qPCR analysis using primers specific to ICP0, ICP27, and Pol sequences. A statistically significant increase in the gene expression of ICP27 was detected in the HEp-2 cells at 6 hours post infection with wt HSV-1 in the presence of a pan-caspase inhibitor.

Oral Presentations: Schedule and Abstracts

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Movement Science and Public Health

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1:40 p.m.	Is Handedness Associated with Turning Preference During Gait? **Abigail Jergenson***, Andrea Rindfleisch, Catherine Stevermer, PT, Ph.D.	30
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Biomedical Sciences

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Human Papillomavirus and Vaccine Knowledge, Beliefs, and Barriers to Vaccinate Among Medical and Physician Assistant Students

Jessica Gustavson[1]*, Julie Schommer[1], Rachel Reimer, Ph.D.[2]

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Specific Goals: The aims of this study were to determine the level of knowledge and beliefs among future healthcare providers about Human Papillomavirus (HPV) and the HPV vaccine. Specifically, we evaluated differences in knowledge, beliefs, and barriers to vaccinate due to political affiliation, religiosity, and class in clinical program.

Methods: Surveys were completed by 373 male and female students in the physician assistant and doctor of osteopathic medicine programs at Des Moines University. Measures incorporated demographic information, sources of information related to HPV, vaccination status, intent to get vaccinated, knowledge and beliefs of HPV and the vaccine, perceptions of future patients' and parent's attitudes and beliefs, intent to recommend the vaccine to future patients, and barriers to recommending the HPV vaccine.

Summary of Results: Results revealed significant associations between religiosity and political affiliation on knowledge, beliefs, and perceived barriers to recommending the HPV vaccine to future patients.

Conclusion: The results of this study demonstrate how political affiliation and religiosity impact the knowledge and beliefs of HPV and HPV vaccination, in addition to perceived barriers to vaccinate.

Review of Pathomechanics of Equinus Deformity: A Proposed Study on Outcomes and Complications Associated with Surgical Treatment

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Equinus deformity, or limited dorsiflexion, is often due to contracture of the triceps surae muscles. Equinus is frequently defined at less than 10 degrees, and more conservatively <5 degrees, of passive dorsiflexion with the knee extended. Because equinus is not well defined, the prevalence of this condition is not well known either. Therefore, equinus deformity is under-diagnosed and under-treated. Equinus causes changes to normal biomechanics of gait including; pronation at the subtalar joint resulting in excessive midtarasal joint movement, changes to heel rise and changes to pressure distribution throughout gait. These changes lead to numerous foot pathologies including plantar fasciitis, metatarsalgia, flat-foot and plantar pressure ulcer formation. Additionally, equinus leads to secondary gait deviations at the hip and knee joints which result in pathologies such as lumbar lordosis and genu recurvatum. Conservative treatment has been shown to be ineffective in resolving equinus deformity, while surgical intervention offers true correction. Gastrocnemius or gastrocnemius-soleus recession is commonly the surgical intervention of choice. Complication rates and outcomes have not been studied extensively for these procedures. Our study will look retrospectively at patient charts with gastrocnemius-soleus recession used for correction of foot pathology. We will assess rates of complications as well as the success of the procedure in terms of range of motion, pain and activity level pre and post operatively.

Is Handedness Associated with Turning Preference During Gait?

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Background: Most people are consistently left-hemisphere dominant and are right handed and right footed. There is ambiguity when associating handedness with directional turning preferences. Some researchers demonstrate handedness as strongly associated with the same side turning preference, but results are inconsistent. The purpose of this project is to determine if handedness is associated with turning preference.

Methods: 53 older adult subjects participated in this study. Handedness was determined for each subject via request. Each participant completed 5 trials of right turns, left turns, and Timed-Up-and-Go (TUG) tests. Turning trials were collected using the GAITRite mat and processed with ProtoKinetics software. Turning velocity, initial turn direction, and TUG turn direction were utilized as indicators of turning preference.

Results: Handedness appeared to be associated with a preference for an opposite initial turning direction (p-value = 0.021). Right handed people turned to the left 98% of the time. Handedness was not associated with turning preferences during TUG tests or turns to the right or left with higher velocities.

Conclusions: Based on the apparent association between handedness and initial turn preference, prediction of favored turn direction seemed possible. However, the lack of association with other turning indicators may suggest the topic needs further exploration.

Changes in Stance Event Times and Rocker Duration Due to Gait Speed

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In the stance phase of the traditional gait cycle, rockers are used to describe which lower body structures are moving with respect to others. These rockers can be defined by the contact and lift events of the heel and forefoot and are generally assumed to maintain a consistent proportion of the gait cycle in healthy individuals. To test this assumption, motion capture data from a recent study was recompiled using kinematic analysis to detect these boundary events consistently. In this analysis, we have found that this assumption may not hold. While these results are limited in scope by the available data, they invite new questions about the traditional gait cycle under various conditions and the effects these conditions may have on various foot pathologies.

Activity Levels of Patients Post Total Hip Arthroplasty

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Introduction: Total hip arthroplasty (THA) is a common surgical procedure used for patients suffering from osteoarthritis of the hip. Osteoarthritis is a painful condition which limits patient function and activity, and the

goal of THA is to restore function and improve activity. Maintaining adequate physical activity is essential to avoid comorbidities such as diabetes and heart disease.

Objective: The goal of the present study was to examine how activity levels change post THA. Specifically, the goals were: to know if THA patient activity level changes following surgery, how THA patient activity levels compare to controls and finally to know if Body Mass Index (BMI) has an influence on activity.

Methods: An accelerometer was used for activity measurement (ActiGraph, GT3X). THA patients (n=35) were recruited from 2 local orthopedic surgeon practices, and healthy cohorts were recruited from faculty and staff as Des Moines University. Subjects came to the Human Performance Laboratory presurgery (PRE), 3 months postsurgery (THREE), 6 months postsurgery (SIX) and 12 months postsurgery (TWELVE). Following this session, they were instructed to wear the ActiGraph on the hip for a 2 week period. 4 activity parameters were examined: total activity minutes, total activity counts, quality activity minutes and quality activity counts. Quality activity was defined as moderate to vigorous intensity.

Analysis: The change in physical activity of the patients post THA and the comparison between the patients and the matched healthy cohorts was evaluated using a two-way ANOVA mixed design (Group x Time) on each of the outcome measures. In examining the effect of BMI on activity levels, the reported data was examined using an ANCOVA, using BMI as the covariate. The Pearson Product Moment Correlation Coefficient was used to test the relationship between the physical activity measures and BMI for the patient group.

Results: Data analysis showed that there were no significant changes in activity levels among THA patients in all activity parameters. This held true across all measured time frames. Group results (THA patients vs. controls) showed that THA patients were less active than controls in quality activity, in the quality activity counts measurement. This result held true at PRE (p=.003), THREE (p=.020) and SIX (p=.034), however no difference was seen at TWELVE (p=.217) All other activity parameters showed no significant difference in activity between THA patients and controls. BMI data showed BMI having little to no influence on activity post THA. We had no significant correlation between BMI and activity, except for total activity minutes at TWELVE (p=.034, Pearson Correlation= -.425)

Conclusion: Activity levels do not appear to significantly change post THA. For the majority of activities, THA patients have similar activity levels to controls. BMI alone does not appear to have a direct correlation with activity levels post THA.

Novel Fluorescent Reporters for the Stromal Interaction Molecule 1

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The stromal interaction molecule 1 (Stim1) is a Ca^{2+} sensor in the endoplasmic/sarcoplasmic reticulum whose Ca^{2+} sensing triggers its oligomerization and subsequent activation of store-operated Ca^{2+} entry via direct interactions with Ca^{2+} channels at the plasma membrane. We have generated a set of fluorescent reporters based on the intraluminal domain Stim1 where dimerization and Ca^{2+} binding take place. These fluorescent reporters consist of a FRET pair (ECFP-EYFPc) flanking the Ca^{2+}-binding loop of the canonical EF hand, the entire canonical EF hand, the hidden EF hand, and the sterile α motif (SAM), or a combination of these fragments. All reporters display enhanced FRET upon Ca^{2+} binding and FRET disruption upon Ca^{2+} chelation from a Ca^{2+}-saturated state. Reporters generated from the unmodified canonical EF domain and the Ca^{2+}-binding loop of this domain display the largest dynamic range in Ca^{2+}-dependent responses. However, double-loop or triple loop chimeras of the linker yield significant improvement in the dynamic range of the biosensors upon interaction with Ca^{2+}. Analyses of spectrofluorometric Ca^{2+} titrations yielded apparent dissociation constants in the millimolar range for these reporters. The highly quantitative nature of the responses will enable highly quantitative studies of factors that affect the Ca^{2+} sensing capability of Stim1 in vitro and in cells.

Efg1/Tup1 Control of Hyphal Growth Determines Boric Acid Resistance in *Candida albicans*

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Although *Candida albicans* can be naturally found in the human flora, it is an opportunistic pathogen that can cause serious fungal infection, especially in immunocompromised patients (Noble et al. 2010). Boric acid (BA) has been shown to inhibit growth of *C. albicans*, though the exact mechanism is not yet known. In this experiment, three mutant strains of *C. albicans* – *Δtup1, Δefg1*, and *Δnrg1* – were observed under varying concentrations of BA. *C. albicans* is unique because it is able to exhibit multiple morphologies: yeast-like, pseudohyphal, and hyphal. These three mutants were selected for study because show abnormalities in the induction of hyphal growth, which has been shown to correlate with increased pathogenicity of *C. albicans*. It was observed that *Δtup1* and *Δnrg1* mutants were unable to repress filamentous growth and demonstrated a heightened sensitivity to BA. In contrast, *Δefg1* mutants do not show hyphal growth and were found to be particularly resistant to BA. It was also observed that BA acts as a fungistatic agent rather than a fungicidal agent.

Purification and Characterization of a Putative Invertase from *Trichomonas vaginalis*

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Trichomonas vaginalis, a flagellated protozoan, is the agent responsible for trichomoniasis, the most common nonviral sexually transmitted infection worldwide. A reported 200 million cases are documented each year with far more cases going unreported. However, *T. vaginalis* is disproportionality under studied, especially considering its basic metabolism. It has been demonstrated that *T. vaginalis* does not grow on sucrose. However, the *T. vaginalis* genome contains some nine putative sucrose transporters and a putative β-fructofuranosidase (invertase). Thus, the machinery for both uptake and cleavage of sucrose appears to be present. We amplified the β-fructofuranosidase from *T. vaginalis* cDNA and cloned it into an *Escherichia coli* expression system. The expressed, purified protein was found to behave similarly to other known β-fructofuranosidases. It had a similar K_m and V_{max} to previously characterized enzymes using sucrose as a substrate and was also active towards raffinose. Thus, *T. vaginalis* has the coding capacity to produce an active β-fructofuranosidase. Since we cloned this enzyme from cDNA, we know that the gene in question is transcribed. Therefore, the reason why *T. vaginalis* is unable to effectively grow on sucrose remains to be determined.

Response of *Salmonella* Clinical Isolates to Environmental Stress Conditions

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One of the defining issues in medical care is the prevention of nosocomial transmission of infection. This imperative has led to increased awareness of the importance of disinfection strategies in patient care. *Salmonella spp.* are not a major source of nosocomial infections, but are a constant concern in food preparation, an environment that has similar disinfection challenges and needs. It has been previously

shown that plasmid carrying strains of *Salmonella* possess evolutionary advantages in the presence of antibiotics, but grow more slowly than wild type variants in the absence of antibiotics. This dichotomy leads to a question of why these resistance gene-carrying plasmids are retained even after several generations of growth in unstressed medium. This experiment sought to identify possible evolutionary advantages of plasmid-containing strains of *Salmonella*, by evaluating the growth rates of five different *Salmonella* strains after exposure to different concentrations of ethanol and sodium hypochlorite (bleach). The results were evaluated for deviation against a control sample that was grown without exposure to chemical stress. During ethanol testing, only one isolate showed reduced cellular growth when compared to the unstressed strain, SA334. Exposure to a 1:50 dilution of 6% sodium hypochlorite (1000 ppm) did result in a notable inhibition in cellular growth from the unstressed sample for all strains. This inhibition in growth after exposure to bleach concentrations considered to be bactericidal by CDC health guidelines is not surprising. However subsequent plating of 1microliter of culture revealed that removal of stress after initial exposure allowed enough bacteria to survive to produce colonies. Further experimentation is necessary to identify the mechanisms *Salmonella* use to survive exposure to bactericidal conditions.

Analysis of Depressive-Like Behaviors in Rodent Chronic Pain Models

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Clinical reports indicate that many chronic pain patients also develop symptoms of mood disorders, especially major depressive disorder (MDD); however, the underlying neural mechanisms linking chronic pain conditions and depressive behaviors are still poorly understood. Our previous studies have demonstrated that rodent models of chronic pain mimic some of the stress-like alterations in intracellular signaling and cellular architecture (e.g., decreased neurogenesis) within the hippocampus, a limbic brain region involved in regulation of mood. In this study, we examined the effects of persistent pain on development of depressive-like behaviors in rodents. Male rats were initially exposed to injection of complete Freund's adjuvant (CFA; model of chronic inflammatory pain) OR spared nerve injury (SNI; model of chronic neuropathic pain). Animals were then monitored for mechanical and thermal hypersensitivity, as well as the presence of anhedonia and anxiety-like behaviors. Our findings indicate that CFA administration produced significant thermal hyperalgesia and mechanical allodynia in the ipsilateral paw, while SNI induced significant mechanical allodynia without thermal hypersensitivity. Furthermore, SNI animals evoked significant reduction in sucrose intake during sucrose preference testing, a behavioral effect indicative of anhedonia – a hallmark symptom of depression. In contrast, the CFA pain model produced less robust effects on sucrose consumption and anxiety-like behavior in novelty suppressed feeding test. The results of this study, in addition to the ongoing molecular tissue analysis, may ultimately contribute towards the identification of new treatment targets and the development of novel clinical strategies to diminish the mental health consequences of chronic pain.

The Effects of Moderate Intensity Exercise Training on the Incidence of Supraventricular Arrhythmias and Atrial Connexin40 Expression in Young and Aged Rats

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Connexin 40 (Cx40) is the primary regulator of electrical conduction within the atria. Alterations of Cx40 expression within atrial tissue are associated with the development of atrial arrhythmias. Aging is also

associated with increased incidence of atrial arrhythmias. We hypothesized aging would result in increased supraventricular arrhythmias accompanied by an alteration of Cx40 expression, while moderate exercise training would counteract these effects. Groups of young (4-6 months) and aged (24-25 months) F344 rats underwent 10-11 weeks of treadmill ET (11-14 m/min, 60 min/day, 5 day/week) or sedentary handling. Subcutaneous electrocardiographic leads were implanted following the young sedentary (n=9), young exercise (n=7), aged sedentary (n=6), and aged exercise (n=6) protocols allowing for electrocardiogram acquisition via the Actiwave telemetry system. The arrhythmic index (AI) was calculated using a modified scoring system totaling supraventricular arrhythmias during a baseline period, sympathoexcitation (isoproterenol s.c. injection), and psychological stressor. Total supraventricular AI was significantly reduced in young compared to aged rats ($p<0.05$). Similarly, the impact of exercise trended toward reducing the supraventricular AI, compared to sedentary rats ($p=0.09$) in both groups. Western blot analysis showed significantly greater atrial Cx40 expression in young exercise rats (n=5) compared to young sedentary rats (n=5) ($p=0.01$). However, atrial Cx40 expression appeared to be similar between the aged sedentary (n=5) and aged exercise (n=2) rats. These preliminary results indicate moderate exercise is cardioprotective through increasing Cx40 expression and decreasing supraventricular arrhythmias in the young rats, however this conclusion cannot yet be made in the aged rat model, although studies are ongoing.

MST-312 Effect on HSV-1 Immediate Early Gene Expression

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Herpes simplex virus (HSV-1) is an infection affecting hundreds of millions across the world. While the initial HSV-1 infection most commonly causes benign cold sores, significant complications can occur under certain circumstances. HSV-1 can cause encephalitis, or migrate to mucosal sites outside of the oral cavity, such that occurs with keratoconjunctivitis. In immunodeficient states, HSV-1 can lead to disseminated infections. Although therapies exist, such as acyclovir, resistance to these agents is developing. It has recently been shown that HSV-1 up-regulates activity of enzymatic telomerase. This enzyme adds nucleotides to the ends of chromosomes, ensuring their stability in normal mitosis. Without this enzyme, chromosomes would shorten at the end of each mitotic cycle and become increasingly fragile. Dr. Nguyen's laboratory has demonstrated that a permeable reversible telomerase inhibitor, MST-312, decreases the extent of HSV-1 infection. Preliminary experiments also suggested that MST-312 is acting on the early phases of the virus life cycle. However, the mechanism whereby this drug is acting on HSV replication it is not completely understood. Using qPCR analysis MST-312's influence on the immediate early genes (ICP0 and ICP27) was determined.

Analyzing the Cytotoxicity of the Telomerase Inhibitor MST-312

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Herpes simplex virus (HSV) is a double stranded DNA virus that attaches to the host cells through glycoproteins on the surface of the virus. HSV is the cause of cold sores and genital herpes. In between outbreaks, the virus remains in neuronal cells. Although there are treatment options available for HSV disease, other treatments may be necessary when antiviral resistance occurs. Therefore, identifying new antiviral targets is important. One such target may be the cellular enzyme telomerase. Telomerase is the enzyme that prevents the shortening of telomeres. Previous research has shown the telomerase activity is increased during HSV infection. Our lab has recently determined that treatment with a telomerase inhibitor, MST-312, dramatically reduces HSV replication. The goal of this study is to characterize the cellular toxicity

of MST-312. To accomplish this, HEp-2 and hTERT-HME1 cells were treated with 2-100 μM of MST-312 for 24 hours. Subsequently, trypan blue exclusion and hemacytometer counts were used to measure toxicity and total cell numbers. There was no significant increase in cell death when MST-312-treated cells were compared to control. However, reduced total numbers of cells were observed following MST-312 treatment, indicating that the treatment was inhibiting proliferation. Further investigation was done using p53 and p21 immunoblots to determine whether MST-312 caused a cell cycle block. The levels of p53 and p21 showed no variation with the MST-312 treatment. Together, these results demonstrate that 2-100 μM MST-312 treatment of HEp-2 and hTERT-HME1 cells is not cytotoxic, but may cause slowing of cell growth.