THE UNIVERSITY of TEXAS

MEDICAL SCHOOL AT HOUSTON

A part of The University of Texas Health Science Center at Houston

2009 SUMMER RESEARCH PROGRAM
STUDENT ABSTRACTS

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Preface

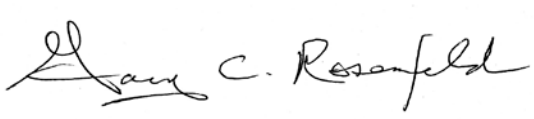
The University of Texas Medical School at Houston (UTMHS) Summer Research Program provides intensive, hands-on laboratory research training for MS-1 medical students and undergraduate college students under the direct supervision of experienced faculty researchers and educators. These faculty members' enthusiasm for scientific discovery and commitment to teaching is vital for a successful training program. It is these dedicated scientists who organize the research projects to be conducted by the students.

The trainee's role in the laboratory is to participate to the fullest extent of her/his ability in the research project being performed. This involves carrying out the technical aspects of experimental analysis, interpreting data and summarizing results. The results are presented as an abstract and are written in the trainees' own words that convey an impressive degree of understanding of the complex projects in which they were involved.

To date, more than 1,700 medical, college, and international medical students have gained research experience through the UTMHS Summer Research Program. Past trainees have advanced to pursue research careers in the biomedical sciences, as well as gain an appreciation of the relationship between basic and clinical research and clinical practice.

UTMHS student research training is supported by a grant from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and/or by financial support from the Dean and the departments and faculty of the medical school.

Biomedical science education remains a vital and integral part of our nation's interests. The UTMHS Summer Research Program, and the dedication of our faculty and administration exemplify the institution's commitment to training and educating the future leaders in our biomedical scientific communities.



Gary C. Rosenfeld, Ph.D.
Director, Summer Research Program
Assistant Dean for Educational Programs

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Acknowledgements

This publication marks the completion of the twenty-fourth year of The University of Texas Medical School at Houston Summer Research Program. The longevity and success of the program are rooted in the overwhelming support received from the deans, faculty, staff and students of UT at Houston Medical School.

Indicative of this support is the administrative assistance and financial support provided by the UTMSH. Sincere appreciation is expressed to Dean Giuseppe Colasurdo M.D. and Patricia M. Butler, M.D., Associate Dean, Office of Educational Programs who continue to insure the yearly success of the Summer Research Program.

Major financial assistance for our Program has also been provided by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) through a short-term research grant (5 T32 DK007676).

Dr. Bryant Boutwell, Associate Vice President for International Programs and Accreditation, has negotiated cooperative agreements with several international medical schools to set up tailored programs for selected international medical students. This international initiative provides the opportunity for our Program to participate in a new area of research education that will be expanded in years to come.

The success of our Summer Research Program depends primarily on the faculty who volunteer to mentor the trainees. These dedicated educators organize and guide the research projects that, for each student, includes data analysis, preparation of an abstract and public presentation of results. Our sincere appreciation to all faculty mentors.

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Lab Research Ownership

Publication and/or Disclosure

Each student participating in this program is required to read, agree to, and sign this disclosure form. The original signed copy is on file in the Summer Research Program office; the student and their faculty mentors are each furnished with a copy.

"In reference to the laboratory research you will perform this coming summer through The University of Texas Medical School at Houston's Summer Research Program, you are required to comply with the standard restrictions regarding participation in the Summer Research Program:

"All of your laboratory research is *CONFIDENTIAL* and although your abstract will be available through our website, you cannot independently disclose or publish any research findings or data in any form (including at meetings or conferences) without the express prior written approval of The University of Texas Medical School at Houston. If you wish to submit your abstract to any third party, you must first contact your faculty mentor no less than three (3) weeks prior to any deadlines in order to obtain the necessary written approvals.

"Because your research was generated from ideas and funds that originated with your faculty mentor and The University of Texas Medical School at Houston, ownership of any data generated by you during the Summer Research Program belongs to The University of Texas Medical School at Houston or the Principle Investigator (PI)."

2009 Summer Research Program
MS1 Students

Last Name	First Name	M	Page #	Department	Faculty Mentor
Aldaz	Sebastian	M	16	Neurology	Jerry Wolinsky
Al-Kalla	Khalid		17	Ophthalmology	Xinping Zhao
Amsbaugh	Mark	J	18	Otorhinolaryngology	Amber Luong
Anderson	Casey	L	19	Surgery	Lillian Kao
Andino	Aldo		20	Internal Medicine	Frank Arnett
Baidwan	Sanjeet	K	21	Integrative Biology & Pharmacology	Stanley Schultz
Basanez	Irving	Z	22	Neurobiology & Anatomy	John Byrne
Bates	Jeremy	R	23	Anesthesiology	Carin Hagberg
Bicknell	Kendall	K	24	Ophthalmology	John O'Brien
Buendia	Francisco	I	25	Surgery	Yanna Cao
Cano	Roxanne		26	Oncology	Joan Bull
Catlette	Gregory		27	Surgery	Anil Kulkarni
Chen	Jared	J	28	Pediatrics	Michael Gambello
Chiu	Caroline		29	Cardiology	Richard Smalling
Chodkiewicz	Hubert	M	30	Orthopaedic Surgery	Terry Clyburn
Claiborne	Paul	M	31	Cardiothoracic and Vascular Surgery	Shelia Coogan
Conner	Christopher	R	32	Neurosurgery	Nitin Tandon
Costales	Anthony	B	33	Orthopaedic Surgery	William Mcgarvey
Cuellar	Derly		34	Neurobiology & Anatomy	Nachum Dafny
Ditzler	Matthew	G	35	Pediatrics	Michael Gambello
Eisemann	Bradley	S	36	Pediatric Surgery	Teichgraeber
Fisher	Stephen		37	Neurosurgery	Timothy Ellmore
Fuller	Clinton	L	38	Pediatric Surgery	Kuojen Tsao
Gutierrez*	Nora		39	Anesthesiology	Carin Hagberg
Harp	Blake	A	40	Ophthalmology	Richard Yee
Heare	Austin		41	Orthopaedic Surgery	Milan Sen
Hiatt	Luke	A	42	Plastic Surgery	David Wainwright
Hiser	Mallorie	T	43	Pediatrics	Jacqueline Hecht
Hogue	Matt	H	44	Orthopaedic Surgery	Milan Sen
Holmes	Michael	G	45	Anesthesiology	Carin Hagberg
Holz	Grant	S	46	Oncology	Robert Amato

Huffsmith	Brooke		47	Surgery	Charles Cox
Johnson	Adam		48	Pathology	Priya Weerasinghe
Kung	David	C	49	Internal Medicine	Yong Jian Geng
Kupsky	Daniel	F	50	Pediatric Surgery	Karen Uray
Levey	Ryan	S	51	Oncology	Robert Amato
Massaey	Colin	J	52	Internal Medicine	Roberto Arduino
McKnight	Brett		53	Ophthalmology	John O'Brien
Medhus	Kristina	A	54	Surgery	Rosemary Kozar
Minor	David	B	55	Ophthalmology	Xinping Zhao
Miranda	Justin	A	56	Orthopaedic Surgery	Catherine Ambrose
Mody	Rayomond	R	57	Oncology	Robert Amato
Moore	Derek	T	58	Microbiology	Heidi Kaplan
Morse	Adrianne		59	Shriners Hospital, Orthopaedic Surgery	Gloria Gogola
Nosrati	Naveed	N	60	Cardiothoracic and Endovascular Surgery	Ali Azizzadeh
Nugent	Cedric	D	61	Cardiothoracic and Vascular Surgery	Shelia Coogan
Nwankwo	Chika	C	62	Ophthalmology	Richard Yee
Ohman	John		63	Neurobiology & Anatomy	Michael Beauchamp
Parry	Joshua	A	64	Orthopedics	Allison Scott
Philip	Asher	S	65	Anesthesiology	Marie Francoise Doursout
Podolnick	Jeremy	D	66	Oncology	Robert Amato
Queen	Joanna		67	Neurosurgery	Raymond Grill
Scerbo	Michelle	L	68	Surgery	John Holcomb
Schakett	Brent	E	69	Surgery	Andrea Hayes-Jordan
Sheikh	Rehman		70	Surgery	Anil Kulkarni
Smallwood	Ashley	K	71	Dermatology	Adelaide Hebert
Spak	David		72	Neurobiology & Anatomy	Anthony Wright
Stavinoha	Tyler	J	73	Orthopaedic Surgery	Thomas Clanton
Syed	Almas		74	Surgery	Anil Kulkarni
Tillman	Ryan	Y	75	Biochem	Cheng Chi Lee

* *The University of Illinois at Chicago Medical School*

2009 International Medical Students

Student Name	Page	University	Faculty Mentor	Department
Hao-yun CHEN	75	China Medical University	Ambro VanHoof	Microbiology
Kuan-Lun FU	76	China Medical University	Nadarajah Vigheswaran	Dental School
Kumiko IMADA	77	University of Tokushima	Anil Kulkarni	Surgery
You LI	78	Southern Medical University	Ali Denktas	Internal Medicine
Chin Han LIN	79	Taipei Medical University	Carin Hagberg	Anesthesiology
Yu-Ling LIU	80	China Medical University	John Byrne	Neurobiology
Yukiya SAKO	81	University of Tokushima	Jeffrey Frost	Integrative Biology & Pharmacology

2009 Summer Research Program
Undergraduate Students

Last Name	First Name	M	Page #	Department	Faculty Mentor
Almohamad	Sam		82	Internal Medicine	Barbara Murray
Bradley	Sherille		83	Pathology	Jun Liu
Busch	Joyce		84	Internal Medicine	Lisa Amitige
Campana	Rodrigo		85	Orthopedic Surgery	Catherine Ambrose
Chatterjee	Totini		86	Microbiology	Hung Ton-That
Cho	Crystal	S	87	Dental Branch	Ken Abramovitch
Clark	Sallie	E	88	Neurosurgery	Ellmore, Timothy
Clark	Tyia	S	89	Integrative Biology & Pharmacology	Guangwei Du
Comeaux	Kelsey	N	90	Anesthesiology	Marie Francis Doursout
Diep	Quynh		91	Dental Branch	Pauline Duke
Eldiwany	Michelle	B	92	Dental Branch	Rade Paravina
Eriksson	Anastasia	L	93	Integrative Biology & Pharmacology	Edgar Walters
Gomez	Daniela		94	Microbiology	Hung Ton-That
Ho	Jonathan	S	95	Internal Medicine	Ah-lim Tsai
Hu	David	K	96	Neurosurgery	Qi Lin Cao
Hyman	Daniel	A	97	Internal Medicine	Diane Milewicz
Iordache	Alice		98	Neurobiology	Valentin Dragoi
Jeng	Melissa	D.	99	Integrative Biology & Pharmacology	Guangwei Du
Killinger	Catherine	E	100	Integrative Biology & Pharmacology	Yi Pig Li
Kubota	Elizabeth	A	101	Emergency Medicine	Richard Bradley
LeBoeuf	William	C	102	Dental Branch	Pauline Duke
Lehmann	Ashton		103	Internal Medicine	Philip Johnson
Leszczynska	Maria	A	104	Internal Medicine	Heinrich Taegtmeyer
Lewis	Rachel	E	105	Anesthesiology	Carin Hagberg
Li	Alexandria	L	106	Dermatology	Stephen Tyring
Li	Qingran		107	Neurology	Sean Savitz
Lynch	Stephanie	M	108	Biochemistry	Jianping Jin
Mandviwala	Taher	M	109	Integrative Biology & Pharmacology	Carmen Dessauer

Matthew	Gena		110	Neurology	Sean Savitz
Mehtani	Siya		111	Psychiatry	Deborah Pearson
Mu	Kathy	S	112	Ophthalmology	Xinping Zhao
Pauls	Lynn	A	113	Anesthesiology	Richard Layman
Pawlik	Claire	E	114	Neurosurgery	Timothy Ellmore
Podder	Daniel	D.	115	Anesthesiology	Carin Hagberg
Raney	Neil	A	116	Dental Branch	Jerry English
Rodiek	Roger		117	Internal Medicine	Philip Johnson
Rothenberg	Daniel	A	118	Integrative Biology & Pharmacology	Catherine Denicourt
Schilling	Matthew	T	119	Internal Medicine	Brandy McKelvy
Shah	Nupur	A	120	Institute for Molecular Medicine	Iraida Sharina
Shouval	Ofer		121	Neurobiology	Nachum Dafny
Smith	Lynsey	C	122	Integrative Biology & Pharmacology	Lenard Lichtenberger
Smith	Carolyne	K	123	Biochemistry	Renhao Li
Sohail	Mahveen		124	Integrative Biology & Pharmacology	Yi Pig Li
Sonne	Blake	R	125	Psychiatry	Alan Swan
Thakkar	Neal	S	126	Integrative Biology & Pharmacology	Alemayehu Gorfe
Wood	Chloe		127	Neurobiology	Valentin Dragoi
Woodie	Daniel	A	128	Neurosurgery	Raymond Grill
Wu	Tiffany		129	Internal Medicine	Richard Kulmacz
Yang	Stephanie		130	Dental Branch	Ryan Quock
Zaidi	Hashim	Q	131	Psychiatry	Katherine Loveland
Zakhidova	Nazima	A	132	Neurosurgery	Nitin Tandon

THE UNIVERSITY of TEXAS
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Medical Students

ABSTRACT

Categorization of MRI-defined pathology and clinical correlates in the combination treatment trial of Multiple sclerosis

SEBASTIAN M. ALDAZ *The University of Texas at Houston Medical School* *Class of 2012*

Sponsored by: Jerry Wolinsky, MD, Department of Neurology

Supported by: Foundation of the Consortium of Multiple Sclerosis Centers, 2U01NS045719-06 Extension of Combination Therapy for Multiple Sclerosis (eCombiRx) from the NINDS

Key Words: Multiple sclerosis, Balo's, neuromyelitis-optica

Multiple sclerosis (MS) is the most common autoimmune demyelinating disease. Some therapies have been developed but it remains an incurable disease. The National Institutes of Health is currently sponsoring the CombiRx Phase III trial to compare treatment efficacy of IM interferon β-1a, SQ glatiramer acetate, and the combination of IM interferon β-1a with SQ glatiramer acetate. Our study analyzed 1102 baseline MRI images from patients considered for the CombiRx trial and categorized them based on lesion manifestation into 13 categories. The categories include Balo's type lesion(s), tumefactive lesion(s), major lesional edema, heavy brainstem load, heavy cerebellar load, heavy cortical load, heavy temporal load, associated hydrocephalus, leukodystrophy-like, neuromyelitis optica-like pattern, typical lesions, and severe global atrophy. Patients displaying phenotypic features of more than one category were grouped in more than one category but were never included in more than three. Rankings were applied such that the most prominent phenotype received the highest ranking. Crucial data analysis will be done at the conclusion of the trial (within a few years) to compare baseline, serial and final patient images. Comparison of pre and post lesion load will yield insight into differences in efficacy of the treatments on categorical lesion evolution. Furthermore, Lucchinetti provides us with a pathological classification of the heterogeneous nature of this disease using histological and molecular examination. Macroscopic examination of tissue lesion evolution is needed to evaluate if there is an MRI counterpart for pathological heterogeneity in MS. A third benefit from this study may be obtained by a planned genetic analysis of individuals within a specific MRI-defined category, such as Balo's, in an attempt to discover genes that may contribute to clinical and imaging manifestations of the disease.

ABSTRACT

A Genetic Screen for Mutations Affecting Embryogenesis in Zebrafish

KHALID T. AL-KALLA *The University of Texas at Houston Medical School* *Class of 2013*

Sponsored by: Xinping Zhao, PhD, Department of Ophthalmology
Supported by: Xinping Zhao, PhD, Department of Ophthalmology
Key Words: Zebrafish, Mutagenesis, Chlorambucil, Embryogenesis

Zebrafish is an attractive animal model for developmental biology and genetics. Because it is a vertebrate, zebrafish is more similar to humans and a better organism for studying human diseases than invertebrate model animals. Moreover, a considerable amount of genetic conservation in zebrafish and humans indicate that gene mutations can be used for studying their normal function in zebrafish and for exploring their utility as models for human disorders. This study is to test if chlorambucil induces gene mutations in zebrafish using a two-generation mutagenesis procedure. Wild type (WT) males were exposed to chlorambucil and then crossed to WT females to produce first filial (F1) generation. F2 lines are then generated by crossing the F1 to the WT strain or F1 in-group mating. Phenotypic screening was performed on F3 embryos from in-group mating of each F2 line. F3 embryos were collected and observed daily over a 5-day period under a dissecting microscope. Abnormal phenotypes were analyzed and documented photographically. Four different types of gene mutations were identified so far. In all of these cases, the mutants accounted for 25% of all the F3 embryos, indicating they are recessive mutations. The first mutant showed abnormal brain, eye, tail and balloon heart on 1-day post-fertilization (dpf). In the second mutant, red-less blood cells were detected on 3 dpf. The color mutant embryos displayed reddish-body on 4 dpf. In the last mutant, no swim bladders were developed on 5 dpf embryos. These results indicate that chlorambucil is an effective mutagen in zebrafish.

ABSTRACT

Effect of Baby Shampoo Nasal Irrigation on Mucociliary Clearance Time in Patients After Sinus Surgery

MARK J. AMSBAUGH *The University of Texas at Houston Medical School* *Class of 2012*

Sponsored by: Amber U. Luong, MD, PhD, Department of Otorhinolaryngology

Supported by: The University of Texas Medical School at Houston Department of Otorhinolaryngology

Key Words: Chronic Rhinosinusitus, Mucociliary Clearance, Functional Endoscopic Sinus Surgery

Although the traditional focus has been on bacterial colonies, it is becoming clear that biofilms may play a substantial role in the etiology of chronic rhinosinusitus. The resistant characteristics of biofilms have lead to the investigation of new treatment modalities that interfere with their formation and development, such as chemical surfactants. Baby shampoo offers an intriguing choice for a therapeutic agent because of its low irritability and combination of three distinct chemical surfactants.

We are currently investigating the effect of a 1% solution of baby shampoo on the mucociliary clearance and symptoms of CRS patients refractory to surgery. A pre-intervention mucociliary function of enrolled subjects is assessed by a saccharine nasal test. Subjects then are randomized into two groups: a control group irrigating with saline and an experimental group irrigating with a 1% baby shampoo solution in saline. A post-intervention saccharine nasal test is repeated at the end of a 4 week period. Symptomatology is measured before and after the intervention with the SNOT-20 questionnaire.

To date, we have recruited 14 subjects (5 males and 9 females) with a mean age of 59 years and averaging 1.8 prior Functional Endoscopic Sinus Surgeries (FESS). The pre-therapy average MCT of 19.2 minutes and SNOT-20 score of 22.7 suggest a baseline ciliary dysfunction when compared to a similar trial done in healthy volunteers at our institution (MCT 12.1 mins). To date, we only have follow-up MCT for 6 patients. Of interest, 3 of the 14 patients with normal gustation could not be enrolled because they were unable to taste saccharine after 45 minutes, suggesting severe sinonasal ciliary dysfunction. We are actively recruiting subjects and hope that investigation of baby shampoo irrigation in patients with refractory CRS may lead to a better understanding of the disease process and possibly a low-cost effective treatment option.

ABSTRACT

Perioperative Near Misses and Adverse Events

CASEY L. ANDERSON *The University of Texas at Houston Medical School* *Class of 2012*

Sponsored by: Lillian S. Kao, MD MS, Department Surgery

Supported by: University of Texas System Patient Safety Research Grant

Key Words: Near miss, adverse event, perioperative care, surgical procedures

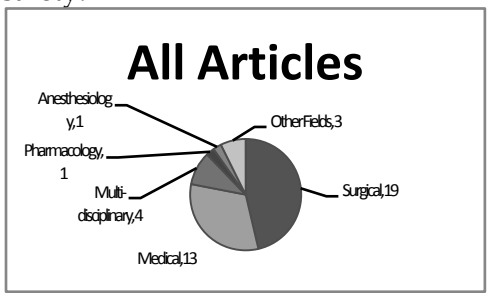
Background: Little research exists detailing peri-operative near misses or adverse events and the effect of a checklist on the incidence of these outcomes.

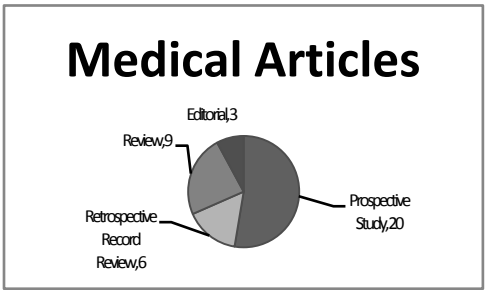
Hypothesis and specific aims: The main hypothesis is that a surgical checklist will decrease peri-operative near misses and adverse events. An approved study was designed to achieve the following specific aims: 1) determine the definition and incidence of peri-operative near misses and adverse events in the literature, 2) prospectively track near misses and adverse events at LBJ General Hospital, and 3) assess the effect of a comprehensive checklist on their frequency.

Methods: To accomplish the first specific aim, a systematic literature search was performed using PubMed, SCOPUS, CINAHL, and Google Scholar including the terms: surgical procedures, peri-operative care, medical error, near miss, adverse event, and communication. The full texts were reviewed and bibliographies were hand searched for additional articles. A questionnaire was developed for specific aim 2 based on the results of the literature review.

Results: The search identified 41 articles; 38 were medically related (see figure) and 17 addressed near misses. Depending upon the method of detection (survey, interview, chart review), the near-miss incidence ranged from 31% to 97%. A questionnaire including 7 screening questions with 16 follow up questions was designed to be used in Specific Aim 2.

Conclusions: There is a paucity of surgical literature describing the incidence and detection methods of near misses in the peri-operative period. Further research is needed to determine how to better track near misses and adverse events, prevent them, and improve operative safety.





ABSTRACT

The Prevalence of Connective Tissue Disease and Rheumatoid Arthritis Autoantibodies in a Mexican-American Population.

ALDO L. ANDINO *The University of Texas at Houston Medical School* *Class of 2013*

Sponsored by: Frank C. Arnett, MD, Department of Internal Medicine Division of Rheumatology

Supported by: UT LASR Fund

Key Words: Autoantibodies, Mexican Americans, Scleroderma, Anti-CCP

Purpose: This study aimed to determine the prevalence of connective tissue disease (CTD) and rheumatoid arthritis (RA) associated autoantibodies, and subsequently these diseases, in Mexican-Americans (MA) which is unknown. **Methods:** In this study, 1633 randomly selected adults (848 unrelated/750 related) from Cameron County (Brownsville), Texas (90% of whom are MA) were tested for anti-cyclic citrillunated peptides (CCP) by ELISA and antinuclear antibodies (ANA) by indirect immunoflourescence (IF). In addition, 528 white controls of European descent were similarly tested. It was hypothesized that due to the higher incidence of rheumatologic disease in Native Americans, there might be a higher prevalence of autoantibodies among Texas MAs due to their Mestizo lineage. **Results:** Among MA samples, 1.95% were positive for anti-CCP, compared to 1.7% in whites (p=.84 CI: .52-2.61, odds ratio: 1.15) and 4.23% were positive for ANA compared to 6.82% in whites (p=.02, CI: .39-.93, odds ratio: .60). Though there was a higher rate of ANA among the white controls, the predominant IF patterns in MAs were more suggestive of underlying CTD. The MA samples had higher rates of anti-centromere (.49 %), anti-nucleolar (.8%) and anti-mitochondrial (.31%) antibodies, thus suggesting possible occult scleroderma and primary biliary cirrosis. Further clinical and epidemiological research is in progress in this population.

ABSTRACT

The correlation between serum zinc levels in diarrheal disease in Mongolian children between 1 month and 5 years of age

Sanjeet K. Baidwan *The University of Texas at Houston Medical School* *Class of 2012*

Sponsored by: Stanley G. Schultz, M.D. Department of Integrative Biology & Pharmacology

Supported by: National Institute of Diabetes and Digestive and Kidney Diseases, 5T35 DK007676-15

Key Words: Diarrhea, Serum Zinc, Mongolia

In some published studies (Bitarakwate, et al) serum zinc concentrations (ug/mL) have been reported to be significantly lower in children suffering from acute diarrhea compared to their normal counterparts. The specific aim of this preliminary study was to determine whether there was a statistically significant difference between serum zinc levels in Mongol children with acute diarrhea than in a control population of children without diarrhea. Serum zinc levels were measured by atomic absorption spectroscopy in 100 children between the ages of 1 month and 5 years. There was no statistically significant difference between the Zn levels in children with diarrhea (n= 101.57) versus those without diarrhea (n=108.73). More detailed balance studies will be needed to explore his matter further.

1. Bitarakwate, Edward. "Serum zinc status of children with persistent diarrhoea admitted to the diarrhoea management unit of Mulago Hospital, Uganda."*African Health Sciences*. 3.2 (2003): 54-60. Print.

ABSTRACT

Modeling the Properties of Neuron B40 in the feeding circuit of *Aplysia*

IRVING Z. BASAÑEZ *The University of Texas at Houston Medical School* *Class of 2012*

Sponsored by: John H. Byrne, PhD, Department of Neurobiology and Anatomy

Supported by: John H. Byrne, PhD

Key Words: *Aplysia*, B40, central pattern generator, buccal motor patterns, SNNAP

Feeding behavior of *Aplysia* is regulated by a central pattern generator (CPG) circuit located in the buccal ganglion. Feeding behavior consists of a simple oscillatory switch between protraction and retraction of the radula, the feeding apparatus. Two types of behaviors, ingestive and egestive, are generated by the same CPG. The purpose of this study was to expand a previously constructed neural circuit model to include neuron B40 and investigate how it effects the function of the circuit. Previously, Cataldo et. al. (2006) used the Simulator for Neural Networks and Action Potentials (SNNAP) to develop a CPG model and run simulations, but the model was only able to simulate egestive buccal motor patterns (BMPs). In the present study, neuron B40, which is active during ingestive programs, was modeled as a Hodgkin-Huxley-type neuron and added to the CPG model. Previously published empirical data (e.g. Jing and Weiss 2002, Jing et. al. 2003) were used to constrain the parameters of the B40 model. These empirical data included the passive properties of B40 as well as the properties of its action potentials, membrane currents, responses to stimuli, electrical coupling, and synaptic connections. The addition of B40 to the circuit model was not sufficient to simulate a switch from egestive to ingestive BMPs. Also, the cells that are currently in the model did not excite B40, suggesting that there may be other unidentified synapses/cells that account for B40 excitation. The duration of the protraction phase, however, was increased, which is consistent with the published observations about B40. We concluded that the present model cannot account for the different of behaviors generated by the CPG, and that additional neurons remain to be characterized in the CPG.

ABSTRACT

An Evaluation of LMA Seal Using Air Vs. Saline: A Mannequin Study

JEREMY BATES *The University of Texas at Houston Medical School* *Class of 2012*

Sponsored by: Carin Hagberg, MD, Anesthesiology, Davide Cattano, MD, PhD., Anesthesiology, University of Texas Medical School at Houston
Supported by: Carin Hagberg, MD, Department of Anesthesiology University of Texas Medical School at Houston
University of Texas at Houston– Office of the Dean
Key Words: LMA, Saline, Air

Background: A laryngeal mask (LM) allows an Anesthesiologist to quickly attain a patent airway as a means of ventilation. The laryngeal mask airway (LMA) was developed in 1982 and has since evolved into several different forms including the LMA Unique (uLMA) and LMA Supreme (sLMA). The major concern for physicians using an LMA is the lack of a proper seal, creating the risk of esophageal regurgitation and subsequent aspiration pneumonitis.
Purpose: As a part of a larger study on LMA cuff pressures and proper sealing during episodes of positive pressure ventilation, we conducted this study to determine if there was a difference in the cuff seal and pressure when using air vs. saline as an inflating agent. We focused our study using the sLMA and uLMA both in and ex-vivo.
Methodology: Fully deflated LMA Unique and LMA Supreme size 3, 4, and 5 cuffs were inflated in an in-vivo (mannequin) and an ex-vivo setting. The cuffs were inflated with air at arterial line pressure gauge. The same procedure was repeated using saline rather than air as a cuff inflating agent.
Results: There was no statistically significant difference in cuff seals or cuff pressures between the two devices in either setting.
Conclusions: Although not statistically significant, there was a trending pattern of increasing pressures at similar volumes when comparing air vs. saline. Equally important was the incompressible nature of saline which allowed the pressures to spike at much lower volumes of inflation (in constrained circumstances) compared to an equal volume air. The next arm of this study will be to test the actual difference in the seal established by the different LMA's using air vs. saline in a cadaveric or Tru-Corp mannequin model. The seal will be tested by applying positive pressure ventilation and determining the volume necessary to prevent leakage at various cm H_20 of PEEP.

ABSTRACT

Association of PDZ-domain proteins with connexin36 in retinal gap junctions

Kendall Bicknell *The University of Texas at Houston Medical School* *Class of 2012*

Sponsored by: Dr. John O'Brien
Supported by: Ophthalmology Department at UT Houston Medical School
Key Words: Colocalization Studies with Connexin 36

Gap junctions are a specialized interconnection formed by connexins (membrane proteins) that create channels between the cells. The channels allow for communication between the cells via electrical means and small molecules. These gap junctions may also allow for transfer of apoptotic signals between neighboring cells leading to a phenomenon known as "bystander killing." This has been hypothesized to account for the spread of apoptotic signals from rods to cones in retinitis pigmentosa (Ripps, 2002). The eventual goal of this research is to develop drugs targeting specific regulatory proteins associated with cone gap junctions leading to decreased gap junction coupling between cells and therefore decreased bystander killing. Previous studies have shown a strong correlation between decreased phosphorylation at specific sites on connexin 36 (Cx36) in photoreceptor gap junctions and decreased gap junction coupling between cells. It has further been determined that the regulation of gap junction coupling is via a signaling cascade that leads to the phosphorylation or dephosphorylation of Cx36. The regulatory proteins associated closely with Cx36 are involved in the control of this phosphorylation, and are presumed to be involved in similar regulation pathways in cone gap junctions. Uncoupling of gap junctions has been shown to depend on dephosphorylation of Cx36 in AII amacrine cells, and this pathway depends on the activity of a protein phosphatase that is activated by Protein Kinase A. It is believed that members of this regulatory cascade are associated with the C-terminus of Cx36, because the regulation by phosphorylation of Cx36 in cultured HeLa cells was inverted by a mutation that eliminated the last 7 amino acids of Cx36, a known PDZ-domain protein binding site. A protein microarray was performed against the Cx36 with the mutation (missing last 7 amino acids) and without the mutation (wild type) and the results were compared. The following proteins: 14-3-3 Gamma, 14-3-3 Eta, 14-3-3 Sigma, PDZ CAP1, Multiple PDZ domain protein (MUPP1), and nNos were found to bind to wild type connexin 36, but did not bind to the mutated connexin 36. The short-term goal of this project will be to use immunocytochemistry to identify which of these Cx36 associated regulatory proteins is also in cone gap junctions. Immunocytochemistry with fluorescently labeled antibodies will be used to tag and locate the regulatory proteins on the cone gap junctions by looking for co-localization of these proteins with Cx35 in photoreceptors in the retina. Immunocytochemistry was performed on rabbit retina fixed with either 2% formaldehyde, 4% formaldehyde, or 4% carbodiamide. The proteins of interest are hypothesized to be regulatory proteins associated with connexin 36 tagged using commercial antibodies and viewed using a confocal microscope. The proteins that showed notable colocalization with connexin 36 were as follows: MUPP1, PDZ-K1, and NHERF2. Currently, immuprecipitation studies are being performed on rabbit retina to verify the apparent colocalization found using immunocytochemistry. If the results of this part of the experiment also verify colocalization then it can be effectively concluded that the colocalization is real. If we can prove the colocalization of these proteins with connexin 36 in cones, drugs can potentially be targeted to these regulatory proteins affecting coupling between gap junctions in the retina.

ABSTRACT

Identification of FFP-induced Tyrosine Phosphorylation on BAD Protein

FRANCISCO BUENDIA S *The University of Texas at Houston Medical School* *Class of 2012*

Sponsored by: Yanna Cao, MD, Department of Surgery
Xiyun Deng, PhD, Department of Surgery
Tien C Ko, MD, Department of Surgery
Supported by: Grant NIGMS P50 GM038529 (T.C.K. and J.B.H.)
Key Words: Hemorrhagic shock, Fresh frozen plasma, BAD, Tyrosine phosphorylation.

Introduction: Resuscitation with Fresh Frozen Plasma (FFP) has beneficial effects on hemorrhagic shock (HS) patients. Previous studies in our lab have demonstrated that FFP has anti-apoptotic effect on endothelial cells by increasing phosphorylation of BAD on currently known sites, i.e., serine residues 112, 136 and 155. This study was designed to explore whether FFP phosphorylates BAD at tyrosine residues.
Methods: Subconfluent, serum-starved human pulmonary microvascular endothelial cells (HPMECs) and human dermal lymphatic endothelial cells (HDLECs) were treated for 30 min with FFP (10% to 50% final concentration) or medium (control). To determine the kinase(s) responsible for BAD phosphorylation, cells were pretreated for 30 min with kinase inhibitors before FFP treatment. Whole cell lysates were analyzed by immunoprecipitation and Western blotting.
Results: Treatment of both HDLECs and HPMECs with increasing FFP concentrations increased phosphorylation of BAD on serine residues 136 and 155, as well as tyrosine sites. Western blot of immunoprecipitated BAD from HPMECs treated with FFP confirmed tyrosine phosphorylation on BAD. A time-course study showed that FFP-induced tyrosine phosphorylation lasted up to 48 h with the highest phosphorylation at 30 min. U0126, a MEK1/2 inhibitor, inhibited phosphorylation of tyrosine while having no effect on serine 136 and 155. Genistein(inhibitor of tyrosine kinases p60src) and AG 490 (inhibits tyrosine kinase EGFR) had no inhibition of BAD phosphorylation on either serine or tyrosine residues.
Conclusions: We identified tyrosine phosphorylation on BAD induced by FFP, which has not been reported in the literature. FFP-induced tyrosine phosphorylation on BAD can be inhibited by tyrosine kinase inhibitor, U0126, indicating that MEK1/2 might be the kinase(s) responsible for tyrosine phosphorylation of BAD by FFP. Further investigations of the tyrosine phosphorylation site(s) on BAD and the functional consequences of FFP-induced tyrosine phosphorylation on BAD are required.

ABSTRACT

A study of immunological effects of thermochemotherapy on MTLn3 mammary carcinoma-bearing rats

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Sponsored by: Joan MC Bull, MD Internal Medicine-Oncology

Supported by: National Institute of Diabetes and Digestive and Kidney Diseases, 2 T35 DK007676-17

Key Words: Thermochemotherapy, immune system, MTLn3, flow cytometry

Previous studies of MTLn3 mammary carcinoma-bearing rats treated with fever-range-whole body-thermal therapy (FR-WB-TT) with dose/time optimized chemotherapy (thermo-chemotherapy) demonstrate that the combined treatment induces a durable immunity to the tumor in 50% of animals. When cured responders to the treatment are reinoculated with MTLn3 tumor cells, they show complete resistance to the tumor. Although oxaliplatin chemotherapy (OX) induced cell killing is important, the data suggests that there is also a critical immune component that appears to be stimulated by FR-WB-TT. The purpose of this study was to investigate the underlying immune mechanisms involved in the treatment regimen. 5 $x10^5$ tumor cells were injected into the inguinal mammary fat pad of Fischer 344 female rats. On day 11 post tumor inoculation, OX in 5% Dextrose/H_2O was injected into an experimental group (n=6) while a control group (n=2) was injected with the drug vehicle. 24 hours after OX treatment, FR-WB-TT was administered to the experimental group for 6 hours at 40°C with 2% isoflurane anesthesia, while controls received sham treatment with 2% isoflurane at 37°C. Blood samples were taken prior to tumor injection and on day 10 post OX treatment. Peripheral blood monocytes (PBMC) were analyzed by flow cytometry to determine changes in T-cell populations (CD4, CD8, CD25). Flow cytometry of PMBCs revealed a trend between responders and non-responders to the treatment. Responding rats had a baseline CD4/CD8 ratio of 1.36-1.45 and 1.98-2.08 on day 10 (43-46% increase). Non-responders increased the CD4/CD8 ratio by only 14-33% from baseline to day 10. Interestingly, CD4+CD25+ regulatory T cells also increased in responders. Importantly, the results suggest not only the critical involvement of the immune system for response to treatment but also the ability to predict response before the start of treatment.

ABSTRACT

Effects of Pre-germinated Brown Rice on Metabolic Syndrome Improvement

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Sponsored by: Anil D. Kulkarni, MSc, PhD, Department of Surgery

Supported by: National Institute of Diabetes and Digestive and Kidney Diseases, 5T35 DK007676-17

Key Words: metabolic syndrome, pre-germinated brown rice (PGRB), homocysteine-thiolactonase (HTLase), hemoglobin A1c (HbA1c)

Metabolic syndrome is a combination of medical disorders including glucose intolerance, hypertension, central obesity, decreased plasma HDL, and increased plasma triglyceride levels that when present lead to a dramatically increased risk of developing cardiovascular disease and diabetes. The purpose of this study was investigate the effects of white rice and pre-germinated brown rice on blood glucose levels, triglyceride levels, and homocysteine-thiolactonase (HTLase) levels on overweight American subjects suffering from metabolic syndrome. The current research on this subject has been done only on laboratory animals and subjects of Asian descent and has shown that a diet high in PGRB leads to notable decreases in plasma glucose, triglyceride, and HTLase levels compared to diets high in white rice. Patients were recruited for the study and then screened to determine eligibility for participation. Once patients are found to have sufficiently high plasma levels of glucose, triglycerides, HbA1c, and a BMI greater than 30 they will be instructed to consume PGBR three times daily for six weeks. For the next six weeks they will be instructed to resume their normal diet. They will then be instructed to consume white rice three times daily for six weeks. At the end of each six week period, blood will be drawn and examined for plasma glucose, triglycerides, HbA1c and HTLase. The effectiveness of a diet high in PGBR compared to a diet high in white rice on mitigating the symptoms of metabolic syndrome will be reported once adequate data is obtained.

ABSTRACT

The effects of *Tsc2* gene deletion on neuronal morphology: An *in vivo* Golgi Study

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Sponsored by: Michael J. Gambello, MD, Ph. D, Department of Pediatrics, Division of Medical Genetics

Supported by: National Institute of Neurological Disorders and Stroke R01NS060804
University of Texas at Houston Medical School - Department of Pediatrics
University of Texas at Houston Medical School - Office of the Dean

Key Words: TSC, Golgi, Sholl, dendritic complexity

Tuberous Sclerosis Complex (TSC) patients exhibit benign tumors in the brain that cause developmental delay, seizures, and behavioral disabilities. Previous studies have shown that the deletion of the tumor suppressor gene, *TSC2*, causes the development of tuberous sclerosis complex. The purpose of this study was to investigate the hypothesis that deletion of *Tsc2* in a mouse model of tuberous sclerosis complex has an effect on dendritic complexity and spine morphology in the cerebral cortex and hippocampal pyramidal layer. A mouse model, *Tsc2* $^{flox/ko}$*;hGFAP-Cre*, was created by the Gambello lab in order to examine biological effects of the disease *in vivo.* Slices of brain were taken from the cortex and hippocampus of wild type and mutant mice and stained with the Golgi stain. Neurons from these slices were selected based on their staining and/or seclusion from other neurons. They were taken from throughout the cortex as well as from the CA1 region of the hippocampus. 14 bright-field images were taken along the z-axis of the neuron, and a compilation of the images were used to trace the neurons. Sholl analysis was then performed on each neuron with circles of diameters ranging from 20 to 120 μm. The results showed significantly greater dendritic complexity in mutant neurons compared to wild type neurons in both the cortex and hippocampus. The longer and more complex dendrites exhibited by mutant neurons might lead to more synapses, hyperexcitability, and seizures. Future studies will be required to determine the cellular mechanisms leading to this abnormal neuronal morphology.

ABSTRACT

Synchronized, Pulsatile Left Ventricular Assist Compared to Continuous Flow LV Assist: Potential Improved Left Ventricular Unloading

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Sponsored by: Richard W. Smalling, MD, PhD, Department of Cardiology

Supported by: Richard W. Smalling, MD, PhD, Department of Cardiology

Key Words: LVAD, heart failure

Heart failure patients who show significant improvement in cardiac function with left ventricular assist device (LVAD) support can have the device removed without need for transplantation. To test the hypothesis that a pulsatile cardiac assist device synchronized with the cardiac cycle results in superior unloading and improved systemic flow compared to a continuous flow VAD at a given VAD output we studied the pulsatile pump TORVAD (TP) compared to the continuous flow pump BioMedicus LVAD (BP). The TORVAD and BioMedicus were extracorporeally implanted in seven Yorkshire/Poulin mixed pigs. The pulsatile pump was actuated immediately after aortic valve closure. Hemodynamics for both pumps were assessed in each pig at baseline and heart failure induced by ligation of the left anterior descending coronary artery. At baseline with TORVAD support cardiac output (CO) increased from 4.5 to 5.9L/m (compared to 5.5L/m with BP support; $P<0.05$), mean arterial pressure (MAP) increased from 73 to 82mmHg (71mmHg with BP support; $P<0.05$), and left atrial pressure (LAP) decreased from 18 to 12mmHg (14mmHg with BP support; $P<0.05$). During heart failure with TP support CO increased from 3.5 to 5.6L/m (compared to 5.1L/m with BP support; $P<0.05$), MAP increased from 55 to 68mmHg (60mmHg with BP support; $P<0.05$), and LAPavg decreased from 19 to 11mmHg (14mmHg with BP support; $P<0.05$). Compared to the BioMedicus at the same VAD output the TORVAD significantly improved ventricular unloading and increased CO to a greater degree.

ABSTRACT

Elimination of Functional Leg Length Discrepancies Post Total Hip Arthroplasty

Hubert M. Chodkiewicz *The University of Texas at Houston Medical School* *Class of 2012*

Sponsored by: Terry Clyburn, MD, Department of Orthopaedic Surgery

Supported by: Terry Clyburn, MD
University of Texas at Houston Medical School - Office of the Dean

Key Words: FLLD, pelvic tilt, THA, pelvic obliquity

A functional leg length discrepancy (FLLD) is a common complication following total hip arthroplasty (THA). When a THA is performed, the hip is brought back in most cases to within 1/4th of an inch of the original length. Yet, the patient may feel as though the operated leg is now actually longer than the opposite leg because of pelvic tilt. Usually the pelvis will return to its natural position, but in some cases it remains tilted resulting in a FLLD. A retrospective chart review study was performed on 33 patients (mean age 61years) undergoing THA between 3/2007 and 3/2009. Variables in the nature of FLLD post-THA and the effects of physical therapy or letting the patient heal naturally by "walking it out" were investigated. All THA patients' medical records and radiographs with 3 month or longer follow-up were reviewed. Pelvic tilt angle, actual and apparent leg length differences, and total FLLD were measured on AP radiographs of the patients' pelvis. Clinically, patients' leg lengths and range of motion (ROM) were also recorded. All measurements were made pre-operatively and at the most recent post-operative visit for non-randomized patients with and without physical therapy. Data indicated that of the 13 patients that had any improvement in FLLD, 11 (85%) did not partake in physical therapy. Further, the non-physical therapy group was worse off pre-operatively as seen by their adduction ROM and had more improvement to that ROM. These results suggest that not doing physical therapy can be beneficial to a patient, possibly due to the patient's own initiative to move more. However, general health is a key factor in each patient's recovery.

ABSTRACT

Early Detection of Bowel Ischemia Using Visible Light Spectroscopy in Patients Undergoing TAAA Surgery

Paul M. Claiborne *The University of Texas at Houston Medical School* *Class of 2012*

Sponsored by: Sheila M. Coogan, MD, Department of Cardiothoracic and Vascular Surgery

Supported by: NIH- National Institute of Diabetes and Digestive and Kidney Diseases

Key Words: ischemia, visible light spectroscopy, thoracoabdominal aortic aneurysm

Bowel ischemia following thoracic and thoracoabdominal aortic aneurysm (TAAA) open repair is a deadly condition increasing both morbidity and mortality in the patient. Bowel ischemia has traditionally been categorized as a difficult and latent diagnosis. Visible light spectroscopy (VLS) is used to measure the oxygen saturation on mucosal surfaces. We will use VLS to provide reproducible real-time, physiological evidence of the presence or absence of bowel ischemia intra-operatively, and these saturation values should be predicative of post-operative bowel ischemia.

The T-Stat 303 VLS device made by Spectros will be used during TAAA surgery to measure the oxygen saturation values of both the small (serosal sensor) and large (rectal mucosal sensor) intestine during know periods of ischemia (ie. aortic cross-clamping). Oxygen saturation measurements that fail to normalize after known periods of ischemia, should predict post-operative gastro-intestinal complications. This study will enroll 100 patients undergoing TAAA surgical repair. This study has been drafted and sent to the University of Texas Health Science Center Institutional Research Board for approval (HSC-MS-09-0343).

ABSTRACT

Electro-corticographic signatures of noun and verb generation

Christopher R Conner *The University of Texas at Houston Medical School* *Class of 2012*

Sponsored by: Nitin Tandon, M.D.
Department of Neurosurgery
Supported by: Nitin Tandon, M.D.
University of Texas Medical School at Houston – Office of the Dean
Key Words: Electrocorticography, brain mapping, language

There is a rich discourse in the literature regarding the neural substrates underlying the generation of nouns as opposed to verbs. Prior scalp EEG studies have shown the spatiotemporal dynamics of these tasks are distributed over differing regions of cortex with, the left anterior and mid temporal lobe are specific for common naming while posterior inferior frontal lobe regions are more specific for verb generation. We sought to study this issue closely in 10 patients with pharmacologically resistant epilepsy scheduled for placement of left hemispheric subdural electrodes for the localization of seizure onset sites.

Electrocortiography (ECoG) data were collected at 1000 Hz while patients named visual stimuli depicting common objects and actions (> 50 trials each). Concurrent audio-video recordings were used to determine articulation times and to exclude trials with erroneous responses. EEG data were time-stamped using a separate marker channel that records TTL pulses at stimulus onset and offset time points. Individual trials were time locked to stimulus onset and time-frequency analysis was performed using sequential power spectral density estimates were computed from 500 to 1523 ms (256 ms Hann window, 128 ms overlap, Welch method). Gamma power (from 50 – 150 Hz) was computed and compared to baseline (-500 to -200 ms relative to stimulus onset). Overlays were generated using percent change in the gamma band with only significant ($p < 0.01$) change displayed.

From 500 to 1500 ms we observed gamma power increases during both conditions over extrastriate, motor, premotor, and subtemporal regions. There was additional gamma power over middle and inferior frontal gyri under both conditions with a greater increase over Broca's are during verb generation. There was also greater gamma increase in subtemporal (posterior fusiform and parahippocampal gyri) regions during verb generation.

We show here that the cortical network involved in both noun and verb generation is broadly disseminated and largely overlapping. However, we demonstrate substantial differences between these to regions that are not typically considered to be essential for either function. Comparisons to fMRI hemodynamics in patients who also had ECoG and coherence between

regions are ongoing.

ABSTRACT

Conservative versus Surgical Treatment of Medial & Lateral Ankle Ligaments Using Allografts

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Sponsored by: William McGarvey, M.D., Department of Orthopaedic Surgery

Supported by: William McGarvey, M.D.

Key Words: deltoid ligament, anterior talofibular ligament, allograft, autograft, ankle sprain

Ankle ligament injuries occur in a vast range of recreational activities as well as competitive sports. Instability is usually the most common complaint associated with these types of injuries. A retrospective chart review from Sept. 1, 2004 through May 31, 2009, was performed to identify the most successful method in approaching the treatment of ruptured medial and lateral ankle ligaments. Patients were screened for the type of treatment used (conservative, autograft, or allograft), the amount of time between injury to treatment, the amount of time between injury to complete rehabilitation, range of motion the patient recovered after treatment, if there was any instability or laxity after treatment, and there was any neural damage during the procedure. So far 325 charts have been reviewed and 9 patients fit the inclusion criteria. Six patients were found to have had the conservative approach, while 1 and 2 patients had an autograft or allograft approach, respectively. Based on initial data analysis, the patients who received an allograft have recovered an average of 4° of dorsiflexion and 25° of plantarflexion over the patients who received an autograft ligament reconstruction. Based on preliminary findings the main advantage to an allograft approach is to provide the patient with an anatomical reconstruction and does not sacrifice normal tissue. Data analysis is ongoing and this continues to be an ongoing study.

ABSTRACT

Age and genetic strains differences in response to chronic methylphenidate administration

DERLY O. CUELLAR III *The University of Texas at Houston Medical School* *Class of 2012*

Sponsored by: Nachum Dafny, PhD, Department of Neurobiology and Anatomy

Supported by: Nachum Dafny, PhD; How and where methylphenidate excretes its effect on the central nervous system - NIH R01 DH027222

Key Words: Methylphenidate, Ritalin, Sprague-Dawley, Wistar-Kyoto, Spontaneously hyperactive rat, locomotor, adolescent, adult, genetic, strain

Methylphenidate hydrochloride (MPD), commonly known as Ritalin is a psychostimulant routinely used in the treatment of attention deficit hyperactive disorder (ADHD) in children and adults alike. Adolescence involves a period of neural development that is highly susceptible to environmental and pharmacological influence, and exposure to a psychostimulant like MPD during this crucial time period may cause permanent changes in neuronal function and formation. Another factor that may influence the level of changes in neuronal function and formation is genetic variability. It has also been reported that genetic variability affects both the initial behavioral response to drugs in general and psychostimulants in particular, and subsequently whether tolerance or sensitization is induced. Thus, the objective of the present study was to investigate the dose response effects of repeated MPD administration (0.6, 2.5, or 10.0 mg/kg, i.p.) using an open field assay to investigate if there are differences between adolescent and adult Wistar-Kyoto (WKY), spontaneously hyperactive rat (SHR), and Sprague-Dawley (SD) rats, respectively, and if the genetic variability between the strain influenced the degree of change in locomotion. The open field assay consists of an automated activity monitoring system that recorded their locomotor activity into four locomotor indices: horizontal activity, total distance traveled, vertical activity, and number of stereotypic movements. The acute and chronic administration of MPD exhibited unique differences in the level of intensity in locomotor activity in each rat strain, with adult rats for the most part having a more intense increase in locomotor activity when compared to their adolescent counterparts. This variability in activity suggests that MPD may affect the same neuronal circuit differently in each strain; furthermore, the unique differences among the individual locomotor indices suggest that each locomotor index is regulated by different neuronal circuits, and MPD affects each circuit differently.

ABSTRACT

Characterization of Cortical and Hippocampal Interneurons in Brain Specific *Tsc2* Knockout Mice

MATTHEW G. DITZLER *The University of Texas at Houston Medical School* *Class of 2012*

Sponsored by: Michael J. Gambello, MD, Ph.D, Department of Pediatrics, Division of Medical Genetics

Supported by: National Institute of Neurological Disorders and Stroke, NIH R01-NS060804;
University of Texas at Houston – Department of Pediatrics;
University of Texas at Houston – Office of the Dean

Key Words: TSC, interneurons, cortex, hippocampus

Tuberous Sclerosis Complex (TSC) is an autosomal dominant, tumor suppressor disorder caused by a mutation in either *TSC1* or *TSC2*, which encode for the proteins hamartin and tuberin respectively. TSC has severe effects on brain development and function, with patients typically displaying cortical tumors, called tubers, as well as subependymal nodules. These lesions often lead to seizures, developmental delay, autism spectrum disorders and other psychiatric disabilities. Dr. Gambello's laboratory has created a mouse model, $Tsc2^{KO/CKO;hGFAP\text{-}Cre}$, for the brain pathology of TSC by selectively removing the *Tsc2* gene from radial glial cells during development using a Cre-loxP system. This mouse model recapitulates many of the brain abnormalities of the human disease. Since pathologic inhibitory stimulation from interneurons can lead to seizures, we hypothesized that loss of *Tsc2* in this model might affect interneuron migration and maturation. An immunohistochemical study was performed on 21 day old mouse brain sections to determine 1) any difference in the number of interneurons within the primary somatosensory, motor, and visual cortices, as well as the hippocampus; and, 2) if there was any difference in cortical interneuron distribution between wild-type mice and mice possessing the disease. Our data showed no significant difference between wild-type and knockout densities of $Calretinin^{+}$ and $Parvalbumin^{+}$ interneurons in the rostral cortex, caudal cortex, hippocampus, and dentate gyrus. This indicates that there is no gross defect in these populations of interneurons; therefore, future projects to explain the neuropathologic mechanism of TSC may investigate interneuronal cell morphology or signaling capability.

THE UNIVERSITY of TEXAS
HEALTH SCIENCE CENTER AT HOUSTON

ABSTRACT

2009 Summer Research Program
Office of Educational Programs
Medical School

Medical Student

COMPUTERIZED ANTHROPOMETRIC MEASUREMENTS FOR PATIENTS WITH METOPIC AND UNICORONAL CRANIOSYNOSTOSIS

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Sponsored by: John Teichgraeber MD, Department of Pediatric Surgery
James J. Xia MD, PhD, MS, Department of Oral and Maxillofacial Surgery
Supported by: Stryker
The University of Texas Medical School at Houston
Key Words: Craniosynostosis, nonsyndromic, anthropometry, 3D reconstruction

The goal of this project is to develop a set of computerized anthropometric measurements to aid in the surgical planning of patients with metopic or unicoronal craniosynostosis. 11 patients with single suture nonsyndromic craniosynostosis were included in the study. They were separated into two experimental groups. The first experimental group included 5 patients with metopic craniosynostosis, and the second group included 6 patients with unicoronal craniosynostosis. All patients underwent a computed tomography (CT) scan prior to surgery. 12 patients with normal head morphology were included in a control group. They were 2:1 matched by age, gender, and race to the patients in each experimental group. All patients in the control group also had a CT scan for a condition other than craniosynostosis. Finally, a set of 3D anthropometric measurements was generated for all patients in each group. Student t-tests were used to compare the differences between the two groups.

UNICORONAL PATIENTS		Unicoronal	Control	P Value
Orbital Width/Height		0.94	1.03	0.003
Unaffected / Affected	Porion-FZ distance	1.19	0.99	2.5E-7
U/A	Nasion-FZ distance (X)	1.16	1.01	0.0002
U/A	Nasion-FZ distance (Y)	0.60	1.05	1.8E-5
U/A	Nasion-FZ distance (Z)	2.62	1.75	>0.05*

METOPIC PATIENTS	Metopic	Control	P Value
Bi-Supraorbital distance / Bi-Infraorbital distance	0.90	1.02	0.004
Bony Intercanthal distance	12.10 mm	15.65 mm	0.007
Nasofrontal Angle	140.99°	150.05°	>0.05*

* Indicates not statistically significant

We have developed a set of computerized anthropometric measurements for patients with metopic and unicoronal craniosynostosis. They represent the characteristics of the deformity and may aid in surgical planning.

ABSTRACT

Functional MRI Correlates of Hemispheric Laterality for Memory

Stephen M. Fisher *The University of Texas at Houston Medical School* *Class of 2012*

Sponsored by: Timothy, M. Ellmore, Ph.D., Department of Neurosurgery

Supported by: The Department of Neurosurgery; The Vivian L. Smith Foundation for Neurological Research

Key Words: fMRI; Working Memory; Hippocampus; Wada Test

Before neurosurgery, patients undergo an invasive procedure – the Wada test - that involves injection of sodium amobarbital into the internal carotid artery (ICA) to identify the hemisphere essential for language and memory so that these cognitive functions may be preserved during resections of tumors or seizure foci. This research seeks to replace this invasive and risky procedure with a safer non-invasive alternative. The dominant hemisphere for language has been shown to strongly correlate (r=0.94) with the results of blood-oxygen-level-dependent functional brain imaging (fMRI) activation during language testing. However, it remains unclear how well functional imaging results correlate with results of the Wada test for memory. To answer this question, patients' memory laterality from Wada testing was compared to brain activation during fMRI of verbal and spatial working memory tasks.

Five epilepsy patients who underwent Wada testing to lateralize language and memory were enrolled: four were classified as left dominant and 1 was classified as right dominant. Each performed working memory tasks during fMRI scanning at 3 Tesla. Analyses were performed in AFNI using multiple regression followed by planned comparisons to assess the significance of activity during: 1) encoding, 2) rehearsal and 3) retrieval. For each patient, a laterality index (L-R/L+R) was computed for each memory task component from the extent of activity (mm^3) in cortical and hippocampal regions that were active in the group statistical analysis.

Individual patient laterality indices computed from hippocampal activity during the retrieval component of the verbal working memory task classified all but one of five patients correctly according to their Wada memory scores. The one that was not classified correctly had a laterality index of zero because there were no active voxels at the threshold level (where p=.05).

This study shows the novel result that functional imaging of hippocampal activity during the retrieval phase of a working memory tasks correlates with results of the Wada test. Further study will assess the reliability of this finding in order to determine whether fMRI may be used as an alternative to the Wada procedure.

Special Thanks: Nitin Tandon, M.D.

ABSTRACT

Risk Factors and Treatment of Port Thrombosis in Pediatric Oncology Patients

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Sponsored by: Dr. KuoJen Tsao

Supported by: University of Texas at Houston, Department of Pediatric Surgery

Key Words: Port, thrombosis, tPA

Background: Implanted central venous access devices (ports) are widely used in pediatric oncology patients. Clinical thrombosis of ports is a common complication which may necessitate removal. Port salvage therapy using tissue plasminogen activator (tPA) in pediatric oncology patients, specifically, has been under-evaluated. The risk factors for port thrombosis and efficacy of tPA therapy were evaluated.

Methods: A retrospective cohort study was performed on all pediatric (≤ 18 years) patients who received a port at the Children's Cancer Hospital - University of Texas MD Anderson Cancer Center from January 2001 to June 2008. A comprehensive database was generated by integrating 3 large institutional databases from pharmacy, operating room, and institutional infusion therapy team. Port thrombosis was defined as clinical luminal occlusion without radiographic evidence of mechanical catheter "pinch off" or malpositioning. An institutional approved protocol utilizing tPA (2mg/ml) with 30-60 minute dwell time (maximum 2 doses) was utilized. Variables including patient demographics and disease (solid tumor or hematological), catheter size, catheter lumina (single or double), catheter tip location (optimal, acceptable, or suboptimal), medications, and operative techniques (vessel utilized, reservoir site) were analyzed. Statistical analysis was performed using logistic regression analysis.

Results: During the study period, 589 PAC's were placed in 488 patients. The median age at PAC placement was 10.5 years (range: 0.3-18.9 years). Catheter sizes ranged from 5Fr to 9.6Fr including 30 double lumen catheters (18.0%). 303 occurrences of thrombosis (median 1.0, range 1.0-7.0 per port) occurred in 167 PAC's (28.4%) in which 161 were treated with tPA protocol and 6 were directly removed/replaced. 146 of 161 (90.7%) ports treated with tPA protocol were salvaged.

Regression analysis demonstrated a significant increased odds for thrombosis including catheter lumina (OR 3.18, 95%CI 1.85-5.48), hematological malignancy (OR 1.56, 95%CI 1.06-2.30), and catheter tip positioning (OR 1.36, 95%CI 1.02-1.81). Variables NOT associated with thrombosis included age at port placement, vessel site, and catheter size.

Conclusion: Although ports are routinely used in the pediatric population, thrombosis is relatively common complication (28.4%). Major risk factors for thrombosis include double lumen catheters, hematological malignancies, and suboptimal catheter tip position. Fortunately, the vast majority (90.7%) of port thromboses can be salvaged utilizing tPA therapy.

ABSTRACT

Preliminary Data on Anticipation of The Difficult Airway: The Preoperative Airway Assessment Form As An Educational And Quality Improvement Tool

Nora Gutierrez | *The University of Illinois at Chicago Medical School* | *Class of 2012*

Sponsored by: Carin Hagberg, MD, Department of Anesthesia
Davide Cattano, MD, PhD, Department of Anesthesia

Supported by: Foundation for Anesthesia Education and Research, and the Hispanic Center of Excellence at the University of Illinois at Chicago Medical School

Key Words: Airway, FAER, Mallampati Classification, Resident Tool

Introduction: Maintaining a patent airway of a patient is top priority for every anesthesia provider. As part of a thorough anesthetic evaluation, it is necessary that the anesthesiologist preoperatively assess their patient's airway. We have created a new preoperative airway evaluation form designed to help identify factors which contribute to a difficult airway. This study will compare the standard form currently used with its newly designed counterpart.

Methods: Resident anesthesiologists were randomly assigned to either use the new assessment form, or current standard model. Additionally, all patients included in the study underwent airway evaluation by a skilled provider, dedicated in airway assessment, using the new form. The new form includes a physical exam assessing body mass index (BMI), neck circumference, inter-incisor distance, thyromental distance, sternomental distance, Mallampati classification, cervical neck mobility and jaw mobility. A history relating to the airway was also included in the assessment.

Results: We screened 510 patients in the month of May using the new preoperative airway assessment form. We have collected postoperative information from 514 patients. Difficult mask ventilation was encountered in 22 patients (4.2 %), difficult laryngoscopy was encountered in 31 patients (6.0%), and difficult intubation was encountered in 13 patients (2.5%). Of the 510 patients screened, 203 were screened by the residents who used the new form, 307 patients were screened by the research team. The residents who used the new form predicted overall airway difficulty with a false negative prevalence of 9.2 %, compared to those who used the old form who had a false negative prevalence of 14.3 %.

Discussion: Our results suggest that using a standard form, assessing factors which contribute to a difficult airway, is better able to guide the anesthesia provider with difficult airway management. This form has decreased the percentage of false negative predictions and as a

result could lead to safer precautionary measures for patients.

ABSTRACT

Determination of Serum Lipid Levels via Routine Examination of Meibomian Gland Expression

Blake A. Harp *The University of Texas at Houston Medical School* *Class of 2012*

Sponsored by: Richard W. Yee, MD, Department of Ophthalmology and Visual Sciences

Supported by: *The University of Texas Medical School, Dr. Richard W. Yee*

Key Words: MGD, Lipid Profile, Meibomian Gland

The meibomian glands are tubulo-acinar, holocrine glands, embedded in the superior and inferior tarsal plates. The meibomian secretion, meibum, is composed of non-polar lipids (cholesterol, cholesterol esters) and polar lipids (phospholipids), whose chief function is to prevent tear evaporation from the eye surface. In patients with meibomian gland dysfunction (MGD) the gland orifices are often clogged or narrowed. This may be attributed to an increase not only in the lipid melting point, but also in the tear-film osmolarity due to an increase in aqueous evaporation or an increase in viscosity of the sebum, which compromises delivery. The characterization of meibum quality and quantity expressed is routinely performed and quantified in ophthalmological practice. This research is aimed at elucidating evidence that would support a correlation between abnormal meibomian gland secretion and high serum lipid profiles. Patients with MGD, whom also have a lipid profile will be included in the study. The cohort will be assessed for an increased prevalence of abnormal lipid profiles in comparison to our historical control, which is based on data from the American Heart Association's "Heart Disease and Stroke Statistics- 2009 Update." 65.2% of patients with abnormal meibomian gland secretion had an abnormal lipid profile result (n=46). 54.34% of patients had elevated cholesterol, compared to 45% in the general population. In conclusion, our data indicate a higher prevalence of abnormal lipid profiles in patients with MGD than in the general population. With further study, a meibomian gland exam could screen for patients at high risk for hyperlipidemia.

ABSTRACT

Infection rates in acetabular fractures with associated laparotomy

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Sponsored by: Milan Sen, MD
Catherine Ambrose, PhD
Supported by: UTHSC Department of Orthopaedics
Key Words: Acetabulum, pelvis, infection, fracture

This retrospective study was conducted to determine if the risk of acute infection in acetabular fractures requiring surgery is increased after a patient has undergone an exploratory laparotomy for associated abdominal trauma. It was our hypothesis that acute infection rates after acetabular fracture fixation are higher in patients with a prior laparotomy. Patients for this study were gathered using the Memorial Hermann Trauma Database, querying from December 2003 to December 2008. All surviving patients over the age of 18 that had exploratory laparotomies, suspected acetabular fractures, and underwent subsequent pelvis surgery were considered. All patients analyzed underwent some type of internal fixation. Those deemed non-operable, or patients with external fixation only, were excluded from the study. The rate of acute wound infection was then calculated for the population and compared to an infection rate of 3%, which is the highest rate reported in current literature for acetabular fracture fixation. Chi-square analysis was used to calculate the statistical significance of our results. There were a total of 37 patients that met our criteria. Of these patients, 30 showed no signs of acute infection before discharge, while 7 patients developed infections confirmed by tissue or aspirate culture of the surgical wound. These results showed an 18.9% infection rate among patients that underwent open reduction and internal fixation preceded by an exploratory laparotomy. Comparing this value to the 3% infection rate of published literature has shown the increased infection rate in our study to be statistically significant with a p-value of less than 0.001.

ABSTRACT

Evaluation of the rate of re-epithelialization of partial thickness skin injuries between different anatomic locations

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Sponsored by: David J. Wainwright, MD, FRCS(C), FACS, Division of Plastic and Reconstructive Surgery
Supported by: The Division of Plastic and Reconstructive Surgery
University of Texas Medical School at Houston
Key Words: Partial thickness, burns, re-epithelialization, dermis, epidermis

Introduction: Partial thickness skin injuries are wounds in which the epidermis and a portion of the dermis are lost, commonly encountered in second degree burns and donor sites of skin grafts. Re-epithelialization of partial thickness skin injuries occurs from two sources: the healthy skin on the periphery of the wound and from surviving epidermal appendages. This healing process results in an advancing wound edge from the periphery as well as circular "islands" of new skin that gradually enlarge. This project aimed to quantify the rate of re-epithelialization in partial thickness injuries and determine how it varies with anatomic site.
Materials and Methods: Patients with second degree burns at multiple anatomic sites were enrolled in the study and their wounds were photographed on a daily basis from the day of admission until the wounds were closed, resulting in a chronological series of photographs for each injury site. Each series of photographs was analyzed using image processing software to determine the rate of re-epithelialization.
Results and Discussion: Early results have indicated similar rates of closure for different sites: 6.7% wound closure per day at the arm, 7.3% at the forearm, and 9.5% at the back. Differences in these rates can be attributed to several factors, including the specific depth of the burn, the thickness of the skin at the site, and the vascular supply at the site. Further research should aim to develop treatment regimens that are specifically tailored based on the location of the burns.

ABSTRACT

Limb Reduction Defects in Texas, 1996-2004: classification, prevalence and risk factors.

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Sponsored by: Jacqueline T. Hecht, PhD, Department of Pediatric Genetics
Supported by: *University of Texas at Houston Medical School*
Key Words: Limb deficiency, Texas Birth Defects Registry, isolated limb anomaly

Congenital limb reduction defects (CLRDs) are structural anomalies characterized by absence or severe hypoplasia of limb structures; they occur as isolated defects or with other malformations. The birth prevalence ranges from 0.31- 1.04 / 1000 live births. Although previously classified by the limb affected, it has recently been suggested that extent and morphology of absent structure(s) may be a more biologically relevant classification. The goal of this study was to use this classification scheme to assess whether any demographic variables were associated with CLRDs. **Methods**: Live-born, singleton babies with limb deficiencies born between 1996 and 2004 were identified through the Texas Birth Defects Monitoring Division. All cases were reviewed by a medical geneticist and classified by type of limb anomaly(s) and by whether it was an upper or lower malformation. Birth prevalence rates and prevalence rate ratios (PRR) for each type of deficiency were calculated and adjusted for gender, maternal age, race, parity, maternal highest education, and public health region. Poisson regression models were used to adjust for covariates. **Results**: A total 1281 limb CLRD cases were identified of which 514 were isolated; 2,730,417 live singleton births were identified during the study period. The prevalence rate for all cases and for isolated CLRDs was 4.69 and 1.88/10,000 births, respectively. Upper limb defects (1.35/10,000) were 2.7 times higher than lower limb defects (0.50/10,000). Terminal defects (loss of a structure and all distal parts) were the most common with a birth prevalence of 1.49/10,000 births. Mothers in the age group less than 18 years had a significantly higher prevalence than the 18-29 age group (PRR= 1.81; 95% CI= 1.17-2.81). Mothers with a parity of 3 or greater had a significantly higher prevalence compared to first parity (PRR= 1.63; 95% CI= 1.18-2.24). Stratification by type of CLRD and affected limb showed similar PRRs across strata. **Conclusion**: This is the largest study of isolated CLRDs. Using two different classification systems, we found that terminal type defects were the most common limb anomaly defect and that younger mothers and those of parity 3 or greater had a higher risk for CLRDs.

ABSTRACT

Outcomes following Open Reduction and Internal Fixation (ORIF) of distal radius fractures using polyaxial locking plates.

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Sponsored by: Milan K. Sen, M.D. Department of Orthopaedics

Supported by: *The University of Texas at Houston Medical School, Dept. of Orthopaedic Surgery*

Key Words: Distal radius, ORIF, polyaxial locking plate

Distal radius fractures (DRFs) have a significant incidence rate in the United States, with more than 750,000 fractures occurring each year. For fractures requiring surgery, open reduction and internal fixation (ORIF) has proven to be a reliable treatment method due to its ability to provide stable fixation and early range of motion. Recently, polyaxial locking plates have been designed that allow for the variation of screw angle by 15° in all directions during operative plate placement. Polyaxial locking plates are still relatively new and little has been published on their efficacy in ORIF treatment of DRFs. This study employed retrospective techniques to examine radiographic outcomes in patients who received these polyaxial implants for their DRF. Patients included in the study were identified by a search using billing (CPT) codes, and also by a query of the Hermann Hospital Trauma Database. From January 2007 to May 2009, 79 patients were identified that fit study criteria, and their medical records were examined to determine the operating surgeon, fracture classification (AO), comorbidities, associated fractures, and type of plate used. 42 of the patients were found to have been treated with the Stryker VariAx Volar radius plate, which is the polyaxial plate that we are investigating. Of those 42 patients, 23 were found to have been followed for an adequate time period to assess long term reduction stability. All patients' pre-op, post –op, and follow up radiographs were measured for radial length, tilt, inclination, articular incongruity, ulnar variance, and distal screw distance to subchondral bone. Analysis of these measurements was performed to determine long term stability and whether fractures treated with these plates lose reduction over time.

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Medical Student

ABSTRACT

PREOPERATIVE USE OF INCENTIVE SPIROMETRY IN PREVENTING PULMONARY COMPLICATION IN THE MORBIDLY OBESE UNDERGOING BARIATRIC SURGERY

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Sponsored by: Carin A. Hagberg M.D Department of Anesthesiology
Supported by: NIH 5T35DA007676-17
Key Words: Incentive Spirometry, Laparoscopic Bariatric Surgery

Background: Morbidly obese patients undergoing general anesthesia for laparoscopic bariatric surgery require special considerations due to an increased risk of postoperative pulmonary complications. The purpose of this study was to determine if the use of incentive spirometry (IS), a lung volume expansion technique, prior to surgery improved respiratory mechanics that may relate to oxygenation and incidence of pulmonary complications postoperatively.
Methodology: At least 3 days prior to surgery, 11 obese patients, BMI > 40 kg/m^2, undergoing bariatric surgery were enrolled in the study during their preoperative consultation with an anesthesiologist. Patients were randomized into 2 groups. The control group was instructed only to use the incentive spirometer for 3 breaths, once per day. The experimental group was instructed to use the incentive spirometer for 10 breaths, 5 times per day. Each patient's greatest inspiratory volume achieved with IS (best of 3 attempts) was recorded during their preoperative consultation, the day of surgery, and postoperative day 1. Lung performance was evaluated by comparing each patient's actual IS inspiratory volumes to a table of "target" IS inspiratory volumes based on age, sex and height.
Results: There were no significant differences preoperatively between the 2 groups. The control group achieved an average of 95% of their "target" IS volume at the preoperative consultation and 91% on the day of surgery. The experimental group achieved an average of 95% of their "target" IS volume at the preoperative consultation and 95% on the day of surgery. There was, however, a statistically significant difference between the 2 groups postoperatively. The control group achieved an average of 71% of their "target" IS volume postoperatively while the experimental group only achieved an average of 50% postoperatively.
Conclusion: The results of this study were unexpected. It appears that preoperative use of incentive spirometry does not significantly improve respiratory function between the initial preoperative consultation and the day of surgery. Of particular importance, there appears to be a decrease in lung function postoperatively in the experimental group compared to the control group. The study was originally designed for 50 subjects but time constraints limited enrollment to only 11 patients. It is believed that the limited patient population had an influence on the efficacy of these results.

ABSTRACT

Circulating Tumor Cells as Prognostic Markers in Hormone-Refractory Prostate Cancer Patients

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Sponsored by: Robert Amato, D.O.
Department of Internal Medicine – Division of Oncology
Supported by: Robert Amato, D.O.
Department of Internal Medicine – Division of Oncology
Key Words: Circulating Tumor Cells, Hormone Refractory Prostate Cancer

Purpose: Prostate specific antigen (PSA) levels are currently used as a marker of prostate tumor activity. However the fact that PSA levels do not always correlate with the extent of disease, and the lack of additional reliable biomarkers, complicates the management of prostate cancer. In this study we evaluated the association of circulating tumor cell (CTC) number with clinical characteristics and survival in patients with hormone refractory prostate cancer.

Methods: From November 2008 through July 2009, samples of blood were drawn from 35 men with hormone refractory prostate cancer treated at UT Oncology Clinic. The samples were analyzed for CTCs using the Veridex CellSearch system. Patient CTC information was linked to clinical information through the use of AllScripts medical record system.

Results: Of the 35 men in the study, 15 (43%) had zero CTCs and 20 (57%) had one or more CTCs. Significantly higher CTC numbers were observed in patients with bone metastasis relative to patients with lymph node metastasis. CTC counts were modestly correlated to type of local therapy, either surgery or radiation. CTC counts were not correlated to the patients' Gleason score or to the number of therapy regimens. CTC number was strongly associated with survival, with higher CTC numbers predictive of decreased survival.

Conclusion: Based on the observed correlation between CTC values and certain clinical characteristics, and the observed correlation between CTC values and survival, our study provides additional evidence of the importance of CTC number as a prognostic marker in men with hormone refractory prostate cancer. Further studies are needed to validate the routine use of CTCs in the treatment of prostate cancer.

ABSTRACT

Autologous mononuclear progenitor cell injection for traumatic brain injury: the effect of injury cavity volume on potential neuroprotection

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Sponsored by: Charles S. Cox, MD

Supported by: Department of Pediatric Surgery

Key Words: Traumatic brain injury, progenitor cell, stem cell, mononuclear, cognition

Introduction: The intravenous injection of autologous mononuclear cells could bypass the significant first pass pulmonary effect leading to the increased potential for neuroprotection. In addition, previous research has shown that the hippocampus is important in long term memory and spatial navigation. We hypothesize that mononuclear cells offer neuroprotection via an interaction with the hippocampus and that increased hippocampal tissue loss would mitigate the potential therapeutic benefit.
Materials and Methods: Two groups of male Sprague-Dawley rats received controlled cortical impact (CCI) injury (moderate and severe groups). Two million autologous mononuclear stem cells were injected via the jugular vein 72 hours after injury. Cognitive testing was completed using the Morris Water Maze (MWM). Injury cavity volumetric analysis and Nissl stain were completed to compare injury severity and cortical/hippocampal tissue loss.
Results: Animals in the moderate injury group showed cognitive improvement compared to controls on days 6 (27.3 vs. 47.5 seconds), 7 (22.0 vs. 33.7 seconds), and 9 (17.3 vs. 31.3 seconds) of training. The severe injury group failed to show cognitive improvement. A significant increase in cortical/hippocampal tissue loss was observed in the severe injury group (13.6 vs. 6.0 mm^3).
Conclusion: The benefit observed from injection of autologous mononuclear stem cells is dependent upon injury cavity volume. The lack of functional recovery of the severely injured group may be due to the increased loss in cortical/hippocampal tissue indicating a potential interaction between the injected cells and hippocampus.

ABSTRACT

Rapamycin-mediated growth inhibition in human neuroblastoma cells

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Sponsored by: Priya Weerasinghe, MD/PhD/MSc, Department of Pathology

Supported by: Maximillian Buja, MD and Robert Brown, MD, Department of Pathology

Key Words: Neuroblastoma, Rapamycin

The objective of this study was to investigate the effects of rapamycin, a drug known to inhibit mediators of the mTOR signaling pathway, on neuroblastoma cells. We cultured human neuroblastoma cells treated with rapamycin at various concentrations and time points. The highest concentration of drug (10μM) proved to inhibit growth on culture plates and western analysis was used to decipher differences in protein expression between samples. Thus far, p70 S6 kinase appears to be increasing in concentration following 24 hour drug exposure, whereas P-STAT3 does not appear to change. After 48 hours of rapamycin exposure, p70 S6 kinase, P-STAT3, and P-AKT all demonstrate decreases in expression as drug concentration is increased from 1 nM to 10 μM. Further testing is still required for 72 hour drug exposure. This study would contribute significantly towards a better understanding of the alterations of the molecular pathways induced by rapamycin in neuroblastoma cells. Elucidating the signal transduction mediators of each type of cancer and studying their regulation through therapeutic intervention are essential to the concept of personalized medicine, which includes finding the most appropriate drug and dosage to a given patient's biological makeup.

ABSTRACT

Aortic Outgrowth within a Fibrin Matrix

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Supported by: National Institute of Diabetes and Digestive and Kidney Diseases, 5T35 DK007676-15

Key Words: Angiogenesis, fibrin, aortic ring model

Angiogenesis, the growth of new blood vessels from pre-existing vessels, is pivotal in many physiological and pathological processes within the body. Tissue repair and regeneration requires the generation of new blood vessels which provides collateral blood to injured tissue, while its inhibition may help combate the growth of tumors. The murine aortic ring model of vascular outgrowth, first described by Nicosia et al, 1982, has become a widely accepted angiogenic assay for testing different factors that either promote or inhibit angiogenesis. Traditionally the murine aortic ring model involves thick or thin collagen gels to support the aorta. Here the viability of the murine aortic ring model using a fibrin gel was investigated. A variety of fibrin gel concentrations was used, ranging from 2.5 to 20 mg/ml. Different cofactors such as poly(ethylene glycol) (PEG), which has been shown by Almany et al, 2005 to decrease the rate of fibrin degradation, were also tested. Whole aortas were collected from mice, humanely euthanized, through a thoracotomy. The aortas were then sectioned and placed in fibrinogen of designated concentrations dissolved in dulbecco's modified eagle medium and polymerized using thrombin. The outgrowth from the aorta was then assessed by light microscopy using a Nikon Eclipse TE-2000U fluorescence microscope. Significant vascular outgrowth was found at higher levels in the fibrin gels with PEG. The observation supports the viability of using a fibrin gel. Further investigation may be conducted to determine the optimal growth conditions within the fibrin gel.

ABSTRACT

Role of NF-kappaB in Intestinal Dysfunction Using a Human Cell Model

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Sponsored by: Karen Uray Ph.D., Department of Pediatric Surgery
Supported by: National Institute of Diabetes and Digestive and Kidney Diseases, 5T35 DK007676-17

Key Words: Edema, NFkappaB, Actin, Intestinal Dysfunction

Intestinal edema has been demonstrated to be a causative agent in intestinal motility dysfunction. Adverse effects in smooth muscle contraction are thought to occur through mechanical stress of smooth muscle altering F:G actin ratios and increasing NF-kappB signaling. The project determined the role of stretches on NFkappaB activation as well as the effects of altered actin polymerization on NFkappaB signaling, and a possible down stream activation of STAT3. Primary human intestinal smooth muscle cells were subjected to either a control cyclical stretch program (CCS) as during basal intestinal contractile activity or an edema cyclical stretch program (ECS) consisting of an increasing cyclical stretch as observed in edematous intestine. NFkappB activation was determined. Stretches were repeated using a 30 uM JSH-23 (Calbiochem) NFkappaB inhibitor and 1 uM cytochalasin-D (Calbiochem) actin polymerization inhibitor. NFkappaB activation was increased in the ECS group compared to the CCS group. A significant difference was seen in STAT3 phosphorylation with NFkappa B inhibited cells lending support to the fact that STAT3 phosphorylation may be downstream of NFkappaB. Inhibition of actin polymerization tended to inhibit ECS induced increases in both NFkappaB and STAT3. We conclude that increased cellular stretch as seen with intestinal edema formation increases NFkappaB activation through altered actin polymerization.

ABSTRACT

Role of Metastatectomy in Renal Cell Cancer Following Use of Molecular Targeted Agents

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Supported by: National Institute of Diabetes and Digestive and Kidney Diseases, 5 T35 DK007676-17; University of Texas Medical School at Houston – Office of the Dean
Key Words: Metastatectomy, Renal Cell Cancer, Molecular Targeted Agents

Background: Renal cell cancer (RCC) is the most common kidney cancer and occurs primarily in adults. It accounts for 2.6% of all adult cancers. The prognosis for metastatic renal cell cancer (mRCC) is poor, with 5-year survival rates of approximately 10-15%. The most recent breakthrough in the treatment for mRCC is the use of molecular targeted agents (MTA). These agents have been helpful in treating tumors as they target specific molecular pathways expressed in an individual patient's cancer. Resection of metastastatic disease has been shown to increase overall survival of some patients. The purpose of this study is to determine whether there is a role of metastatectomy in kidney cancer patients that have been treated with MTAs.

Methods: From October 2005 to July 2009, 18 male patients with mRCC were treated with a MTA. Inclusion criteria for the study were predominantly clear cell RCC, progressive measurable metastases, and no active CNS involvement. After achieving stable disease (SD) or partial response (PR) to therapy, these patients underwent metastatectomy.

Results: Of the 18 men in the study, 6 achieved surgical complete remission (sCR). 16 of 17 patients evaluated achieved negative surgical margins during metastatectomy. In patients treated with angiogenesis inhibitors, only 3 of the 14 patients had post-operative complications associated with bleeding. Just 2 of the 18 patients have not survived to this day. Due to low power, the study was unable to find any significant correlations or predictors.

Conclusions: As a preliminary study, the data is promising. The patients are healthy, have few complications with surgery, and achieve negative surgical margins. 66%of the patients did have recurrence of disease and most within 5 months. Further study is needed to fully evaluate the safety and efficacy of treating mRCC patients with MTAs followed by metastatectomy.

ABSTRACT

High Prevalence of Carotid Atherosclerosis among HIV-Positive Young African American Smokers

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Sponsored by: Dr. Roberto Arduino, Department of Internal Medicine – Infectious Disease

Supported by: Dr. Roberto Arduino, Department of Internal Medicine – Infectious Disease

Key Words: Human Immunodeficiency Virus, CART, & CIMIT

Background: Recent data indicate a high prevalence of subclinical atherosclerosis among patients infected with Human Immunodeficiency Virus (HIV). Information is limited regarding ethnic populations and HIV infected smokers. We used carotid ultrasound imaging to evaluate the prevalence of subclinical atherosclerosis among African American (AA) HIV infected patients.

Methods: African-American participants (n=45) of a large study evaluating smoking cessation in an HIV infected cohort were recruited for this study. B-mode ultrasound testing was used to determine the carotid intima-media thickness (CIMT) and the presence of carotid plaque. Plaque was defined as a discrete area of thickening, protruding into the lumen with a thickness >50% of the surrounding walls. Risk factors for coronary artery disease (RF), duration of Combination Antiretroviral Therapy (CART), CD4 cell count, HIV viral load (VL), and markers of inflammation (homocysteine, IL6, CRP) were evaluated.

Results: 21 female and 24 male subjects were evaluated with a mean age of 44 yr (range 24-63 yrs) 12 subjects had CIMT >75th percentile for age and mean CIMT was 0.69±0.16. A positive correlation between CIMT and age (p=.0001) was found. CIMT did not correlate with CD4 count or markers of inflammation. CRP correlated inversely with CD4 and homocysteine, and correlated directly with VL (p<0.02). 24 subjects (53%) were found to have abnormal carotid plaquing. There were significant differences in age (49±6 vs 37±7, p=0.002), average CIMT (0.75±0.15 vs. 0.61±0.13, p<0.005) and dyslipidemia (11 vs. 2, p=0.019) in the group with plaque vs. those without plaque. There were no significant differences in duration of CART, VL, CD4 count, number of RF, or biomarkers between groups.

Conclusion: There is a high prevalence of subclinical atherosclerosis in this cohort of HIV+ young AA smokers. Especially noteworthy was the high occurrence of abnormal carotid plaquing which is over 10 times the frequency seen in AA subjects. This has not been described before. Age, CIMT, dyslipidemia were significantly increased in subjects with carotid plaquing versus those who did not. This study highlights the need for aggressive traditional RF modification with particular attention to dyslipidemia in AA smokers. Further studies are required to determine the exact nature of the interplay between HIV, smoking, inflammation and RF that contribute to atherosclerosis.

ABSTRACT

Light induced model of retinal degeneration in zebrafish.

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Sponsored by: Dr. John O'Brien, MD, Ophthalmology
Supported by: Dr. John O'Brien, MD, Ophthalmology
Key Words: Zebrafish, outer nuclear layer

The specific aim of this project was to develop a model of macular degeneration in Zebrafish, by using light induced apoptosis. Theories have been proposed suggesting that cells undergoing apoptosis can spread certain "pro-apoptotic factors" through gap junctions between photoreceptor cells, which promotes "bystander killing," ultimately destroying the retina (Ripps, 2002). We exposed the fish to 14,000 lux light for 24 hours of constant light. Both the control and light-lesioned tanks were maintained at 29º C. Four fish were placed in each tank. The lights were kept on for three days and the fish were then allowed to recover for four days. One fish from the control and one from the experimental groups were sampled at four, seven, and nine days. The most effective stain was with an APO-BrdU TUNEL kit. We examined a standardized portion of the ventral retina of each fis, because it sustains the most damage from the UV rays (Vihtelic and Hyde, 2002). Measurements were taken to measure the thickness of the outer nuclear layer (ONL) of the retina, which contains the nuclei of the photoreceptors. Apoptotic nuclei were also counted in 100 μm squares of ONL. The data obtained indicates that our model of macular degeneration is causing appreciable apoptosis in the ONL, however enhanced degeneration would be beneficial in standardizing the amount of degeneration in the ONL. Further degeneration may also show a change in the thickness of the ONL which was not seen in our model. A higher intensity of light or a smaller tank may be beneficial in inducing higher levels of apoptosis in future studies. Once higher and more predictable levels of apoptosis are generated, the potential benefits of treatment with an adenosine receptor antagonist (A2) that uncouples gap junctions in the ONL can be effectively evaluated.

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Vihtelic TS, Hyde DR (2000) Light-induced rod and cone cell death and regeneration in the adult albino zebrafish (Danio rerio) retina. J Neurobiol 44:289-307.

ABSTRACT

Effect of plasma treatment on endothelial cells subjected to *in vitro* model of hemorrhagic shock

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Sponsored by: Rosemary A. Kozar, MD PhD
Department of Surgery

Supported by:

Key Words: hemorrhagic shock, endothelial, plasma, FFP, hypoxia, VEGF, HUVEC

Objective: This study sought to examine the effect of age of plasma on hypoxia-induced endothelial cell dysfunction.

Background: Resuscitative strategies using high ratio plasma are associated with improved outcome in patients requiring massive transfusion during hemorrhagic shock, though the mechanism is unknown. Preliminary laboratory data suggests that plasma's protective properties may be linked to the injured endothelium. We therefore hypothesized that plasma would reverse endothelial cell dysfunction after shock. As aged red cells have been shown to have detrimental effects following transfusion, we also hypothesized that fresh plasma would provide enhanced protection compared to aged plasma after shock.

Methods: HUVECs were grown to confluence then treated with 5% plasma thawed day 0 (fresh) or day 5 (aged) and compared to controls (media only) following hypoxia (1% O_2 for 24 hours) and reoxygenation. To validate this *in vitro* hypoxia model, HUVECs were transfected with VEGF then lysates analyzed for expression (Luciferase) and compared to normoxic controls. Functional assays for endothelial function included: proliferation (Beckman-Coulter counter), and migration which was quantified following HUVEC monolayer scratch assay using Kodak Digital Science 1D Software. The reciprocal of the denuded area was used as an index of migration. Results were analyzed by one-way ANOVA with Tukey post hoc, mean ± SEM, $p<0.5$ significant.

Results: There was significant up regulation of VEGF in hypoxia treated cells vs. normoxia controls (1.4±.3 *vs.* 0.5±.1, $p<.05$). Cell proliferation and migration were enhanced by fresh plasma compared to aged plasma (Table).

	Controls	**Fresh Plasma**	**Aged Plasma**
Proliferation	**1.3±.01**	**2.3±.02***	**1.3±.02**
Migration	**1.0±.2**	**1.7±.2***	**1.3±.2**

*P<.05 versus control and aged plasma

Conclusion: Fresh but not aged plasma significantly enhanced endothelial cell function following shock in an *in vitro* model of hypoxia/reoxygenation. These findings may have important clinical implications for patients requiring massive transfusion.

ABSTRACT

Enhancer Trapping in Zebrafish with Ear Specific Expression of Green Fluorescent Protein

*David Minor*David Minor *The University of Texas at Houston Medical School* *Class of 2012*

Sponsored by: Xinping Zhao, PhD, Department of Ophthalmology and Visual Science

Supported by: Xinping Zhao, PhD, Department of Ophthalmology and Visual Science

Key Words: Enhancer trapping, *Danio rerio*, zebrafish, ear

Zebrafish, *Danio rerio*, is a useful animal model for genetic studies because it shares a high level of genetic conservation with humans and is easy to study due to small size, short life cycle, transparent embryos, and high rates of breeding. We used a technique known as enhancer trapping to better characterize the functions of zebrafish genes that may share homology with genes causing human disease. In this method, an expression vector is randomly inserted into the zebrafish chromosome. A unique expression pattern of the reporter (green fluorescence protein, GFP) is observed if the vector is integrated to a genomic region where an enhancer resides. We crossed stable transgenic fish with unique GFP expression patterns to a wild type fish and observed the progeny by fluorescence microscopy. Embryos showing novel GFP expression patterns were collected for genomic DNA isolation, which was then digested with restriction enzymes and amplified by inverse PCR in order to obtain sequences flanking the integration site. The PCR product or its cloned colonies was sequenced by the Sanger method. The sequence data was then compared to the known sequence of the zebrafish genome to determine the locations of the DNA inserts. This analysis mapped the integration site in the enhancer trapping line that displays GFP signals only in the ear and to chromosome 21. The location was near one gene whose function is yet unknown. It is likely that the enhancer influencing the unknown gene is trapped in our transgenic fish.

ABSTRACT

DNA Persistence of Nonviable Bacteria in Osteomyelitis

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Sponsored by: Catherine Ambrose, PhD, Department of Ortopaedic Surgery
Supported by: Department of Orthopaedic Surgery
Key Words: PCR, *Stapholycoccus aureus*, biofilm infection, osteomyelitis

The polymerase chain reaction (PCR) has recently become a useful diagnostic test to detect bacterial pathogens without the need for culture. However, PCR amplifies all DNA present, regardless of whether the source of DNA is live or dead cells, making it difficult to determine if the amplified DNA is from an active infection. Studies in the Chinchilla middle ear *in vivo* model have shown that the DNA from dead bacterial pathogens persists for only a few days after cell death. However, it is thought that the DNA from pathogens in environments with limited perfusion, such as bone infections, may persist longer. This is the first study to define the length of time that DNA from dead bacterial cells can be detected in osteomyelitis tissue samples. Using *Staphylococcus aureus*, the major causal agent of osteomyelitis, *in vitro* biofilms were grown on stainless-steel rods. These rods were heat-treated (80°C for 25 min) to kill the *S. aureus* cells, while maintaining their cellular structure. Cell death was confirmed using the fluorescent BacLight LIVE/DEAD cell viability kit and imaged with a Ziess 510 Meta Confocal microscope. A Petroff Hausser cell counter was used to confirm that cell lysis did not occur during heat treatment. Using this method, rods covered with a dead biofilm will be placed into a rat femur to simulate a previously cured bone infection. Analysis of the tissue sample using PCR amplification of the 16s rRNA gene will be used to determine the *in vivo* persistence of pathogenic DNA over time.

ABSTRACT

Comparison between FDG-PET (F-18 Fluorodeoxyglucose(FDG) Positron Emission Tomography(PET)) and Response Evaluation Criteria in Solid Tumors (RECIST) in Detection and Duration of Response to mTOR Inhibitor

Raymond Mody *The University of Texas at Houston Medical School* *Class of*

Sponsored by: Dr. Roberto Amato, MD, Oncology Department

Supported by: Dr. Roberto Amato, MD, Oncology Department

Key Words: FDG-PET, mTOR Inhibitor, RECIST

Background: FDG-PET, based on the concept of enhanced glucose metabolism in malignant tumors, can be an early sensitive marker of tumor response to anticancer drugs by monitoring changes in glucose metabolism in tumors, thus, identifying responding and non-responding tumors early in course of therapy. Response to therapy on FDG-PET is identified at a much earlier stage than conventional imaging (CT) since metabolic changes show up weeks or months before decrease in tumor size. We analyze the timeframe and duration of metabolic response (PET) in comparison to CT in patients with metastatic Renal Cell Carcinoma (RCC) on Everolimus treatment, an oral mTOR inhibitor.

Methods: We performed a retrospective review of patient data from a phase II study assessing the activity of everolimus in patients with metastatic clear cell RCC. The study protocol included CT scans and PET scans at baseline, and then every 8-12 weeks thereafter while on study. We documented and compared the site of metastatic lesions on CT (measured by RECIST) and the correlated metastatic sites on PET scans (measured in SUV units). We measured time to best response for comparable lesions on CT and PET scans. We also evaluated time to progressive disease per RECIST criteria and time to progressive disease on PET scan (defined as >10% in SUV uptake) for each patient. Calculations of percent change in initial PET response were made. Duration of therapy data is also included in this study.

Results: 41 patients were originally enrolled in this phase II study. Of those, 37 presented with data evaluable for this study. Ten patients in this study had progressive disease (PD) based on both RECIST and PET criteria (in this study, we established PD for PET as a 10% increase in SUV from smallest recorded value since initiation of treatment). Of these 10 patients, 8 had recorded PD on the PET scan before PD was recorded on CT. The other two patients showed PD for PET and CT at the same week interval. Twenty-two patients were evaluable for comparison of percent change in RECIST at first metabolic response vs. percent change in first PET response. Of these 22 patients, 21 of them had larger percent decreases on PET than on CT. The average change for initial metabolic response was 38.3% while for RECIST at the initial metabolic response it was 9.5%. Twenty-three patients were evaluable for comparison of time to best response for RECIST and PET. Of the 23 patients, 8 had earlier best response for PET, 11 had earlier best response for RECIST, and 4 had best response for each at the same week interval.

Conclusion: In comparing data of patients evaluable for progressive disease based on both RECIST and PET criteria, our data shows that PET criteria (definition of PD as a 10% increase in SUV) was a earlier predictor of progressive disease compared to RECIST. Data from twenty-two patients evaluable for comparison of percent change in RECIST at first metabolic response vs. percent change in first PET response showed that PET had a larger change in initial metabolic response than RECIST at the same interval. From the twenty-three patients evaluated for comparison of time to best response for RECIST and PET, PET was not an earlier indicator of best response.

ABSTRACT

Effect of Glucose Concentrations on *Staphylococcus aureus* Biofilm Formation in an *In Vitro* Model for Diabetic Foot Ulcer Infections

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Sponsored by: Heidi B. Kaplan, PhD, Department of Microbiology and Molecular Genetics

Supported by: National Institute of Diabetes and Digestive and Kidney Diseases, 5T35 DA007676-17

Key Words: Diabetes, biofilms, confocal microscopy, infections, *Staphylococcus aureus*

Over 20 million Americans have diabetes mellitus, with 90% of these being type II diabetics. Bacterial infections that lead to biofilm formation in diabetic patients are extremely difficult to eradicate. These infections can have serious consequences including loss of limbs or in severe cases can threaten a patient's life. Here, we have adapted an *in vitro* biofilm model developed previously in our lab to serve as a model of a diabetic foot ulcer infection (DFUI) by modulated glucose levels in our synthetic interstitial fluid (SIF) to mimic those of a non-diabetic (75 mg/dL), a treated type II diabetic (125 mg/dL), and an untreated type II diabetic (175 mg/dL). For the model, *Staphylococcus aureus*, which is the most common etiological agent of DFUIs, was grown on discs of polymethylmethacrylate (PMMA) at 37°C in SIF. The biofilms were stained with the fluorescent BacLight LIVE/DEAD cell viability kit, imaged using a Ziess 510 Meta Confocal microscope on days 3, 4, and 5, and analyzed with the nPHLIP 2.0 software developed previously in our lab. The greatest biovolume was detected on day 4 for all glucose concentrations, and 125 mg/dL provided the optimal glucose concentration for biofilm growth. While it has often been presumed that compromised vascularity is the main cause of the severity of infections in diabetics, our data indicate that glucose levels should also be taken into account. Our results suggest that restoration of blood glucose levels to normal levels might reduce the incidence or severity of DFUI.

ABSTRACT

Functional Outcome of Carpal Wedge Osteotomy in Children with Arthrogryposis Multiplex Congenita

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Sponsored by: Gloria Gogola, MD, Department of Orthopaedic Surgery

Supported by: Thomas E Cain, MD, Educational Trust Fund: Shriners Hospitals for Children-Houston
University of Texas Medical School at Houston – Office of the Dean

Key Words: Carpal Wedge Osteotomy, Arthrogyrposis, Functional Dexterity Test

INTRODUCTION: Children affected with arthrogryposis have multiple joint contractures from birth with significant functional limitations. Carpal wedge osteotomy has been described as a surgical technique to reduce the flexion contracture at the wrist. The procedural goal is to establish a better position from which to execute functional motor tasks of the hand such as feeding, writing, and hygienic self-care.

METHODS: An IRB approved, retrospective study was designed to evaluate functional outcomes in children with arthrogryposis who have undergone carpal wedge osteotomy. Preoperative versus postoperative changes in resting wrist position, passive and active range of motion about the wrist, as well as dexterity patterns as determined by Functional Dexterity Test (FDT) were analyzed. Fifteen children were evaluated. The average age at surgery was 6.5 years, and the average length of follow up was 20 months.

RESULTS: Analysis of resting position showed a preoperative mean flexion of 77°, with a mean postoperative flexion loss of 41° for the cohort ($p<.001$). The mean passive range of motion arc pre to post showed a loss of 24° flexion ($p<.001$) and a gain of 26° extension ($p<.001$). Similarly, the active range of motion mean arc from pre to post showed a mean active flexion decrease of 29° ($p<.0001$) and active extension gain of 25° ($p<.0001$).
The FDT, composed of 16 wooden on a peg board, evaluates a patient's ability to perform in hand manipulation. Ten patients had complete FDT video exams for analysis, which showed in every case an increase in speed per peg turn and a faster total time postoperatively on both the dominant and non-dominant hand. Five subjects demonstrated a change from a passive hand grip pattern before surgery to an active grip pattern.

CONCLUSION: We conclude that carpal wedge osteotomy as indicated in children with arthrogryposis significantly improves wrist position, which translates into positive functional

gains in dexterity.

THE UNIVERSITY of TEXAS
HEALTH SCIENCE CENTER AT HOUSTON

2009 Summer Research Program
Office of Educational Programs
Medical School

Medical Student

ABSTRACT

A comparison of patency rates in brachiocephalic arteriovenous fistula patients versus upper arm tapered arteriovenous graft patients at UTHCVS from 2006-2009

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Sponsored by: Ali Azizzadeh, MD, Department of Cardiothoracic and Vascular Surgery

Supported by: National Institute of Diabetes and Digestive and Kidney Diseases, 5T35 DK007676-15

Key Words: Arteriovenous fistula, arteriovenous graft, polytetrafluoroethylene, Propaten, hemodialysis access, heparin bonded PTFE

Background: Arteriovenous fistulae (AVF) are the preferred type of vascular access for hemodialysis patients. However, many patients do not have acceptable veins in the upper extremity and require prosthetic arteriovenous grafts (AVG). Several groups advocate using a graft that is tapered at the arterial anastomosis and widened at the venous anastomosis. We analyzed patency rates and 30-day complication rate by retrospectively comparing brachiocephalic AVF and upper extremity AVG.

Methods: We analyzed all patients who had a permanent vascular access procedure at our tertiary referral center from 2006 to 2008. 181 different patients had a permanent access procedure created by members of our department. Factors presumed to affect patency and morbidity rate included age, previous failed access procedures, and comorbid conditions, such as diabetes. Per surgeon preference, minimum vein diameter was 2.5 mm for AVF. We compared complication rates, reinterventions, primary, primary-assisted, secondary, and functional access patency rates using logistic regression and accounting for correlation among observation coming from the same subjects.

Results: Of the 181 vascular access patients, 67 had brachiocephalic AVF, and 66 had tapered brachial-axillary AVG. Ten patients were excluded from 1-year analyses because follow up data were not available. All grafts were expanded polytetrafluoroethylene (PTFE) with a 4- to 6-mm or 4- to 7-mm taper. Of the AVGs, 29 were heparin-bonded and 33 were standard-walled. 30-day postoperative complication rates of AVF versus AVG were 4.4% and 16.7%, respectively (OR 0.34, 95% CI 0.06-1.91). 1-year primary, primary-assisted, and secondary patency-rates of AVF vs. AVG were 80% vs. 72.6% (OR 1.13, 95% CI 0.37-3.46), 93.8% vs. 87.1% (OR 0.92, 95% CI 0.22-3.9), and 89.2% vs. 74.2% (OR2.3, 95% CI 0.7-7.4). Overall functional access patency of brachiocephalic AVF was 83.3% compared with 58.2% in AVG (OR 1.33, 95% CI 0.41-4.32). 1-year thrombosis rates between standard-walled and heparin-bonded PTFE were 39.4% and 27.6% (OR 1.32, 95% CI 0.29-6). Age, body-mass index, dyslipidemia, hypertension, diabetes, and history of previous access made no statistical difference in complications or patency rates.

Conclusions: Native AVF is the preferred long-term vascular access for hemodialysis. However, when upper extremity veins are inadequate, tapered AVG has acceptable results. The results we obtained from tapered grafts compare favorably to the use of non-tapered, straight prosthetic grafts in the published literature. Comorbid conditions did not affect the complication or patency rates of brachiocephalic AVF or AVG. Heparin-bonded tapered PTFE did not perform better than standard-walled PTFE and may not justify the additional expense.

ABSTRACT

Determining CT Findings That Will Necessitate Surgical Intervention of Type B Aortic Dissection

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Sponsored by: Anthony L. Estrera, MD, FACS, Department of Cardiothoracic and Vascular Surgery
Supported by: NIH National Institute of Diabetes and Digestive and Kidney Diseases
Key Words: Aortic dissection, Stanford Type B, Computed tomography, CT

Aortic dissections are common and occur at a rate of 2.6 to 3.5 per 100,000 persons per year. Of those afflicted, nearly 50% will die within the first 48 hours if the dissection is left untreated. This study specifically examined Stanford type B dissections which are located within the descending aorta distal to the left subclavian artery. While 85.5% of dissections are successfully treated with a medical course of action, the remaining percentage require surgical repair of the aorta. It is the purpose of this study to determine what characteristics set that 14.5% of patients apart from the rest. Following IRB approval a list of patients with aortic dissections was compiled. The list was then narrowed down to only those patients with a type B aortic dissection. Information from the charts was collected retrospectively for each patient and entered into a Microsoft Excel spreadsheet. Computed tomography (CT) scans were then examined for each patient and measurements were taken at standardized locations. This data was also entered into an Excel spreadsheet. As this is a continuing study, the data collected has yet to be fully compiled and analyzed. Upon completion, a multivariate analysis will be performed with the data in order to determine what correlations, if any, exist between a patient's signs and symptoms and the necessity for surgical intervention.

ABSTRACT

Evaluation of the Efficacy of Various Topical and Eyelid Cleansing Agents on the In Vitro Killing of Ocular Demodex

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Sponsored by: Richard W. Yee, MD, Department of Ophthalmology

Supported by: Hermann Eye Fund

Key Words: Demodex spp., Anterior Blepharitis, Tea tree oil

Anterior blepharitis caused by ocular *Demodex folliculorum* is an inflammation of the eyelids that causes red, irritated, itchy eyelids and the formation of cylindrical dandruff-like scales on eyelashes. The aim of this study was to determine which agent from a selection of topical agents and commonly used eyelid cleansing solutions would be most effective at killing demodex mites. The topical agents used include Restasis, Azasite, Zymar, Lumigan, and Tobramycin. The kill time of these agents were compared to those of commonly used eyelid cleansing agents such as 50% baby shampoo, provodone iodine, new sterilid, and Tea Tree Oil. We selected patients who exhibited cylindrical sleeves on their lashes and performed a slit lamp exam to determine which lashes would be epilated. The lashes were then placed on a slide and immersed in 20 micro liters of the agent being tested. A light microscope was used to determine the presence of the demodex mites and the amount of time it took for the agent to completely kill the mites. Kill time was determined by the cessation of leg movements of the mites for a period of 10 minutes. Kill times range from 2 minutes (50% tea tree oil) to over 3 hours (Azasite, Restasis, 50% baby shampoo, Zymar, provodone iodine, Tobramycin, and Lumigan). The kill times for agents that failed to kill the mites after 3 hours were not determined. In conclusion, we were able to determine that 50% tea tree oil was the most effective at killing the demodex mites.

ABSTRACT

Disruption of Time Encoding in Human Primary Visual Cortex

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Sponsored by: Michael S. Beauchamp, PhD, Department of Neurobiology & Anatomy
Supported by: Michael S. Beauchamp, PhD, Department of Neurobiology & Anatomy
Key Words: V1, TMS, fMRI, time

A recent study in rats (Shuler & Bear, Science 2006 Mar 17;311(5767):1606-9) implicated an unexpected brain region in time perception: primary visual cortex (V1). After training, V1 neurons responded not only to the presentation of a visual stimulus that was delivered before a reward, but also to the presentation of the reward itself. An important question is whether the V1 activity contributed to the rat's knowledge of the length of the delay between the visual stimulus and the reward. Due to the difficulty of answering this question in rats, we posed a similar question in humans. Our hypothesis was that disrupting human V1 would interfere with the ability to accurately estimate time intervals.

To assess the role of V1 in time keeping, subjects were first trained to judge a 2 second interval using 40 trials of response-determined feedback. Then, the subjects were presented with 40 trials in which the stimulus was either repeated at a random delay in the same location, the opposite quadrant, or not at all. The results demonstrated a significant increase in mean response time in the trials with the stimulus at the same location (2521.6 ms vs. 2370.5 ms, $p = 0.0004$) and the opposite quadrant (2446.3 ms vs. 2370.5 ms, $p = 0.004$) compared to the trials without a second stimulus. A significant increase also exists between same and opposite quadrant trials (2521.6 ms vs. 2446.3 ms, $p = 0.006$).

Transcranial magnetic stimulation (TMS) was then used to disrupt human V1 by creating a focal magnetic field and electrical current in the nervous tissue underlying the TMS coil. To measure this disruption a 4 alternative forced-choice task involving the orientation of a stimulus was used. Among 10 subjects (6 male, 4 female, average age = 25.3 ± 5.6, all right-handed) performance was reduced from 90.6% ± 4.6% (no TMS) to 51.8% ± 8.5% (with TMS).

In an adaptation of the first experiment the second 40 trials were replaced with 20 TMS trials interleaved with 20 no TMS trials. TMS did not change the subjects estimate of the length of the 2 second delay (mean response time, 2146 ms ± 278 ms without TMS versus 2146 ms ± 364 ms ($p = .9916$). However, TMS increased the standard deviation of the subject's estimate of the length of the delay. That is, on a trial by trial basis, they were less precise at judging the delay when TMS was delivered to V1 (SD 364 ms ± 119 ms vs. 278 ms ± 79 ms, $p = 0.0148$). This change in precision was not observed when a TMS pulse was applied to a control site (282 ms ± 174 ms, $p = 0.919$). These results support a role of V1 in the perception of time.

ABSTRACT

Hypovitaminosis D in Pediatric Orthopaedic Patients

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Sponsored by: Allison Scott, MD, Department of Orthopaedics

Supported by: National Institute of Diabetes and Digestive and Kidney Diseases, 5T35 DK007676-15

Key Words: Vitamin D, Hypovitaminosis D, Pediatrics, Spina bifida, Orthopaedics

Objective: Hypovitaminosis D is increasingly diagnosed among children worldwide. This study examines the prevalence and various factors of low 25(OH)-D among pediatric orthopaedic patients. **Methods:** 25(OH)-D levels were obtained from two groups of pediatric orthopaedic patients from a specialty hospital in Texas. The first group consisted of 70 children admitted for surgeries requiring bone healing. The second group consisted of 45 children with spina bifida. 25(OH)-D levels were correlated with age, sex, ethnicity, season, and region (Mexico vs. U.S.). Additionally, the surgical group's 25(OH)-D status was correlated with the diagnosis, BMI, and BMI percentile. The spina bifida group's status was also correlated with PTH levels, PODCI, and ambulation. **Results:** In the surgical group, the median 25(OH)-D concentration was 20.9 ng/ml, and 90% had insufficient 25(OH)-D levels < 32 ng/mL, 51% had < 20 ng/mL, and 16% had deficient levels <12 ng/mL. African descendants, older age, and cold seasons were significantly associated with hypovitaminosis D, but diagnosis, region, BMI, $BMI^{\%tile}$, and gender were not. The spina bifida group's median 25(OH)-D concentration was 20 ng/mL, and 89% had insufficient levels < 32 ng/mL, 58% had < 20 ng/mL, and 18% had deficient levels < 12 ng/mL. Ethnicity, PTH, and PODCI mobility score were significantly associated with 25(OH)-D status. There was a trend for 25(OH)-D levels to decrease with older age and wheelchair ambulation. Gender, season, and region had no association. **Conclusion:** Hypovitaminosis D is prevalent in these pediatric orthopaedic patients and several factors increase their risk. The effects of low 25(OH)-D on their overall health should be evaluated and more research is needed to clarify optimal 25(OH)-D concentrations in children and what degree of supplementation maintains it.

ABSTRACT

Role of Nitric Oxide in Hemorrhaged and/or Resuscitated Rats

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Sponsored by: Marie-Francoise Doursout, Ph.D
Department of Anesthesiology

Supported by: Marie-Francoise Doursout, Ph.D
Key Words: Hemorrhagic shock, Nitric Oxide, HPLC

Hemorrhagic hypotension leads to a well-characterized sequence of events which includes decreases in cardiac output and blood pressure, the release of vasoconstrictors, hyporeactivity, and vascular decompensation. An key substance induced in this physiologic response is nitric oxide (NO), a molecule that decreases blood pressure when it is released from the vascular endothelium. Nitric oxide is the physiological activator of soluble guanylyl cyclase (sGC), an enzyme which catalyzes the formation of cGMP, leading to a vasodilatation. An overproduction of NO has been described in the pathophysiology of hemorrhagic shock. It is well known that NO reacts with superoxide anion to form peroxynitrite, a protein that damages organ tissues and will be measured in future experiments The goal of our study was to assess NO production in hemorrhaged animals with and without resuscitation. In our experiments, rats on a nitrate-restricted diet were hemorrhaged at 2ml/kg over 10 minutes, and were either left untreated or resuscitated using Ringer's solution, lyophilized plasma, Day 0 plasma, or Day 5 plasma. Blood samples were collected before hemorrhagic shock (HS), and at 1, 2, 3 4, and 6 hrs after hemorrhagic shock. The plasma was analyzed for nitrite and nitrate, metabolites which represent the final products of the nitric oxide (NO) oxidation pathways and are assessed as an index of systemic NO production. We measured these concentrations using high performance liquid chromatography (HPLC). Preliminary results show that nitrate levels increase in all treatment groups after HS, and treatment with Day 0 plasma leads to the induction of fewer nitrates than treatment with Day 5 plasma. We will continue experiments to increase the samples size of each treatment group and make more definitive conclusions. Future work will include analyzing cytokine release after HS and examining tissue sections for pathology.

ABSTRACT

Clinical Factors and Pathological Correlates Associated with Outcomes in Patients with Metastatic Renal Cell Carcinoma Treated with Modified Vaccinia Ankara Delivering Tumor Antigen 5T4 (TroVax)

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Sponsored by: Robert Amato, DO
Department of Internal Medicine – Division of Oncology
Supported by: National Institute of Diabetes and Digestive Kidney Diseases, 5 T35 DK007676-17
Key Words: TroVax, metastatic renal cell carcinoma, cancer vaccine

Purpose: Metastatic renal cell carcinoma accounts for 3% of all adult cancers, and the five year survival rate is only 5%. The TroVax vaccine is a modified Vaccinia Ankara virus (MVA) that has been engineered to deliver the tumor antigen 5T4, which is highly expressed on carcinomas of the kidney and is retained in metastatic lesions. Two separate studies have been conducted to study the efficacy of TroVax, and both have shown that TroVax was well tolerated and generates an immune response. In this study, the baseline characteristics of patients who received TroVax were examined to determine the clinical and pathological characteristics that predict a greater progression free survival and overall survival.

Methods: A total of 53 patients received the TroVax vaccine alone or with IL-2 or IFN. Their baseline laboratory data, clinical data, and demographic data were collected and analyzed to determine the baseline characteristics that predict a good overall response to the TroVax vaccine. A correlation analysis and two linear regression analyses were performed.

Results: Of the 53 patients who received the TroVax vaccine alone or in combination with IL-2 and IFN, 11 (20%) are still alive with an average overall survival of 36.7 months. It was hypothesized that LDH, HGB, performance status, Fuhrman grade, histology, platelet count, and neutrophil count, and metastatic site and number of lesions would be predictive of overall survival and progression free survival. A regression analysis showed that the number of previous treatments ($p = 0.046$) predicts overall survival, as does a lack of metastatic spread to the lymph nodes ($p = 0.041$). Receiving TroVax in itself predicted a greater progression free survival ($p = 0.017$).

Conclusions: This analysis shows that the only baseline characteristics predictive of greater progression free survival and overall survival in patients who received the vaccine are number of previous treatments, lack of metastatic spread to the lymph nodes, and receiving the TroVax vaccine. Further analysis and studies should be done in order to support these findings.

ABSTRACT

Spinal Cord Injury Causes Failure of the Blood-Testes Barrier

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Sponsored by: Raymond Grill, PhD, Department of Integrative Biology and Pharmacology

Supported by: NINDS RO1 NS 049409

Key Words: Contusion, Permeability, Endothelial

Spinal cord injury (SCI) disrupts spinal vascular barrier function. Barrier failure allows the influx of blood-born molecules that produce a devastating inflammatory response that continues long after the initial insult. The pathological response to SCI is not limited to the local spinal environment. SCI elicits adverse alterations systemically that contribute to a permanent loss of quality of life. It has been reported that men suffering from chronic SCI exhibit lowered testosterone and altered sperm production. We hypothesize that acute SCI elicits a systemic attack of endothelial barriers, including that of the testes. Adult male rats received a thoracic-level SCI. Testicular barrier integrity was assessed at 3 days post-SCI by measuring permeability to albumin, a serum protein, and gadolinium, an MRI-sensitive dye. Testicular structural deficits were assessed via histology.

A significant reduction of testicular albumin extravasation was detected at 3 days. We also assessed testicular permeability using dynamic contrast enhanced MRI (DCE-MRI). This pilot study indicated a profound increase in SCI-dependent testicular vascular permeability. Qualitative morphological analysis showed increased numbers of activated mast cells in the testes from SCI-subjects. Cellular stress was evidenced by upregulation of activating transcription factor-3 (ATF3). Finally, blood vessels within the testes of SCI-subjects exhibited reduced expression of the endothelial barrier antigen (EBA), a marker associated with enhanced vascular barrier function.

These findings support the hypothesis that SCI disrupts blood-testes barrier integrity. We next propose to test the hypotheses that these acute responses to injury contribute to the long-term deficits associated with testicular dysfunction in chronic SCI.

ABSTRACT

Reliable Reduction of Trauma Overtriage Based on Prehospital Data: A Conservation of Scarce Health Care Resources

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Sponsored by: John B. Holcomb, MD, Department of Surgery
Supported by: *John B. Holcomb, MD*
The University of Texas at Houston Medical School – Office of the Dean
Key Words: Overtriage, Trauma, Prehospital

Introduction: Fifty percent of the Code 2 patients that arrive to our Level 1 trauma center via helicopter (LF) are discharged after arrival. Code 2 patients are hemodynamically stable, but have a mechanism that could indicate a potentially serious injury. Prehospital triage is currently based on vital signs, mechanism of injury and anatomical location of injury. An overtriage rate of 50% is considered acceptable, however this historic rate contributes to overcrowding and delayed care to the more seriously injured. **Objective:** We hypothesized that there is a signal within the prehospital physical exam and vital signs that differentiates admitted versus discharged Code 2 patients. **Methods:** This IRB approved, retrospective study evaluated adult (>18 years) Code 2 patients (n=1758) transported by LF from May 2007 - May 2009. Due to time constraints, a subset (n = 490) of this cohort was analyzed. Prehospital data from each patient, including demographics, mechanism and vital signs were analyzed using linear regression and Student's t-test to compare the discharged (n=287) and admitted (n=203) groups. **Results:** Utilizing simple univariate analysis, these data do not show a clinically significant difference within current prehospital measurements that allowed an accurate method of prehospital triage for Code 2 trauma patients. **Conclusion:** Based on the current analytic method and cohort size, admitted or discharged patients cannot be discriminated. Within the next 60 days we will perform multivariable logistic regression modeling using our complete dataset to identify the factors most strongly associated with admission compared to discharge. If this new analysis does not show a difference, then new methods of prehospital triage may distinguish these two groups. Electronic capture and analysis of serial prehospital vital signs, including novel methods of ECG and pulse oximetry waveform interrogation will likely be required.

ABSTRACT

Outcomes of Pulmonary Metastases in Ewing's and Osteosarcoma

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Sponsored by: Andrea Hayes-Jordan, MD, Department of Pediatric Surgery

Supported by:

Key Words: Ewing's, Osteosarcoma, Pulmonary Metastases,

Ewing's and osteosarcoma are the two most common bone malignancies in children, adolescents, and young adults. Combinational therapies including radiotherapy, chemotherapy, and surgical techniques have substantially improved the overall survival for patients with localized disease. The survival rate of patients with pulmonary metastases is substantially lower than it is for those with localized disease only. At the moment, there is no precedent for therapy of patients with pulmonary metastases. A retrospective study was designed to determine if surgical resection of the pulmonary metastases had an effect on survival rate. One hundred and sixty-six Ewing's or osteosarcoma patients from MD Anderson were analyzed to determine the combinational and singular effects of radiation and pulmonary resection. The presence of unilateral or bilateral pulmonary metastases and the number of pulmonary nodules was also examined. The data retrieval and analyses is still underway, as the longevity of the research has extended beyond the scope of the ten-week summer research program. More patients will be added to this retrospective study to enhance results. This study aims to determine if surgical resection improves the survival rate of patients with pulmonary metastases from Ewing's or osteosarcoma and to postulate a standard, more effective methodology for these patients.

ABSTRACT

Ceramide containing multivesicular emulsion application as a skin hydration treatment for feet of subjects with non-insulin dependent diabetes mellitus

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Sponsored by: Adelaide A. Hebert, MD, Department of Dermatology

Supported by: National Institute of Diabetes and Digestive and Kidney Diseases, 5T35 DK007676-17

Key Words: Non-insulin dependent disbetes, xerosis, TEWL

The American Diabetes Association reports that over 20 million people in the United States have diabetes. Patients with diabetes experience a high incidence of foot xerosis, cracks, fissures, and erosions. Many diabetics have peripheral neuropathy and do not inspect their feet daily for ulceration and infection. Adverse sequelae from these complications include amputations and a reduced quality and length of life. These concerns highlight the importance of basic skin care measures in this population.

We are currently investigating whether skin hydration in non-insulin dependent diabetics can be enhanced by twice daily application of a ceramide containing multivesicular emulsion. This study is currently enrolling subjects. Changes in barrier function of the skin are being assessed before and after application of the study cream using tewametry, which measures transepidermal water loss, and corneometry, which assesses moisture content of the stratum corneum. Thirty subjects with non-Insulin dependent diabetes mellitus will be treated with a ceramide containing multivesicular emulsion twice daily for 14 days. Following treatment, subjects will be assessed weekly over a 21 day period for improvement from baseline based on tewametry, corneometry, and investigator xerosis assessment scores.

In a previous study, patients with insulin dependent diabetes were treated and measured with these same methods as the study described above. In that study, twice daily application of a ceramide containing repair cream reduced xerosis of the feet in patients with insulin dependent diabetes mellitus by facilitating barrier function in the skin. These therapeutic strategies may help prevent diabetic foot complications.

ABSTRACT

Proactive Interference of Human Visual Working Memory

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Sponsored by: Anthony A. Wright, Ph. D., Department of Neurobiology and Anatomy
Supported by: Anthony A. Wright, Ph. D., Department of Neurobiology and Anatomy
University of Texas at Houston Medical School – Office of the Dean
Key Words: Visual Working Memory, Visual Memory Processing, Interference

This study investigated the effects of proactive interference (PI) upon human visual working memory. PI occurs when memory from a previous event interferes with the recall of a more recent event.

Ten participants each completed 128 trials of a list memory task. A trial consisted of six color kaleidoscope images presented in quick succession on a touchscreen computer. After the sixth image and a delay of five seconds, a kaleidoscope image (probe) appeared alongside a white box. The participants were instructed to choose the kaleidoscope image if it was seen in the previous six images or to choose the white box if the image was not seen. During select PI test trials, an image viewed in a previous trial (1, 2, 4, or 8 trials prior) was shown as the probe in order to create interference. Subjects might incorrectly categorize these items as belonging to the current trial's list due to the PI effect.

Accuracy was analyzed across list position (RM ANOVA) and a significant linear trend was found, $F(1, 9) = 14.529$, $p = 0.004$, $\eta = 0.617$. Planned comparisons showed the last list position to be significantly different than the first, $p = 0.017$. List position analysis led to a hypothesis that only interfering items from the first list position interfere with memory performance. Using binomial regression, a significant difference was found for interfering items in the first list position between trials just witnessed ($n = 1$) and trials further in the past ($n = 2$, 4, and 8), $p = 0.041$.

This result of interference from the first item in the list is consistent with the primacy effect, and shows evidence that items that are well remembered in the past can interfere with visual working memory performance.

Acknowledgements:
John Magnotti

ABSTRACT

Calcaneal Fractures: Indirect Reduction and External Fixation

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Sponsored by: Thomas O. Clanton, Department of Orthopaedic Surgery

Supported by: University of Texas at Houston Medical School
Key Words: Calcaneus, external fixation, Ilizarov, os calcis, ORIF

The current treatment of displaced intra-articular calcaneal fractures has been surgical fixation. The objective of this study was to evaluate the use of indirect reduction with Ilizarov external fixation as a viable alternative to open reduction internal fixation (ORIF) in the surgical treatment of calcaneal fractures. Medical records of 113 patients with 122 fractures of the calcaneus that were seen at Memorial Hermann Hospitals between January 1, 1999 and May 1, 2009 were retrospectively analyzed for their fracture type, time to surgery, time of hospital stay, post-operative infection, post-operative pain, need for additional surgical intervention, and time to weight bearing. Follow-up ranged from 6 months to 4 years. Statistical analysis revealed that patients receiving external fixation of calcaneal fractures spent more time in the hospital ($p<.001$), had longer time to weight bearing ($p=.001$), had greater chance of infection ($p=.005$) and had increased occurrence of pain ($p=.036$). Continued analysis, including radiographic data analysis, is being performed to verify these conclusions.

ABSTRACT

Use of 5′-AMP mediated hypothermia to treat cardiac ischemia

RYAN Y TILLMAN *The University of Texas at Houston Medical School* *Class of 2012*

Sponsored by:
Supported by: Cheng C Lee, PhD., Department of Biochemistry and Molecular Biology
Key Words: Hypothermia, ischemia/reperfusion, 5′-AMP

Introduction: Therapeutic hypothermia is a widely accepted method for improving patient outcome following an ischemic event. The metabolite 5′-adenosine monophosphate (5′-AMP) plays a central role in determining cellular energy equilibrium and has recently been shown to rapidly induce a deep hypometabolic state and loss of thermoregulation. The core body temperature of mice rapidly assumes target temperatures without the use of paralytics. Based on these observations we hypothesized that 5′-AMP induced hypothermia will reduce inflammation and preserve cardiac function in a mouse model of ischemia/reperfusion injury.
Methods: Male C57BL/6 mice were instrumented for electrocardiographic (ECG) analysis and underwent a left thoracotomy followed by ligation of the left anterior descending coronary artery (LAD) for duration of 45 minutes. Ischemia was confirmed by development of ST segment elevation on Lead II ECG. Prior to reperfusion, mice were randomly assigned to a normothermic control group, a 5′-AMP control group, or a 5′-AMP induced deep hypothermia (IDH) group. 24hours post-operatively, mice underwent ECG analysis followed by cardiac tissue collection for immunostaining of the inflammatory cytokine tumor necrosis factor alpha.
Results: Conduction abnormalities at 24hrs post-surgery, including ventricular tachycardia, were present in 50% of both control groups (n=16) as opposed to 27% of the 5′-AMP-IDH group (n=11). Immunostaining for TNF-a was inconclusive and further experimentation will be required.
Conclusion: 5′-AMP induced hypothermia shows promise in decreasing pathological hallmarks of ischemia. However, further experimentation including functional assays will be required to shed light on this treatment.

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International Medical Students

ABSTRACT

Characterization of a Type IV pilus-like gene cluster in *Corynebacterium diphtheriae*

Hao-Yun Chen *China Medical University* *Class of 2014*

Sponsored by: Hung Ton-That, Ph.D., Department of Microbiology & Molecular Genetics

Key Words: *Corynebacterium diphtheriae*,, type IVb pili

Backgorund: *Corynebacterium diphtheriae*, an aerobic Gram-positive bacterium, is the causative agent of diphtheria, a historically deadly disease. Recent bioinformatic analysis revealed a type IVb-like pilus gene cluster in *C. diphtheraie*. Type IVb pili, also called Flp (fimbrial low-molecular-weight protein) have been shown to be associated with biofilm formation and pathogenesis of both Gram-positive and Gram-negative bacteria. To define the role of Type IVb pili in the pathogenicity of *C. diphtheria*, the function of Type IVb pili in *C.diphtheriae* should be investigated first. In the present project, my aim is to construct knock-out mutants of all genes in the Type IVb-like pilus gene cluster for comparison of the mutants versus wild-type *C. diphtheriae* in functional assays such as biofilm formation and adherence of epithelial cells.
Method: To generate conjugative plasmids for knock-out mutants, approximately 1kb upstream and downstream fragments of the target gene were PCR-amplified and a second step of PCR amplification was introduced to ligate the two DNA fragments. Next, ligated PCR products were digested and inserted into the linearized conjugative plasmid pK19mobsacB. Conjugative plasmids were transformed into *Escherichia coli* DH5α for propagation and then re-transformed into *E. coli* strain S17-1 which expresses F-pilus for conjugation. S17-1 *E. coli* containing conjugative plasmids were then mixed with *C. diphtheria* to allow conjugation to occur. *C. diphtheria* cells, in which the conjugative plasmids had integrated into the bacterial chromosome, were selected on heart infusion agar (HIA) plates containing nalidixic acid and kanamycin. Corynebacterial mutants, as the result of second homologous recombination, were then selected on HIA plates containing 10% sucrose and further screened by PCR analysis.
Result: Due to time constraint, I have only finished constructing a conjugative plasmid targeting *tadZ*, the first gene in the locus. I am in the process of selecting corynebacterial co-intergrants. Although I don't have enough time to finish the project, I have learned a lot of molecular biology techniques this summer.

ABSTRACT

Cytotoxic activity of Gemcitabine and Docetaxel against murine squamous cell carcinoma cells

Kuan Lun Fu *China Medical University , Taiwan* *Class of 2012*

Sponsored by: ***Nadarajah Vigneswaran*** BDS, DMD, Dr. Med. Dent Professor of Oral and Maxillofacial Pathology, Department of Diagnostic Sciences

Supported by: NIH grant R21DE019956 (NV)

Key Words: CD147, Gemcitabine, Docetaxel, Cisplatin, S-phase arrest, cytotoxicity

Background: Patients with head and neck squamous cell carcinoma (HNSCC) require a combination of chemotherapy. Cisplatin (CP), Docetaxel (DOC) and Gemcitabine (GEM) are regimens showing a high response rate in advanced HNSCC patients. However, the poor therapeutic response with these regimens show up because of acquired multidrug resistance mediated by CD147. To determine whether siRNA-mediated silencing of CD147 would improve the treatment of HNSCC in mice is important. **Aim**: To investigate ***in vitro*** cytotoxic activity of DOC/GEM singly or in combination with CP against B4B8 and LY2 cells. **Methods**: Cell viability was determined using the XTT-assay. IC_{50} of drugs was calculated. Special staining for proliferating cell nuclear antigen (PCNA) and cleaved Caspase 3 (Casp-3) were performed to determine the proliferation and apoptosis rates, respectively. Cells were treated with GEM alone or in combination with CP and stained immunohistochemically using the antibodies against PCNA and Casp-3. Positive cells were counted by image analysis program. **Results**: B4B8 cells were mostly resistant to GEM but DOC killed B4B8 in a higher concentration. Combining CP (5μM) with GEM did not enhance its cytotoxicity against B4B8 cells whereas DOC with CP revealed synergy in killing B4B8 cells. LY2 cells were highly susceptible to killing by GEM than DOC .The mean apoptosis rates for LY2 cells treated with GEM (250nM) alone or in combination with CP were 21% and 27%, respectively. Apoptosis rates for the B4B8 cells treated with GEM (250nM) alone or in combination with CP were 12% and 16%, respectively. There were no significant differences in the cell proliferation rate of B4B8 cells between untreated control (88%) and GEM (86%) treated cells. Interestingly, LY2 cells treated with GEM (250 nM) had markedly higher PCNA positive cells (76%) than untreated control cells (28%). **Conclusion:** LY2 cells in syngeneic mice are more susceptible by chemotherapeutic drugs GEM /DOC than B4B8 cells. GEM exerts greater cytotoxicity against LY2 cells than DOC. Increase in PCNA positive cells within the LY2 cells treated with GEM compared to untreated controls cells is most likely caused by S-phase arrest. Our data suggests that PCNA should not be used to determine the cell proliferation rates of tumor cells treated with GEM.

ABSTRACT

Cholesterol Crystals and Survival of Vascular Smooth Muscle Cells from Murine Aortas

YOU LI *Southern Medical University, Guangzhou, China* *Class of 2012*

Sponsored by: Ali. Denktas MD, Assistant Professor, and Yong-Jian Geng, MD, PhD, Professor, Division of Cardiology, Department of Internal Medicine

Supported by: UT-Houston Summer Research Program

Key Words: Atherosclerosis , Crystallization, Smooth Muscle Cells cholesterol

Atherosclerosis is a chronic arterial disease, with two life-threatening complications: heart attack and stroke. A well-defined risk factor is hypercholesterolemia which can cause vascular plaque formation. Smooth muscle cells migrating and proliferating from the arterial intima constitute a major cellular component in fibrous plaques. This research aims to compare the cholesterol and 7-ketocho-lesterol in their biological effects on smooth muscle cellproliferation and death. Smooth muscle cells (SMC) were isolated and grown from C57BL/6J aortas in Iscove's Modified Dulbeccos Medium(IMDM). They were incubated with cholesterol or the oxysterol 7-ketocholesterol for 48 hours after washing with PBS. SMCs' viability was assessed by fluorescent microscopy with nucleic acid-binding fluorocheromes. Cholesterol crystals were detected by polarized microscopy. Their images were taken and collected via a digital camera and analyzed with the NIH Image software. SMCs were evaluated by immunocytochemistry to determine whether they expressed SMC specific antigens. There was evidence that in the presence of oxidized cholesterol, crystals appeared in large amounts in the cultures similar those seen in advanced atherosclerotic lesions. Additionally, the oxidized cholesterol showed a more significant negative effect on the viability of SMCs, when compared to cholesterol. In conclusion, vascular SMCs exposed to oxidized cholesterol can develop cholesterol crystals and have lower viability.

ABSTRACT

PRELIMINARY DATA ON ANTICIPATION OF THE DIFFICULT AIRWAY: THE PREOPERATIVE AIRWAY ASSESSMENT FORM AS AN EDUCATIONAL AND QUALITY IMPROVEMENT TOOL

Lin Chin Han(Kenny Lin) Taipei Medical University *Class of 2013*

Sponsored by: Carin A. Hagberg, MD, Department of Anesthesiology, The University of Texas Health Science Center at Houston
Supported by: Foundation for Anesthesia Education and Research
Key Words: Mallampati score, Wilson score

One of the responsibilities of anesthesiologists is to maintain patients' airways during surgical procedures. However, failure to secure the airway resulting in death or hypoxic brain injury is the leading cause of medical malpractice cases for these physicians. Many of these cases were due to an inadequate preoperative airway examination. Therefore, the preoperative assessment performed by anesthesiologist including an appropriate airway examination is very important. Unfortunately, a very useful preoperative airway assessment form for patients does not exist. We developed a new form to facilitate prediction of the difficult airway. This study compares which assessment form is more predictive of difficult airway management.

We randomized all anesthesiology residents at the University of Texas Medical School at Houston in July 2009 into 2 groups. Patients under 18 years of age or with external airway devices were excluded. The new form involves much more data collection to predict a difficult airway. Both two groups are required to perform postoperative assessments to determine if those features on the preoperative form are predictive of a difficult airway.

We have screened 365 patients in July 2009. The mean age and BMI were 48.9 yrs ± 12.2 yrs (SD) and 30.61 kg/m^2 ± 8.25 kg/m^2 (SD), respectively. The experimental group predicted an overall airway difficulty with a false negative prevalence of 11.2% vs 14.3% and a false positive prevalence of 20.9% vs 27.8%, as compared to the control group. Prediction of the research team had a false negative prevalence of 13.4% and a false positive prevalence of 30.6%.

Our study demonstrated that the new airway assessment form will improve the prediction of a difficult airway. These results suggest that BMI, neck circumference, inter-incisor distance, thyromental distance, sternomental distance, Mallampati score, neck mobility, mandible mobility are good indexes for the evaluation of difficult airway. The decrease of the false negative prevalence rate demonstrates that the new form performs better than the old form, thus is likely to replace the current form.

ABSTRACT

Development of New Methodology to Detect Gene Expression of the Three Isoforms of Adenylyl Cyclase in Neuron B51

YU LING LIU *China Medical University* *Class of 2015*

Sponsored by: John H. Byrne, PhD, Department of Neurobiology and Anatomy

Key Words: Operant conditioning, *Aplysia*, adenylyl cylcase

Operant conditioning is a form of associative learning, which is produced when an animal's behavior is modified by reinforcement. The invertebrate marine mollusk *Aplysia* has a simple and thoroughly understood nervous system, making it a suitable model system to examine the mechanisms of operant conditioning. Conditioning can now be understood at the level of changes in the activities of single cells such as the "decision making" interneuron, B51 in the buccal ganglion. Recently, Lorenzetti et al (2008) have found that the cAMP-dependent pathway was ciritically involved in meditating operant conditioning. This work suggested that adenylyl cyclase (AC), an enzyme that converts ATP to cAMP, could be involved in the molecular mechanism of operant conditioning. Three isoforms of AC exist in the *Aplysia*, but the expression of only two (AC-a and AC-b) have been detected previously in B51. The goal of my experiment is to modify the methodology to detect gene expression of the three isofroms of AC in B51 using single-cell polymerase chain reaction (PCR) with a modified nested PCR procedure. After confirming the gene expression of the AC isoforms, the roles of existent ACs in B51 during the operant conditioning will be examined. The positive control contained templates from the cDNA library of plural pedal ganglia. Two negative controls were designed, one controlled the reverse transcription stage, excluding reverse transcriptase from the sample; the other controlled the PCR stage, where nuclease free water replaced cDNA templates. The results showed sharper and consistent expression of isofroms AC-a and AC-b, which further confirms their existence in B51. Although detectable in sensory neurons, AC-c has yet to be detected in B51. Due to the lack of positive control results (sensory neuron Single-Cell PCR), my experiment could not assert its lack of gene expression in B51.

Reference:
Lorenzetti, F.D., Baxter, D.A. and Byrne, J.H. (2008). Molecular mechanisms underlying a cellular analog of operant reward learning. *Neuron 59(5)*,815-28

ABSTRACT

Ku70 interacts directly with Net1 without the aid of other proteins.

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Sponsored by: Jeffrey A Frost PhD Integrative Biology and Pharmacology
Supported by: University of Texas Medical School at Houston – Office of the Dean
Key Words: Ku70, Ku80, Net1, DNA damage

Ku proteins play a key role in nonhomologous DNA-end-joining (NHEJ) repair, which is responsible for repairing a major fraction of DNA double-strand break (DSB). Ku proteins consist of a complex of two protein subunits, Ku70 and Ku80. Previous work indicated that both Ku70 and Ku80 interact in vitro with the C-terminus of the Rho GEF Net1 (neuroepithelioma transforming gene 1). This was significant because Net1 regulates cell survival in response to DNA damage. Thus, the identification of Ku70/Ku80 as Net1 interacting proteins may serve as the mechanism by which Net1 protects cells from DNA damage induced apoptosis.
The goal of this project is to determine whether Ku proteins interact directly with Net1 in vitro. We transformed BL21DE3 E. coli with expression plasmids for His-tagged Ku70, GST, GST-Net1 (502-591), GST-Net1 (502-595) and GST-Net1 A (full length)] and purified each protein using NiNTA-agarose or glutathione-agarose affinity chromatography. We then tested the interaction of Ku70 with the GST proteins in vitro by pulldown assay followed by Western blotting. We observed specific interaction of His-tagged Ku70 with GST-Net1 (502-595). This result indicates Ku70 interacts directly with Net1 without the aid of other proteins. Future studies will identify domains within Ku70 that mediate interaction with full length Net1. Completion of these studies will shed light on the mechanism by which Net1 controls DNA-PK activity and ultimately cell survival.

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Undergraduate Students

ABSTRACT

Influence of isolate origin and presence of various genes on biofilm formation by *Enterococcus faecium*

SAM HUSAM ALMOHAMAD *University of Houston* *Class of 2010*

Sponsored by: Dr. Barbara Murray, MD, Internal Medicine
Supported by: Dr. Barbara Murray, MD, Internal Medicine
Key Words: Enterococcus faecium, biofilm

Background. *E. faecium* is often associated with medical devices and endocarditis. The ability to form biofilm may help enterococci cause such infections, however, very little is known about *E. faecium* and biofilm.

Methods. 61 *E. faecium* isolates (21 from *E. faecium* endocarditis, 19 from other *E. faecium* infections, 10 from healthy volunteer stools and 11 from animal sources) were evaluated. For biofilm, bacteria were grown in tryptic soy broth-0.25% glucose in polystyrene microtiter plates for 24 h at 37°C and plates were processed as previously described. The presence of *esp* (enterococcal surface protein) and *fms* genes (MSCRAMMs-like faecium surface protein) were evaluated using DNA colony lysates and high stringency hybridizations.

Results. OD_{570} for biofilm ranged from 0.01 to 1.3 and allowed the 61 *E. faecium* to be categorized into 4 groups (i) OD_{570}, ≥1: 5 isolates [8%]; (ii) OD_{570}, ≥0.5-1: 8 isolates [13%]; (iii) OD_{570}, ≥0.2-0.5:15 isolates [25%]; and (iv) OD_{570}, ≤0.2; 33 isolates [54%] (defined as non-producers). 19 of 40 (48%) clinical isolates, 3 of 10 (30%) isolates from healthy community volunteers, and 6 of 11 isolates (55%) formed biofilm. The *esp* and *fms* genes were found to be present in isolates of all four biofilm categories.

Conclusions. Although the clinical and animal isolates showed higher biofilm formation than the isolates from healthy community volunteers, the difference was non significant. Neither *esp* nor *fms* genes appear to be essential; however, the presence of ebp_{fm} operon (*pilB*) and *fms21* (*pilA*) locus was associated with higher amounts of biofilm.

ABSTRACT

A Comparative analysis of the morphology and motility of Treponema Pallidum *and* Borrelia Burgdorferi

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Texas State University-San Marcos

Sponsored by: Dr. Jun Liu ,PhD, Department of Pathology and Laboratory Medicine

Supported by: The University of Texas at Houston Medical School - Summer Research Program

Key Words: Syphilis , Lyme disease , Motility

Treponema Pallidum, the causative agent of syphilis and *Borrelia Burgdorferi*, the causative agent of Lyme disease, two very prevalent diseases, are from a group of bacteria known as Spirochetes. In research related to disease control and prevention, Spirochetes are of special importance due to their distinct morphology and motility. Both these organisms possess the ability to begin as a localized infection and later disseminate throughout the body, affecting the central nervous system, cardiovascular system and other parts of the body. In particular *T.pallidum* presents a difficult challenge to scientists, because of the strict conditions, such as sensitivity to oxygen and low metabolic capabilities, which restrict it from being continuously cultured in a laboratory. Due to these problems in cultivation, little is known about the specifics of the cellular structures of this organism. With the use of an emerging microscopic technique, Cryo-electron Tomography, which allows for 3D images to be taken of organisms, we have been able to view images of these bacteria that have led to a better understanding of the cellular architecture of these organisms. This study was conducted to compare the morphology of these organisms in order to better understand how the motility correlates with the high invasiveness and pathogenesis of these bacteria. There are differences within the protein make-up of the motors that power motility. For future studies other structural differences between these organisms can further be studied to expand our knowledge on this unique group of bacteria.

ABSTRACT

Expression of a *Mycobacterium tuberculosis* gene in *E. coli*

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Sponsored by: Lisa Y. Armitige, MD, PHD, Department of Internal Medicine, Division of Infectious Diseases
Supported by: University of Texas at Houston Medical School – Summer Research
Key Words: *Mycobacterium tuberculosis*, tuberculosis, Ag85C

Mycobacterium tuberculosis (Mtb), the causative agent of the disease tuberculosis, kills 2 million people worldwide every year. Diagnostics currently in use for tuberculosis do not differentiate between people who have had the disease in the past and those who are currently infected.
The goal of this study is to produce a protein sufficient for testing reactivity of cells from tuberculosis patients and healthy volunteers to Mtb.

We chose the gene *fbpC* which encodes for the protein Antigen 85C for our studies. In order to express the protein we chose Mtb laboratory strain H37Rv from which to amplify the gene. Through Polymerase Chain Reaction (PCR) we amplified the gene for cloning. Restriction endonuclease sites for *Bam*HI and *Hin*dIII were engineered into the PCR primers. Gene Ag85C (*fbpC*) and plasmid vector PQE30 were digested via endonucleases at restriction sites *Bam*HI and *Hin*dIII on both the gene and plasmid vector. The gene and vector were ligated together. Codon Plus RP, an *E. coli* bacterium, was chosen because of its ability to translate genes from GC-rich genomes, such as Mtb; and to express large quantities of proteins. Through transformation the recombinant Mtb gene was transferred into Codon Plus RP. The bacteria were plated on selective plates and the transformed bacteria grew. Twenty-four bacterial colonies were picked from agar plates into broth. Plasmid Prep was performed on all twenty-four colonies. Through random sampling the colonies proved to have cloned the plasmid vector PQE30 and the gene Ag85C has yet to be identified through gel electrophoresis. Currently, additional transformants are being screened for the cloned gene.

ABSTRACT

Dietary Nucleotides to improve Spinal Cord Injury outcomes in Rats

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Sponsored by: Catherine G. Ambrose, PhD, Department of Orthopaedic Surgery
Supported by: The University of Texas at Houston Medical School – Summer Research Program
Key Words: Dietary Nucleotides, Spinal Cord Injury, Rats

Spinal Cord Injuries, or SCI, have devastating effects on the bodies of all organisms who suffer them. Bone studies conclude that after a SCI, bone mineral density (BMD) and bone mineral content (BMC), as well as volumes and mechanical strength of the bone significantly decrease. To try to diminish these changes in the bone, SCI rats in this study were given one of 3 nucleotide diets for six weeks after injury. After sacrifice, bilateral femora were removed from each animal and the bones were scanned using Dual Energy X-ray Absorptiometry (DXA) to determine BMD and BMC. Using Archimede's Principle, the volumes of the bones were calculated. The mechanical strength of the bones was assessed using a servohydraulic testing machine (MTS 810). The bones were then ashed at 580 ^{o}C for 24 hours. The results demonstrated that the nucleotide diet consisting of 0.5%RNA resulted in a significant improvement in the strength of the femurs at the femoral neck. Although the diet improved bone strength at the midshaft of the femurs, the differences were78 not significant. In a separate arm of this study completed earlier, the 0.5%RNA diet was also found to significantly reduce the scarring in the spinal cord at the level of the injury, corroborating the bone results presented here.

ABSTRACT

Sequencing *Corynebacterium diphtheriae* clinical isolates

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Sponsored by: Hung, Ton-That
PhD
Microbiology and Molecular Genetics

Supported by: University of Texas Health Science Center R01.AI061381

Key Words: *Corynebacterium diphtheriae* SpaA operon

Corynebacterium diphtheriae, the causative agent of cutaneous and pharyngeal diphtheria in humans, assemble on their surface three different pilus structures, namely the SpaA, SpaD, and SpaH-type pili, that mediate specific adherence to difference tissues. Each pilus is made of a major pilin forming to the pilus shaft and two minor pilins located at the tip region and at the pilus base. Pilus assembly requires a specific transpeptidase enzyme called sortase, whose gene is associated with pilus genes in a pilus gene cluster. It is known that the concentration of a major pilin determines the length of pili. Previous work done in the lab has shown that some clinical isolates express pili with various lengths as compared to those of the type strain. The aim of this study was to sequence the SpaA pilus gene cluster of clinical isolates that produce highly extended pili in order to determine the mechanisms that regulate pilus polymerization. For the purposes of this study, only one clinical isolate, obtained from the Center for Disease Control and Prevention, was studied. Using a primer walking method, sets of primers, based on the spaA locus sequence of the type strain, were designed to amplify 500 bp PCR products, which were then cloned into the cloning vector pCR2.1. The resulting plasmids were transformed into *Escherichia coli* DH5α cells. Positive transformants, i.e. white colonies grown in X-gal plates and 500 bp DNA products by colony-PCR, were subject to plasmid DNA purification, and the DNA templates were submitted to sequencing. Seven of the twenty regions of the spaA locus were obtained, analyzed and compared with the type strain sequence. Future work will focus on completing the entire gene locus.

ABSTRACT

Comparison of CBCT Mandibular Trabecular Bone Density in Osteoporotic Versus Non-Osteoporotic Patients

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Sponsored by: Kenneth Abramovitch, DDS, MS, Department of Diagnostic Sciences, Section of Radiology

Supported by: The University of Texas at Houston Dental Branch - Summer Research Program

Key Words: osteoporosis, CBCT, trabecular bone

Osteoporosis is a skeletal disorder that can lead to bone weakness and subsequent fracture. It is common in people, particularly women, of advanced age. The disease is often asymptomatic until debilitating fracture-related injuries occur. Cone-beam computed tomography (CBCT) is quickly becoming a prevalent diagnostic tool in dentistry. It has well-documented efficacy for dentoalveolar implant surgery and prosthodontics and for assessment of inferior alveolar nerve proximity to third molars prior to third molar extraction. A recent pilot study with CBCT demonstrated that there was statistically significant decreased mandibular cortical bone density in female osteoporotic patients when compared to age matched control patients. Using CBCT software, the relative bone densities in the mandibular cancellous bone of three groups of female patients were measured and compared at six specific points of interest. These groups were: osteoporotic patients older than 45 years, non-osteoporotic patients older than 45 years, and non-osteoporotic patients aged 18 to 25 years. This study aimed to establish whether or not a significant difference exists between these groups, in CBCT derived densities of cancellous mandibular bone. Analysis of measured bone densities revealed no statistically significant differences among the three groups. This trend, along with the incidence of the large standard deviations in the cancellous bone density measurements, suggests that the variability inherent in the density of cancellous bone prevents a reliable assessment of mandibular osteoporosis.

ABSTRACT

Separate and overlapping cortical circuits for language and working memory

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College of Charleston

Sponsored by: Timothy Ellmore, Ph.D., Department of Neurosurgery
Supported by: UTHSC-Houston Department of Neurosurgery
Vivian L. Smith Foundation for Neurological Research
Key Words: Working memory, language, fMRI, Wada test, epilepsy

Pre-surgical planning prior to resection of tumors or seizure foci involves the identification of eloquent cortex critical for language, memory, and motor function. One outstanding question is what is the spatial relationship between brain areas important for language and memory function. While theoretical models of language processing posit a strong dependence on working memory during language production - which would suggest a high degree of overlap - there is little empirical evidence showing how these two cognitive processes tap into the same neural circuits.

Four epilepsy patients with language and memory function lateralized to the left hemisphere by Wada testing were imaged in a 3T MRI with a blood-oxygen-level-dependent sequence. Each performed visual verbal and spatial working memory tasks, and three covert visual language production tasks. Functional image analysis was done with AFNI using multiple regression. Significant task related activity was quantified separately for the memory and language tasks in each subject's cortical mantle (i.e., gray matter) using an automated labeling approach.

The degree of overlap, quantified by a group conjunction analysis of voxels active in both language and memory tasks divided by the number of voxels active in either task was 2.3%. Individual conjunction analyses of individual patient datasets showed some variability in the degree of overlap, ranging from 2.2% to 10.9% (mean 6.7% +/- 2.5). Areas of activation common to both memory and language tasks included Brodmann area 45 (-45, +32, +10 mm, MNI Coordinates) and the superior temporal gyrus (-43, -39, +14 mm, MNI coordinates) near to Brodmann area 41.

A quantitative comparison between cortical areas active during language production and working memory was conducted and showed surprising little overlap. These results suggest functional recruitment of different neural circuits during language and memory processing, which may be important to take into account during pre-surgical mapping to preserve eloquent cortex.

Acknowledgements:
Nitin Tandon M.D.
Stephen Fisher

ABSTRACT

Examining Phosphatidic Acid Signaling Using a New Sensor

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Sponsored by: Guangwei Du, Ph.D., Department of Integrative Biology and Pharmacology
Supported by: The University of Texas at Houston Medical School - Summer Research Program
Graduate Student Education Committee
Key Words: phosphatidic acid (PA), phosphatidic acid binding domain (PABD), transactivator of transcription (TAT), retrovirus

Phosphatidic acid (PA) is a phospholipid located on the cellular membrane. It plays a key role in cell proliferation, membrane traffic, and cytoskeletal reorganization. It has also been proposed that the dysregulation of PA may contribute to cancer and cardiovascular diseases. Therefore, it is important to study signaling pathways regulating PA production. To do this, a phosphatidic acid binding domain (PABD) recently characterized by our laboratory is used as a biosensor to monitor the change of PA level in live cells. Since it is difficult to deliver the plasmid encoding PABD to some cell lines by regular transfection methods, we have designed two more efficient strategies to deliver PABD into cells. The first method is to infect the cell with a retrovirus construct carrying a green fluorescent protein (GFP)-tagged PABD. We have completed the construct and have used it to deliver the GFP-PABD into HCC1806 cells, which are very difficult to transfect. The second method is to purify the PABD expressed in *E.coli*. This PABD is tagged with a peptide derived from the transactivator of transcription (TAT) protein, which carries the PABD into the cell at high efficiency without transfection reagents. These two methods will provide better ways to study PA-mediated signaling. Understanding PA-mediated functions may assist in designing therapeutic treatments of cancer and other diseases.

THE UNIVERSITY of TEXAS
HEALTH SCIENCE CENTER AT HOUSTON

2009 Summer Research Program
Office of Educational Programs
Medical School

Undergraduate Student

ABSTRACT

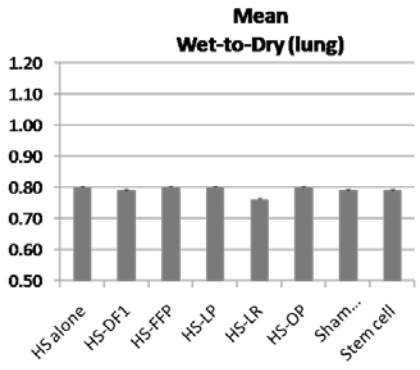
Is the lung edematous in hemorrhaged rats subjected to resuscitation fluids?

KELSEY COMEAUX *Prairie View A&M University* *Class of 2011*

Sponsored by: Marie-Françoise Doursout, PhD, Department of Anesthesiology
Supported by: The University of Texas at Houston Medical School - Summer Research Program
Key Words: hemorrhage, edema, resuscitation fluids

It is generally recognized that the major cause of battlefield deaths in conventional warfare is acute hemorrhage, accounting for 50% of fatalities. Therefore research is needed to overcome the deleterious effects of hemorrhage. It has been demonstrated that conventional resuscitation fluids induced edema mainly in the gut. However no data are currently available on the effects of resuscitation fluids in the lung. Thus, the goal of our study was to determine if the lung was edematous in hemorrhaged rats subjected to various resuscitation fluids e.g. Lactated Ringer (LR), Lyophilized plasma (LP) and Fresh Plasma (FP).

Rats were anesthetized under isoflurane and ventilated. Tygon catheters were introduced into the femoral artery for blood pressure and heart rate measurements and into the jugular vein for blood sampling. Hemorrhage was induced by withdrawal of 2 ml/kg of blood over 10 min. Resuscitation fluids (LR, LP, FP) were administered 1 hr after hemorrhage. Animals were sacrificed at t=6hrs. Lungs were removed and weighed (wet weight), then disposed overnight in an oven. Weight of the lung was measured at t= 24 hrs (dry weight). As shown in the table, our data demonstrates that resuscitation fluids did not induce edema in the lungs.



Conclusion: Although no edema was recorded in the lung in hemorrhaged rats with or without resuscitation fluids, further studies using combined resuscitation fluids are wanted. Furthermore, additional ratios need to be studied in further experiments.

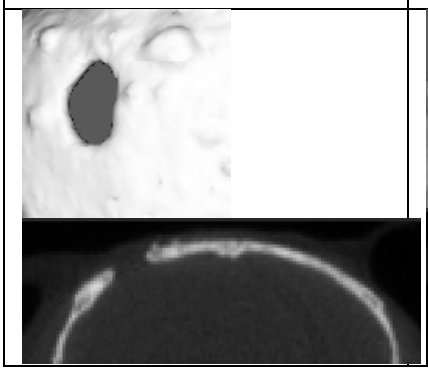
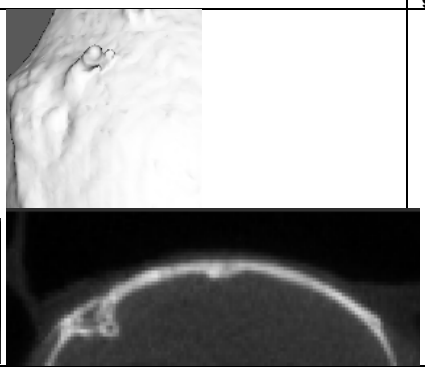
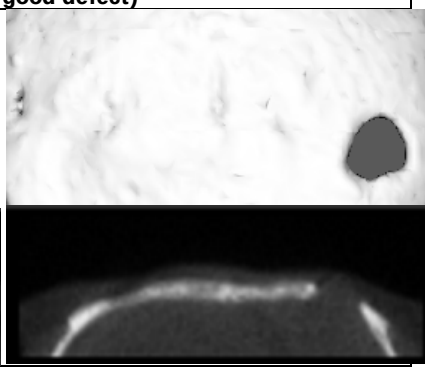
ABSTRACT

MicroCT Scans of Defects in Mice Skulls: One Year Post-Surgery

QUYNH DIEP *University of Houston* *Class of 2010*

Sponsored by: Dr. Pauline J. Duke, PhD., Department of Orthodontics Research
Supported by: UTHSC Office of Biotechnology
Key Words: microCT, one year, skull defects

In our lab, we have previously used bone-forming cartilage to heal bone. There has been a continued effort to further this usage. Results have shown that implanting a 2mm defect in a mouse skull with cartilage engineered in a rotating bioreactor results in healing of the defect in about 3 weeks as indicated by μCT scans and histology sections of the defect region. In the current study, μCT scans of implanted and control animals after one year are compared. μCT scans were taken at several time intervals at M.D. Anderson and analyzed using a GE MicroView software to thoroughly view the skull and corresponding defect or implant. The scans have shown the presence of non-healing defects in the control mice even a year after the procedure. This has important implications on the lack of mechanisms for self-repair and possibly further usage of promoting factors for cartilage transforming into bone. There is an obvious thickening in the region of the defect indicating remodeling around the defect edge. With the implants, it still holds true that there is a lack of complete remodeling even at a year post-surgery. The implanted nodule seems to be well into its process of shape reformation into the skull defect but still remains quite bulky and possibly protruding into the brain, which was seen in the initial scans. Histological sections of the defect regions will be carried out to determine how much of the implant remains after one year, and what the cause of the thickened edge in the non-healing defect. The question remains to determine whether complete reformation and reshaping of the skull occurs, and if so, how long does it take?

53383 (control)	53316 (implant)	53385 (control; 1 poor defect, 1 good defect)
		

ABSTRACT

SPECULAR COMPONENT AS PREDICTOR OF GLOSS OF RESIN COMPOSITES

MICHELLE B. ELDIWANY *University of Texas at Austin* *Class of 2012*

Sponsored by: Rade D. Paravina, DDS, MS, PhD, Department of Restorative Dentistry and Biomaterials

Supported by: The University of Texas Dental Branch at Houston- Summer Research Program

Key Words: Polymerized composite, spectrophotometer measurement (ΔL*, ΔE*)

Purpose of the study was to evaluate relationship between differences in color parameters (ΔL*, ΔE*) recorded using two specular component modes (SCI-included and SCE-excluded) and gloss (GU) of resin composites. Shades A1 and A3 of Venus Diamond (Haraeus Kulzer), Tetric EvoCream (Ivoclar Vivadent), and Filtek Supreme Plus (3M ESPE), and M1 and M5 shades of Ceramo X mono (Dentsply Caulk) were used. The polymerized composite specimens were polished using Venus Supra (Haraeus Kulzer) polishers for 40 seconds: 20 seconds pre-polishers and 20 second high gloss polishers. Color evaluations were made by a spectrophotometer and gloss data was performed by a small-area gloss meter. We found that with the increase in gloss, the difference in lightness and color difference increased. Analysis of variance showed significant differences among composites and between shades ($p<0.0001$; power=1.000). Fisher's PLSD intervals ($p=0.05$) for comparisons among composites and between shades were 0.3 and 0.2 for ΔL*and 0.4 and 0.3 for ΔE*, respectively. It was concluded that ΔL* and ΔE* values obtained in two specular component modes (SCI-included and SCE-excluded) were good predictors of gloss (GU) of resin composites.

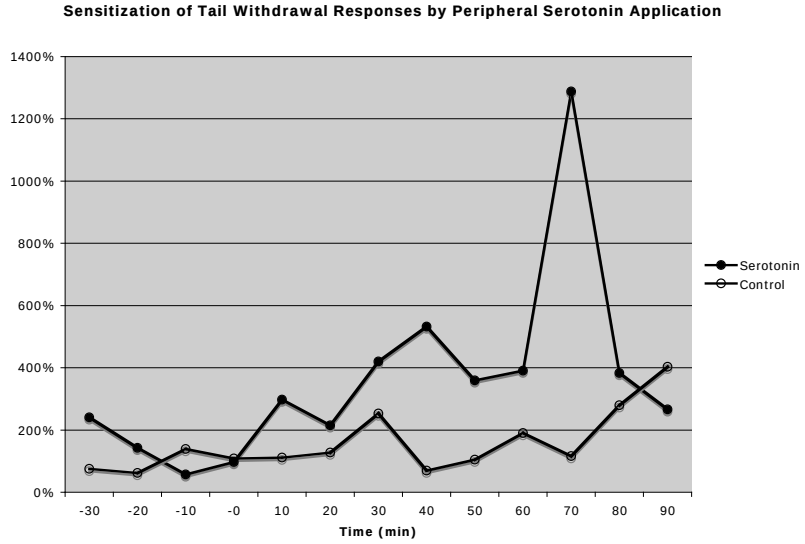
ABSTRACT

Sensitization of Tail Withdrawal Responses in *Aplysia californica* After Application of Serotonin

Anastasia L. Eriksson *Barnard College, Columbia University* *Class of 2010*

Sponsored by: Edgar T. Walters, Ph.D., Department of Integrative Biology and Pharmacology
Supported by: National Institute of Neurological Disorders and Stroke 1 R01 NS35979-14

The marine snail, *Aplysia californica*, long used as a research animal to elucidate basic neural processes, is also a useful model animal for the study of human pain mechanisms, despite our wildly divergent evolutionary histories. As a result, we have undertaken to study the effects of a pain- and memory-related neurotransmitter 5-hydroxytryptamine (5-HT or serotonin), on a peripheral withdrawal response of Aplysia.
Preparations made of a small portion of the tail of Aplysia were utilized. The tail, severed from the body and central ganglia of the animal, was pinned down and attached to a strain gauge to measure contractions. While being constantly perfused with artificial seawater (ASW), the preparation was given moderate intensity mechanical stimuli (brief pokes with a von Frey hair) every 10 minutes. After at least 2 baseline responses it then underwent perfusion for 2 minutes with either a solution of serotonin (10^{-6} M) in ASW or a control ASW solution, administered in a blind fashion. Test stimuli continued at 10-minute intervals until 90 minutes after 5-HT or sham treatment.
The post-treatment responses were scaled to the recorded baseline responses. Analysis of the data (n=6 preparations in each group) showed a significant difference in the behavior of the experimental and control preparation; though there was much response variance due to the difficulty of producing consistent stimuli, 5-HT still produced a large increase in amplitude of the withdrawal responses that persisted for most of the testing period. These data show that the peripheral nervous system and/or musculature of Aplysia is capable of long-lasting enhancement of responsiveness to nociceptive stimulation induced by relatively brief exposure to 5-HT. This model system may be useful for comparative studies of primitive peripheral mechanisms that in humans may contribute to persistent pain and some forms of memory.



ABSTRACT

Purification of His-Tagged Proteins for Antibody Production

DANIELA M. GOMEZ *Sam Houston State University* *Class of 2011*

Sponsored by: Hung Ton-That, Ph.D, Department of Microbiology & Molecular Genetics

Supported by: The University of Texas at Houston Medical School - Graduate Student Education Committee

Key Words: protein purification, antibodies

Protein purification is extremely important in biomedical research; for example, purified proteins can be used to generate rabbit-raised polyclonal antibodies for protein detection with Western blotting and ELISA assays. In this application, animals are immunized with purified proteins, and after three sequential immunizations, the animal antiserum is obtained. To minimize cross-reactivity of the generated antibodies, individual proteins should be highly pure and free from other protein contaminants. Protein purification using affinity chromatography can be used to achieve this goal. My summer project involves purification of histidine-tagged proteins that will be used for antibody production later. In this project, I employed *Escherichia coli* BL21 (DE3) that harbor a plasmid expressing a His-tagged protein upon induction with IPTG. Bacterial lysates were obtained by French Press and the clear lysates were passed through a Ni-NTA column to allow His-tagged proteins to bind to the Ni-NTA resin. Unbound proteins were washed away by sequential washing steps. To elute the His-tagged proteins, I used Elution buffer that contains 0.5 M imidazole, which displaces the His-tag from Nickel co-ordination, thus releasing the His-tagged proteins from the resin. Purified proteins were visualized by gel electrophoresis and Coomassie staining. I found out that some other proteins were copurified with my His-tagged proteins and that inclusion of 10 mM imidazole in the wash buffer reduced this non-specific binding. Future experiments will optimize conditions to obtain highly purified proteins.

ABSTRACT

The Binding of Nitric Oxide Synthase to Prostaglandin H Synthase

JONATHAN HO *Duke University* *Class of 2012*

Sponsored by: Ah-Lim Tsai, PhD, Department of Internal Medicine, Hematology Division
Program in Biochemistry and Molecular Biology

Supported by: The University of Texas at Houston Medical School – Undergraduate Summer Research Program

Key Words: Prostaglandin H Synthase, nictric oxide synthase, cross-talk

Nitric Oxide (NO) and prostaglandins (PGs) are key mediators for many important physiologic and pathologic processes such as basic cardiovascular homeostasis and inflammation. Cross talk between NO and PGs occurs at different levels and was suggested to occur via binding between nitric oxide synthase (NOS) and prostaglandin H synthase (PGHS) (Snyder, *Science* 2005, pg 1966). Snyder and his coworkers, based on their immunoprecipitations of stimulated macrophage cell homogenates, assert that iNOS (or inducible NOS) and inducible PGHS (or PGHS-2) undergo binding interactions that increase the activity of PG biosynthesis by PGHS-2. However, his approach fails to prove direct binding between iNOS and PGHS-2, as additional macromolecules could mediate the interaction. To confirm whether or not iNOS and PGHS-2 cross talk is caused by direct binding, we decided to study the protein interactions using purified PGHS-2 and iNOS (or its subdomains). $iNOS_{ox}$ and truncated iNOS containing FMN/heme domains ($iNOS_{FMN+Heme}$) containing multiple histidine tags were mixed with PGHS-2 and a cobalt resin that selectively binds His-tagged proteins; Western blot using either anti-iNOS or anti-PGHS2 antibody analysis demonstrated the absence of binding between purified functional proteins, implying that additional molecules may mediate the iNOS/PGHS2 cross talk. We will assess this by using stimulated macrophage-like cell soluble and membrane fractions via the same immunodetection approach utilized previously. Such studies will shed light on the underlying mechanism of NO and PG cross talk at the protein level.

ABSTRACT

Title: Transplantation of neurotrophin-expressing neural stem cells promotes functional recovery after spinal cord injury

DAVID K. HU *University of Texas at Austin* *Class of 2010*

Sponsored by: Qi Lin Cao, M.D., Department of Neurosurgery
Supported by: The University of Texas at Houston Medical Branch – Summer Research Program
Key Words: Spinal cord injury, Glial-restricted precursor cells, GRP-derived astrocyte, neural stem cell, transplantation, neurotrophic factor

New therapeutic strategies are urgently needed for spinal cord injury (SCI), a significant cause of disability and mortality. Neural stem cells (NSC) have the potential to replace the damaged neural cells and enhance the endogenous repair and therefore, could be a new promising therapy for SCI. In this study, we tested whether transplantation of NSCs or precursor cells would improve the functional recovery after SCI. We further investigated the underlying mechanisms for functional recovery. Adult Sprague Dawley rats received the moderate contusive SCI at thoracic vertebral level 9 and randomly divided into five groups receiving grafts of control medium, NSCs, glial-resitricted precursor (GRP), GRP-derived astrocyte (GDA), and multi-neurotrophin D15A expressing GDA, at 7 days after SCI. Rats were then tested for locomotor function using the Basso-Beattie-Bresnahan (BBB) locomotor rating scale once weekly and for Treadscan every other week for 8 weeks. Then histological and immunohistochemical analyses were performed on the injured spinal cord for tissue sparing, cell survival, differentiation, axonal regeneration, and remyelination. Our results showed that BBB scores were not significantly different among all groups at 1 week after injury, before transplantation. However, BBB scores were significantly higher in animals receiving grafts of D15A-expressing GDA compared to all other groups from 1 to 7 weeks after transplantation. The histological results showed that all transplanted cells survived and integrated into the host spinal cord. Other detailed histological analysis as well as the analysis for Treadscan test are still undergoing. Our results show that transplantation of D15A expressing GDA significantly improved the locomotion function after SCI, suggesting combinatorial treatment of GDA transplantation and increasing expression of neurotrophic factors is effective therapeutic strategy for SCI. The undergoing histological analyses will help us understand the mechanism(s) that will further help us to identify the optimal therapeutic approaches in future studies.

ABSTRACT

Copy Number Variation Analysis of theDTX4* Gene in Sporadic Stroke Patients

DANIEL A. HYMAN *Brown University* *Class of 2011*

Sponsored by: Dianna Milewicz, MD, PhD, Department of Medical Genetics
Mark Wang, PhD., Department of Medical Genetics

Supported by: The University of Texas at Houston Medical School - Summer Research Program

Key Words: Stroke, DTX4*, pPCR, Agilent Array

Recent studies have suggested that Copy Number Variation (CNV) may be an important mechanism for genetic disease development. The *DTX4** gene, encoding one of the contractile proteins in smooth muscle cells, was previously found to be associated with several types of cardiac vascular disease but the underlying mechanism remains to be elucidated. In our current study, we examined copy number variation of the *DTX4** gene in sporadic stroke patients. Genomic DNA isolated from stroke patients and controls were screened by Taqman probe-based *Quantitative Polymerase Chain Reaction* (*qPCR)* assay. In total, 433 stroke patient samples were screened (275 non-Hispanic Caucasian, 38 Hispanic, 111 African American and 9 other races). We have identified deletion of *DTX4** in 2 stroke patients (1 Caucasian and 1 African American), but no duplication of the gene has been identified. These two DNA samples showing *DTX4** deletion were further examined by our customized Agilent microarray and the deletion status was confirmed. For comparison, we screened 330 controls (240 Caucasian and 90 African American), and found no duplication or deletion of the *DTX4** gene in control samples. From these data, together with data from other published resources, we now speculate that deletion of the *DTX4** gene may be a potential mechanism for stroke development. Further research will focus on increasing sample size and pinpointing the exact deletion region. Investigation of *DTX4** CNV in other cardiac vascular diseases will also be pursued.

*Name of gene has been changed to protect gene identity pending publication.

ABSTRACT

Receptive field structure of neurons in non-human primates V1

ALICE IORDACHE *University of Houston* *Class of 2010*

Sponsored by: Dragoi Valentin, Ph.D., Department of Neurobiology and Anatomy
Supported by: The University of Texas at Houston Medical School - Summer Research Program
Key Words: receptive fields, visual cortex, electrophysiological recordings

The receptive field of a visual neuron is the area of space where the presentation of stimuli will lead to the firing of that neuron. It is therefore essential that before running any electrophysiological experiment to determine the receptive field of the recorded neurons in order to locate the area in which the stimuli of interest will be presented. The project was aimed at determining the receptive fields of all neurons and consisted of running an experiment that displayed randomly distributed, small (0.3 degrees) rectangular gratings on a large region of the computer monitor. Activity of several neurons from V1 area of a rhesus macaque monkey was recorded. The monkey was required to maintain fixation on a small rectangular spot in the center of the screen while the eye position was monitored using an EyelinkII eye tracking system. The recordings were made using a 16 contact laminar multielectrode and several single platinum-iridium electrodes advanced with a computer controlled NAN microelectrode drive. Evoked action potentials during the presentation of the targets were analyzed using a program written in Matlab and the location of the receptive fields was determined in "almost" real time. Following completion of the main experiment, the receptive field data was further analyzed in detail to determine other properties of the receptive fields. Due to the neuronal response delay the process is more complex. In order to obtain an optimal result, both a mathematical cluster analysis method and a visual inspection of the maps was used for a given delay range. Data from 14 days (one day had anywhere from 1 to 4 receptive field recordings) of experiments was analyzed. The results show that the receptive fields of the recorded neurons were located in the proximity of the foveal region, shifted down and to the left side of the screen. The size of the receptive fields was about 1-2 degrees.

ABSTRACT

Role of Lipin in Autophagosome Formation

MELISSA D. JENG *Rice University* *Class of 2012*

Sponsored by: Guangwei Du, PhD, Department of Integrative Biology and Pharmacology
Supported by: The University of Texas at Houston Medical School - Summer Research Program
Key Words: lipin, lipid synthesis, autophagy, autophagosome, GFP-LC3

Autophagy is a process by which cells destroy old, damaged, or mutated organelles as an anti-ageing or cell death mechanism. A double-membrane vesicle surrounds the waste organelle and then fuses with a lysosome to be degraded. An unanswered question is from where autophagosomes obtain lipid membrane necessary for vesicle formation. Four models of autophagosome formation have been proposed. One of them is de novo lipid synthesis, in which lipid molecules or micelle clusters attach to and elongate a pre-autophagosomal membrane. In our research, we test this hypothesis through inhibition of some key enzymes involved in de novo synthesis, using a stable cell line expressing a GFP-LC3 tag to mark autophagosomal formation. One enzyme we study is lipin, which converts phosphatidic acid to diacylglycerol (DAG) for downstream phospholipid synthesis. To observe the role of lipin in autophagy, we have generated retroviral constructs expressing various lipin splicing isoforms and the GFP-LC3 cell line. We are examining the correlation of lipin inhibition and autophagosome suppression when the cells are put under an autophagy-inducing condition. Our research might give us a better understanding of autophagy and provide insight to therapeutic methods.

ABSTRACT

Regulation of TNF-⟨ release by Macrophages

CATHERINE E. KILLINGER *Vanderbilt University* *Class of 2010*

Sponsored by: Dr. Yi-Ping Li, PhD, Department of Integrative Biology and Pharmacology
Supported by: The University of Texas at Houston Medical School – Summer Research Program
Key Words: Macrophage, TIMP3, TACE, LPS

TIMP3 is an endogenous inhibitor of the enzyme TACE which releases TNF-α, an important inflammatory cytokine, from the plasma membrane. It was previously shown that TACE release of TNF-α from myogenic cells is critical for the activation of p38 MAPK during myogenesis. Macrophages infiltrate regenerating muscle and influence myogenesis via releasing cytokines. Thus, to a large extent, macrophage release of TNF-⟨ regulates myogenesis. In order to understand the regulation of macrophage release of TNF-⟨ we investigated the regulation of TIMP3 and TACE activity in the macrophage-like cell RAW 2647 activated by LPS. RAW 2647 cells were treated with PBS or LPS (100 ng/mL). RNA was then extracted for RT-PCR (realtime) analysis, and cell lysates were analyzed by Western Blot of TIMP3 and TACE. We observed a downregulation of TIMP3 mRNA levels at 24 hours of LPS treatment. At the same time, TIMP3 protein levels also decreased. In addition, an active form of TACE protein (phosphorylated) increased at 2 hours of LPS treatment. These preliminary data suggest that in activated macrophages TACE activity is regulated by dual mechanisms: a down-regulation of TIMP3 expression and an upregulation of TACE activity via phosphorylation. More experiments will be required in order to reach final conclusions.

THE UNIVERSITY of TEXAS
HEALTH SCIENCE CENTER AT HOUSTON

2009 Summer Research Program
Office of Educational Programs
Medical School

Undergraduate Student

ABSTRACT

Survey of Airway Management Protocols for Patients with Traumatic Brain Injury Treated By Ground-Based Emergency Medical Services

ELIZABETH A. KUBOTA *University of Texas at Austin* *Class of 2011*

Sponsored by: Dr. Richard N. Bradley, MD, Department of Emergency Medicine
Supported by: The University of Texas at Houston Medical School - Summer Research Program
Key Words: Drug assisted intubation, endotracheal intubation, EMS

OBJECTIVE: To determine the current protocols and practices of ground-based emergency medical services (EMS) agencies regarding endotracheal intubation (ETI) in patients with traumatic brain injury through a cross-sectional survey.
METHODS: A survey will be sent to all of the qualified agencies listed on the 2008 JEMS 200 City Survey Bonus Content. Qualifications from the JEMS list are an advanced life support, 911 agency and a primary ETI provider of their area. Several contacts were made per agency for inter-rater reliability. The items for the survey were generated through the Delphi technique, in which each investigator was given the opportunity to submit and rank the items. The items were divided into 5 domains: system need, procedural experience, monitoring equipment, oversight/quality assurance, and methods of drug-assisted intubation (DAI). The top scoring items from each domain had priority for inclusion in the survey. An online version of the survey was also generated through www.SurveyMonkey.com.
RESULTS: A pre-enabling study was successfully set up, as a cross-sectional survey, in which to evaluate current ground-based EMS protocols of endotracheal intubation.
DISCUSSION: Upon Committee for the Protection of Human Subjects approval, potential participants will be mailed the survey, followed by 3 potential reminder letters. When the response time ends, the returned surveys will be de-identified and data will be analyzed using basic statistical methods. Anticipated results: (1) A majority of agencies will utilize DAI in ETI; and (2) There will be a correlation between survival rates and operating room training. Assessment of the data is pending.

ABSTRACT

Presence of Vascular Endothelial Growth Factor (VEGF) in Cartilage Nodules Engineered in a Rotating Bioreactor

WILLIAM C. LEBOEUF *Our Lady of the Lake College* *Class of 2011*

Sponsored by: Dr. Pauline J. Duke, PhD. Department of Orthodontics
Supported by: UTHSC office of Biotechnology
Key Words: vascularization, angiogenesis, VEGF

One of the most vexing issues in engineering of bone for replacement and repair is that of vessel penetration into the implant. Our lab uses engineered bone-forming cartilage for healing of skull defects. When implanted, this cartilage turns into bone via endochondral ossification, which includes a vascularization process. Penetration of vessels into the implant is seen in skulls fixed after 2 and 4 weeks of implantation. In the current study, the ability of the engineered cartilage to promote angiogenesis was investigated by use of an antibody to the angiogenic molecule VEGF. Angiogenesis is a process by which new capillaries are formed from pre-existing blood vessels in physiological or pathological contexts. This neovascular mechanism is mediated by the vascular endothelial growth factor (VEGF) family of cytokines. The cartilage nodules for the histological study will be derived from mouse embryonic limb bud cells, cultured in a rotating bioreactor. Nodules will be fixed in 10% buffered neutral formalin, embedded in paraffin, sectioned and stained with the PolyVue AP/PermaRed Detection kit for assessment of vascularization located in the cytoplasmic, cell membrane, and extracellular matrix. The antibody to VEGF used for staining reacts with a 19-22 kD (reduced) protein. VEGF is a homodimeric, disulfide-linked glycoprotein involved in angiogenesis, which promotes tumor progression and metastasis. This antibody reacts with 165, 189 and 121 amino acid splice variants of VEGF of human, to a lesser extent, mouse and rat. In summary we propose that VEGF is actively responsible for hypertrophic cartilage neovascularization through a paracrine release by chondrocytes, with invading endothelial cells as a target.

ABSTRACT

Institutional Review Board Preparation for *The International HIV Controller Study*

ASHTON LEHMANN *Middlebury College* *Class of 2009*

Sponsored by: Philip C. Johnson, M.D., Dept. of Internal Medicine
Robin L. Hardwicke, Ph.D., RN, AACRN, FNP-C, Dept. of Internal Medicine

Supported by: The University of Texas at Houston Medical School – Summer Research Program
Tom and Emily Ryan through the T. Ragan Ryan Foundation

Key Words: Institutional Review Board (IRB), Committee for the Protection of Human Subjects (CPHS), Informed Consent, HIPAA, Protected Health Information (PHI), HIV, Controller

To ensure the ethical protection of the rights and welfare of human subjects participating in academic research, all proposed research involving human subjects requires review and approval by an Institutional Review Board (IRB) before study initiation. The University of Texas Health Science Center at Houston's IRB, the Committee for the Protection of Human Subjects (CPHS), protects the autonomy, safety, emotional health, and financial considerations of human subjects by assessing submitted protocols for minimization of risks to subjects and that the anticipated benefits (to subjects directly or to scientific knowledge) outweigh such risks, assurance of subject safety, documentation of informed consent, and protection of subject privacy. I prepared the IRB application and associated informed consent and HIPAA documents for submission to the CPHS to allow for the University of Texas at Houston Medical School's collaboration with Harvard Medical School's *International HIV Controller Study*, which aims to study the viral, host genetic, and immunologic contributions of 1,000 HIV positive individuals who are able to "control" the effects of HIV by maintaining undetectable viral loads in the absence of antiretroviral therapies. This study requires the release of subjects' medical histories and blood sampling for laboratory testing. Although all Protected Health Information (PHI; which would allow for personal identification) will be removed prior to release, the risk of improper disclosure of HIV status or genetic information cannot be entirely avoided. Such ethical concerns and preventative measures were fully documented in the IRB materials such that subjects will be fully informed before consenting to participate.

ABSTRACT

The Role of mTOR Signaling in the Heart

Maria A. Leszczynska *University of Florida* *Class of 2011*

Sponsored by: Heinrich Taegtmeyer, MD, D. Phil, Department of Cardiology
Supported by: The University of Texas at Houston Medical School- Summer Research Program
Key Words: mTOR signaling in the heart, cardiac hypertrophy, substrate metabolism

Heart disease is the leading cause of death in the United States, due in large part to the increasing prevalence of heart failure. Cardiac hypertrophy and altered substrate metabolism are two phenomena closely linked to heart failure. Moreover, many of the signaling pathways that appear to regulate cardiac hypertrophy, such as the mTOR signaling pathway, also modulate glucose metabolism. The target of rapamycin (TOR) is an evolutionary conserved kinase which is vital for the regulation of cell growth in response to nutrients in all eukaryotic cells. In the heart, mTOR is an important regulator of cardiac hypertrophy. We proposed that glucose metabolism regulates the mTOR pathway in the heart in response to insulin. To test this hypothesis, Sprague-Dawley rats (300-350 g), received standard laboratory food and water ad libitum. The rats were anesthetized by intraperitoneal injection of chloral hydrate (60 mg/100 g body wt), heparinized (100 U), and the hearts were rapidly removed and transferred into cold saline. Utilizing the isolated working rat heart perfusion apparatus, hearts were perfused under a variety of nutrient conditions. After 30 min of perfusion and nutrient manipulation, both ventricles were freeze clamped. Protein was isolated from the hearts and western blots were performed using the antibodies for mTOR and its downstream targets p70S6K1 and 4EBP1. We demonstrated that in the isolated rat heart, phosphorylation of mTOR and both of its downstream targets p70S6K and 4EBP1 required exogenous glucose. Moreover, phosphorylation of p70S6K by glucose was attenuated by rapamycin, indicating that mTOR is required for glucose-dependent signaling. Our findings suggest that glucose serves not only as a substrate for energy provision, but also as an intracellular signal, regulating protein synthesis and, ultimately growth of the heart.

ABSTRACT

A Comparison of the Infant Truview EVO2 Video Laryngoscope and the Macintosh Laryngoscope Blade in Pediatric Patients

RACHEL LEWIS *The University of St. Thomas* *Class of 2011*

Sponsored by: Carin A. Hagberg M.D, Maria Matuszczak M.D.,
Supported by: The University of Texas at Houston Medical School - Summer Research Program
Key Words: Video laryngoscopy, pediatric anesthesia, Truview

Background: The Infant Truview EVO2 (Truphatek International Ltd., Netanya, Israel) provides an enlarged laryngoscopic view of the airway structures. The purpose of this study is to compare the glottic view obtained by the Infant Truview EVO2 to that seen with the standard Macintosh blade in pediatric patients.

Methods: Patients less than one year of age and without difficult airway documentation were enrolled once informed parental consent was obtained. General anesthesia was induced by inhalation of Sevoflurane and 100% oxygen, followed by intravenous administration of propofol, fentanyl, and rocuronium. Laryngoscopy was performed with both devices in a random, cross-over manner, using the Cormack-Lehane scale and POGO score to assess the laryngoscopic view. View of the glottis during passage of the ETT was facilitated with the second laryngoscope and recorded. Duration of intubation, number of attempts for successful endotracheal intubation, subjective level of difficulty in the performance of intubation, and vital signs throughout the procedure were recorded.

Results: Thirty-nine infants participated in this study, 19 of which were intubated with the Truview and 20 with the Macintosh blade. The POGO score was higher when evaluated with the Truview (97 ± 13.41) than with the Macintosh blade (75.31 ± 22.76). Mean duration of intubation was 52.71 ± 27.91 s in the Truview group and 36.31 ± 15.75 s in the Macintosh group. The Truview did not provide an obstructed laryngeal view while the Macintosh provided six obstructed views.

Conclusion: The Infant Truview EVO2 video laryngosocpe provides a laryngoscopic view equal to or better than that provided by the Macintosh laryngoscope blade in pediatric patients less than the age of one. Although time for intubation with the Infant Truview is longer, its ability to improve the laryngoscopic grade could improve conditions in blind or difficult-to-intubate cases.

ABSTRACT

Detection of Merkel Cell Polyomavirus (MCPyV) in Squamous Cell Carcinoma of Skin

ALEXANDRIA L. LI *Rice University* *Class of 2012*

Sponsored by: Dr. Stephen K. Tyring, M.D., Ph.D., M.B.A.
Supported by: The University of Texas at Houston Medical School - Summer Research Program
Key Words: NMSC, SCC, MCPyV

Nonmelanoma skin cancers (NMSC), which include squamous cell carcinoma (SCC), account for the most common forms of cancer in the United States. The pathogenesis of SCC of the skin has been linked to viruses. To determine the presence of viral infection in a SCC sample that was histologically described as a well-differentiated, crateriform, squamous cell carcinoma, human papillomavirus (HPV) and Merkel cell polyomavirus (MCPyV) detections were performed. Three different consensus primer sets were utilized in PCR assays for detection of a broad spectrum of HPV types. A primer set specific to the small T antigen region was also used for detection of MCPyV. No HPV types were present in the sample; however, a putative MCPyV DNA fragment was detected by PCR. The cloning, sequencing of the fragment, and computer analysis of the obtained sequencing data verified the presence of MCPyV. This recently discovered polyomavirus is found in Merkel cell carcinoma, a rare, highly aggressive, neuroendocrine NMSC. Further research will be necessary to determine if MCPyV plays a role in the carcinogenesis of squamous cell carcinomas.

ABSTRACT

Measuring the Decrease of Forepaw Use in Ischemic Rats with the Vermicelli Handling Test as a Novel Test of Motor Function for Stroke

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Sponsored by: Sean I. Savitz, MD, Department of Neurology
Supported by: The University of Texas at Houston Medical School – Summer Research Program
Key Words: Ischemic infarct, Vermicelli handling test, Motor Function, Animal model

Even though there are many behavioral tests that evaluate loss of motor function in rats with brain disorders, few behavioral measures assess digit function that are easy to administer and applicable to motor deficits observed in patients. The Vermicelli handling test quantifies the forepaws' fine digit movements. Previous research has found that this test is sensitive to lateralized impairments in forepaw function. Thus, it has the potential to be applied as a valuable model that measures motor function for stroke in rats. The purpose of this study was to examine the changes in digit function in ischemic rats using the Vermicelli handling test. Reversible middle cerebral artery occlusion (MCAO) in the left hemisphere was induced in Long Evans rats for two hours (n=9). 1mL saline was administered intravenously 24 hours after ischemia. The Vermicelli handling test was administered before treatment and once a week for four weeks after treatment. The test was scored by tallying fine digit movements of the ipsilateral and contralateral forepaw. Compared to pretest scores, the number of forepaw adjustments decreased significantly from two weeks after stroke to the end of the study period ($p<0.050$). Therefore, the focal ischemia model caused a quantifiable deficit that could be applied as a novel test of motor function for stroke.

ABSTRACT

Creation of a conditional knockdown cell line of human ubiquitin genes

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Sponsored by: Jianping Jin, Ph.D

Key Words: Ubiquitin, shRNA

Ubiquitin is a powerful signaling molecule that can control the protein proteolysis through the 26S proteasome in eukaryotes. Ubiquitin has seven lysines, each of which can be engaged in polyubiquitin chain formation. Different ubiquitin chains could determine different fates of ubiquitylated proteins. Human genome contains four genes expressing 14 copies of ubiquitin precursors that will be processed before integrated into an ubiquitin signaling pathway. Moreover, two of the ubiquitin genes, S27a and UBA52, are synthesized as an ubiquitin fusion protein with small subunits of ribosome. Therefore, it is very difficult to do any genetic manipulation to control the expression of ubiquitin without perturbing the function of ribosome. Our goal is to create a condition knockdown cell line of human ubiquitin genes to facilitate the ubiquitin study. Our strategy is to apply RNA interference techniques (shRNA) to silence four ubiquitin genes simultaneously. Meanwhile, shRNA-resistant ubiquitin cDNA will be fused with both small ribosome subunits and expressed in the same cell line. The tetracycline-inducible system will be used to manage the expression of both ubiquitin shRNA and two ubiquitin-ribosome fusion proteins. By this approach, we can introduce mutations of ubiquitin systematically to study their functions in vivo.

ABSTRACT

Various Adenylyl Cyclases N-termini interaction with G Proteins

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Sponsored by: Carmen W. Dessauer, PhD, Department of Integrative Biology and Pharmacology

Supported by: The University of Texas at Houston Medical School – Summer Research Program

Key Words: Adenylyl Cyclase, G-proteins, N-terminus

Adenylyl cyclase (AC) catalyzes the conversion of ATP to 3'-5'-cyclic AMP or cAMP and pyrophosphate which plays an important role in physiological functions. There are nine mammalian membrane bound adenylyl cyclases that are regulated by G-proteins, anchoring proteins (AKAPs), forskolin and protein kinases. AC is a membrane bound protein which is composed a cytosolic N-terminus (NT), two cytoplasmic domains known as C1 and C2, and two transmembrane domains known as M1 and M2. The C1 and C2 domains are roughly 40% identical and form the catalytic core. The NT is the most variable region within the different AC isoforms and has been the least studied domain. Our lab has shown that N-terminus of AC5 scaffolds inactive G-proteins (Gsαβγ). We wanted to test if this is a general paradigm among all AC isoforms and whether N-termini of other AC isoforms also scaffold inactive G-proteins. I tested the NT's of AC 1, 2, 3, 5, 6, and 9 for binding of G-proteins (GDP bound Gαs and Gβγ) by using a GST-pull down assay. I found that all the GST-tagged AC NT's bound Gβγ and GDP-Gαs (GST was used as control and did not bind). This was surprising since activities of various AC isoforms are uniquely regulated by Gβγ and GTP-Gαs. Gαs stimulates all isoforms but Gβγ effects are isoform specific. Gβγ inhibits AC's 1, 3, and 8, stimulates AC's 2, 4, 5, 6, and 7, and has no effect on AC 9. Thus, ACs bind to inactive G-proteins via N-termini. Further GST-pull down assays will be performed to test synergy of the G-proteins for binding to N-termini of various AC isoforms.

THE UNIVERSITY of TEXAS
HEALTH SCIENCE CENTER AT HOUSTON

2009 Summer Research Program
Office of Educational Programs
Medical School

Undergraduate Student

ABSTRACT

Motor Functions in Ischemic Rats with Bone Marrow Stem Cells

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Sponsored by: Sean I. Savitz, MD, Department of Neurology
Supported by: University of Texas Houston Medical School Summer Research Program
Key Words: Ischemic infarct, bone marrow stem cells, motor function

Intravenously injected bone marrow stem cells are being used in the study of therapeutics for stroke. Previous research has shown that treatment with bone marrow stem cells induces functional recovery and decreases neurodegeneration after ischemia in rats. The purpose of this study was to assess the effects of different dosages of bone marrow stem cells on gross motor functions in ischemic rats. Long Evans rats (n=20) were divided into 3 treatment groups: saline (n=7), 1 million cells (n=6), and 5 million cells (n=7). Both the control and experimental groups underwent reversible middle cerebral artery occlusion (MCAO) for 3 hours. The stem cells were intravenously injected 24 hours after stroke. The 3 treatment groups underwent behavioral testing using the circling and cylinder test. The tests were conducted once before induced ischemia, and then once a week for 4 weeks. In the circling test, there was a significant decrease in the total amount of circling to the left and right side except during week 2 on the left side and week 3 on the right side (all p's<0.05). The cylinder test showed a significant group by test interaction between the saline and cell treated groups. The treatment groups differed by test only at week 2, which indicated that right paw usage in the saline group was greater than in the cell treated groups at week 2. There was a trend at week 4 showing that the group treated with stem cells had less circling to the left compared to saline controls (p=0.1). These results suggest that the concentrations of stem cells studied did not consistently improve motor function use in ischemic rats.

ABSTRACT

ASD Versus ASD-ADHD Comorbidity

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Sponsored by: Deborah A. Pearson, PhD
Supported by: The University of Texas at Houston Medical School - Summer Research Program
Key Words: ASD, ADHD, comorbidity

Objective: Many children and adolescents with autism spectrum disorders (ASD; e.g., Autistic Disorder, Asperger's Disorder) also have significant behavioral and emotional concerns. The purpose of this study was to compare the comorbidity of other psychiatric diagnoses in children with an ASD who did or did not have significant levels of Attention-Deficit/Hyperactivity Disorder (ADHD; i.e., hyperactivity, impulsivity, and inattention) symptoms. **Methods**: Participants were 157 children and adolescents (ages 7-17 years; IQs 52-147) who met DSM-IV criteria for an ASD (130 boys; mean age=10.5 yrs.; mean IQ=87). Of these children and adolescents with an ASD, 124 (101 boys; mean age=10.2 yrs; mean IQ=85) also had clinically significant levels of ADHD symptoms (the "ASD-ADHD" group), while 33 (29 boys; mean age=11.6; mean IQ=95) did not (the "ASD-only" group). Chi-square analyses were used to compare the frequencies of particular psychiatric disorders in both groups. **Results**: With one exception (other than ADHD), the prevalence of comorbid psychiatric disorders in the two groups was similar. Only the prevalence of Oppositional Defiant Disorder (ODD) was found to be marginally different in the two groups: 30.6% (n=38) of the ASD-ADHD group met DSM-IV criteria for ODD, compared with 15.2% (n=5) of the ASD-only group ($\chi^2(1) = 3.15$, p=.076). **Conclusions**: Findings suggest that, for the most part, comorbid psychiatric symptomatology was similar in children and adolescents with ASDs who did or did not have significant levels of ADHD symptomatology. However, it should be noted that the number of children and adolescents without significant ADHD symptoms in this present sample was relatively small. These findings underscore the importance of obtaining a comprehensive assessment of behavioral and emotional symptoms in children and adolescents with autism spectrum disorders.

ABSTRACT

Screening of Transgenic Zebrafish

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Sponsored by: Xinping Zhao, PhD, Department of Ophthalmology and Visual Sciences
Supported by: The University of Texas at Houston Medical School – Summer Research Program
Key Words: Glaucoma, transgenic, zebrafish, Metronidazole

Glaucoma is the second leading cause of blindness and is commonly associated with the trabecular meshwork blockage in the anterior angle of the eye. The zebrafish is a useful model organism for the study of visual conditions because its eye structure and genetic regulation closely resemble that of a human's. To study glaucoma, we expressed a toxic gene in the cells within the anterior angle of the zebrafish eye. Cell death in the anterior angle may disrupt its structure and function in regulation of the ocular fluid, leading to glaucoma-like phenotypes, such as retinal ganglion cell (RGC) death and optic nerve (ON) damage. The stable transgenic line, gsnl1-NTRmCherry, expresses the mCherry and *E. coli* nitroreductase (NTR) fusion protein specifically in the anterior angle. NTR converts Metronidazole to a toxic compound to kill the NTR-expressing cells, which can be detected by a reduction of the mCherry fluorescent signal. To facilitate the detection of glaucoma-like phenotypes, we crossed this transgenic fish to a transgenic fish in which RGC and ON are labeled with the green fluorescent protein (GFP). The GFP signal can aid in identifying glaucomatous phenotypes. The double transgenic embryos were incubated with Metronidazole at various time points and observed under fluorescence microscope at 5 days post-fertilization (dpf). Those treated at 3 dpf showed reduced mCherry signal compared to untreated embryos. Further analysis of these treated embryos at later time points allows us to evaluate whether or not the destroyed the anterior angle cells can result in RGC death and ON damage.

ABSTRACT

Anesthesia Quality Improvement via Preoperative Assessment

LYNN A. PAULS *Rice University* *Class of 2012*

Sponsored by: Richard M. Layman, MD, Department of Anesthesiology
Supported by: The University of Texas at Houston Medical School - Summer Research Program
Key Words: quality assurance, anesthesia, preoperative assessment

Quality improvement initiatives have become a standard practice in many departments to assess patient satisfaction, care, and safety by guiding improvement in health care delivery, efficiency and service. Through examining anesthesia preoperative patient assessment and care, this study provides information designed to inform the Anesthesiology professional of quality assurance issues within the department and identify areas for improvement, along with educational programs and purposes. METHODS: Adult patients were selected at random by case availability and followed into the OR where stethoscope availability and usage were observed for five minutes or until auscultation was witnessed. Non-observational data, consisting of ASA classification, vital signs, Mallampati class, and lung examination, were collected from randomly selected adult cases that could not be witnessed concurrently or within an eight hour time frame. RESULTS: Amongst all providers, auscultations were observed in 50% of cases within 5 minutes after intubation. Of the remaining 50%, auscultation was documented on the anesthesia record 97% of the time. Auscultations performed within 5 minutes after intubation were observed twice as often by Faculty and CRNAs (both 60%) compared to CA2 and CA3 residents (32% and 35%). T-moders and CA1 residents exhibited statistically equivalent stethoscope usage, 47% and 50% respectively. ASA classifications were documented on 94% of all cases. Of documented ASA classifications, 98% of providers recorded correct ASA status. Twenty percent of CA1 residents incorrectly identified ASA status. Amongst all providers, vital signs, Mallampati airway, and Lung examination were documented 93%, 83%, and 52% of the time, respectively. CONCLUSION: From this study it is suggested that auscultation by residents is decreasing with years in residency, ASA classifications are accurate and precise, and more attentive preoperative lung examination as well as intraoperative lung evaluation can be performed.

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ABSTRACT

Unilateral Anterior Temporal Lobe Resections and Confrontation Naming

CLAIRE PAWLIK *Rice University* *2011*

Sponsored by: Timothy Ellmore, Ph.D., UTHSC-H Department of Neurosurgery
Supported by: Cris Hamilton, Ph.D., Rice University
Nitin Tandon, M.D., UTHSC-H Department of Neurosurgery
Key Words: anterior temporal lobectomy, language

The exact function of the anterior temporal lobes (ATLs) is unknown. One idea is that they store information about meaning (e.g., names of objects and people), as bilateral atrophy is present in patients with semantic dementia. Neurosurgical patients undergoing unilateral resection of the ATL represent a unique population to test hypotheses about how language and semantic knowledge are organized because the resection is focal, whereas atrophy in semantic dementia is diffuse and often bilateral. In the present study, it was hypothesized that the ATL is critical for confrontation naming. It was predicted that resection of the dominant ATL as determined by sodium amytal (Wada) testing would result in a decrement in naming accuracy. Eleven patients performed up to 6 different covert language production tasks in an MRI scanner before and after resection of their dominant or non-dominant anterior temporal lobe. Tasks included visual naming of common objects, famous faces, famous places, and actions, completing word stems, and naming based on auditory descriptions. The dependent measure consisted of whether a patient reported that he/she could name each object as indicated by a button press. Pre- and post-resection data was compared to identify possible language deficits. Data were analyzed with a 2 (Lesion Side: Dominant or Non-Dominant Hemisphere) x 6 (Task) x 2 (Time: Pre- or Post-Resection) mixed analysis of variance (ANOVA). Lesion side was treated as a between-subjects factor, and Task and Time were treated as within-subjects factors. There were significant main effects of Task, $F(9,45) = 22.33$, $p < .05$ and Time, $F(1,9) = 13.29$, $p < .05$, but no significant interaction between Time x Lesion Side. Patients had particular difficulty with the auditory naming task, and deficits on this task were more pronounced. These results suggest that ATL resections correlate with certain naming deficits, but it is necessary to consider the details of the surgeries and validity of the language tests in considering the results. In several cases, the resected area extended beyond the anterior temporal lobe and this may account for some variation in performance. Finally, tasks that more accurately and impartially assess naming accuracy are important to consider for future studies of brain-behavior relationships.

ABSTRACT

Preliminary Data of the Difficult Airway: The Preoperative Airway Assessment Form as an Educational and Quality Improvement Tool

DANIEL D. PODDER *Rice University* *Class of 2012*

Sponsored by: Carin A. Hagberg, MD, Department of Anesthesiology
Supported by: The University of Texas at Houston Medical School - Summer Research Program
Key Words: preoperative assessment, intubation, difficult airways

Introduction: Airway-related difficulties can put patients under serious risk during surgery. We have begun this long-term study to see whether a more thorough preoperative evaluation could better predict difficult airways in patients than the standard method of airway assessment.
Methods: We divided all anesthesiology residents at Memorial Hermann Hospital (MHH) into two groups. The control group continued performing MHH protocol preoperative airway assessments on all adult patients; the experimental group was given a new, more detailed preoperative form to complete. For quality assurance, a group of trained airway assessment experts also independently screened patients using the experimental form.
Results: In May 2009, we screened 333 patients using the experimental form, and there were a total of 52 cases (15.6%) of difficult airways. Residents using the standard form predicted difficulties with a false positive prevalence of 55.8% and a false negative prevalence of 13.3%. Residents using the experimental form had a false positive prevalence of 13.9% and a false negative prevalence of 11.9% (Chi test, $p=2.15 \times 10^{-111}$). The experts had a false positive prevalence of 14.3% and a false negative prevalence of 6.6% (Chi test, $p=5.31 \times 10^{-240}$).
Conclusions: Our preliminary results suggest that a more thorough preoperative investigation is more accurate in screening for the difficult airway, reducing both type-I and type-II errors. We believe that use of the new preoperative airway assessment form would be beneficial to clinical practice since the anesthesiology team would be better prepared for encountering difficult airways in patients, thus reducing risk to these patients. In addition, the new assessment form could be a useful tool in the education of anesthesiology residents regarding the anticipation of the difficult airway.

ABSTRACT

Shear Bond Strength and Adhesive Remnant Index Comparison of Commercial Adhesive-Bracket Combinations for Orthodontic Bonding

NEIL A. RANEY *Rice University* *Class of 2011*

Sponsored by: Jeryl D. English, DDS, MS, Chair, Brian Penton, DDS, Department of Orthodontics, University of Texas Dental Branch at Houston

Supported by: The University of Texas at Houston Medical School – Summer Research Program

Key Words: shear bond strength, adhesive remnant index, orthodontic brackets, orthodontic bonding, enamel

Strong bonds between brackets and the enamel of teeth and safe de-bonding of these brackets are of primary importance to orthodontists. Nine combinations of brackets and adhesives attached to bovine teeth were tested for maximum shear bond strengths. Bracket-adhesive combinations were de-bonded with an Instron™ testing machine both immediately and 24 hours after bonding. The brackets tested included ceramic 3M Unitek™ Clarity, plastic Ormco Damon™ D3, and ceramic American™ Radiance. The adhesives tested included 3M Unitek™ Transbond XT Light Cure (control) and two color-changing adhesives, 3M Unitek™ Transbond Plus Color-Change and Ormco™ Blugloo. The adhesive-bracket bond strength was expected to be highest for matching manufacturers of the primer and adhesive. The Clarity brackets with XT adhesive tested 24 hours after bonding exhibited the highest bond strength of all combinations tested. The Blugloo-bracket bond strengths for most brackets tested weaker over 24-hour periods compared to immediate tests. The majority of all measured bond strengths are high enough to be clinically acceptable (8-9 MPa). Also, it was desired to have more adhesive left on the teeth (higher adhesive remnant index) following de-bonding because such an occurrence reflects a decreased likelihood for the enamel to break off from the tooth during de-bonding. In general, the brackets with XT adhesive tested 24 hours after bonding exhibited the highest adhesive remnant indexes compared to all other brackets with different adhesives or testing times. Statistical analyses are not included for these shear bond strength or adhesive remnant index values.

ABSTRACT

Antiretroviral Effects on HIV Positive Pregnancies

ROGER RODIEK *Vanderbilt University* *Class of 2011*

Sponsored by: Dr. Philip Johnson, MD, Internal Medicine, Dr. Robin Hardwicke, PhD NP AACRN

Supported by: The University of Texas at Houston Medical School – Summer Research Program

Key Words: HIV infection, antiretroviral (ARV) regimen

Since 1996, the HIV/AIDS virus has proven vulnerable to the growing list of antiretroviral protease inhibitors on the drug market. As research and development of the HIV infection continues to progress, the risk of vertical transmission during gestation or at birth from mother to child has significantly decreased for HIV positive pregnant women and researchers continue to find a direct correlation with a proper antiretroviral (ARV) regimen and HIV negative infants. Depending on the patient's resistance to certain drugs, a normal ARV cocktail for pregnant women includes any number of combinations of antiretroviral agents. A lingering concern with this ARV regimen comes with its effects on the potential mental and physical damage done to the fetus during gestation and birth. I have had the opportunity to research and analyze labor and delivery charts at Memorial Hermann Hospital and follow both retrospective and prospective HIV positive pregnancy cases from first enrollment into clinic through delivery. Research outcome included APGAR, gender, head circumference, birth length and weight, and HIV status. This research suggests that the overwhelming majority of infants show no developmental abnormalities at the time of birth and within the following year. A proper ARV regimen is essential for the health of both the mother and the infant during pregnancy. While there has been growing concern of ARVs' effect on the infant during gestation, the research conducted suggests that there is little to no risk that ARVs administered during gestation will affect the health of the infant.

ABSTRACT

The Effects of p27 Cleavage in Breast Cancer Cells

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Sponsored by: Catherine Denicourt, PhD, Department of Integrative Biology and Pharmacology

Supported by: The University of Texas at Houston Medical School – Summer Research Program

Key Words: p27, cell cycle, breast cancer, apoptosis

The protein p27 is a member of the cyclin-dependent kinase inhibitor (CIP/Kip) family. p27 negatively regulates cell cycle progression by binding to cyclin-CDK complexes leading to arrest in the G1 phase of the cell cycle. In normal healthy cells, p27 is localized exclusively in the nucleus. However, in approximately 40% of breast cancer cells, p27 becomes aberrantly localized in the cytoplasm. This mislocalization of p27 not only deregulates the cell cycle, but it also makes the cell more resistant to apoptosis and promotes cell migration and metastasis, correlating with poor prognosis. p27 contains two caspase cleavage sites following aspartic acid 108 (D108) and aspartic acid 139 (D139). Our hypothesis is that caspases cleave p27 in breast cancer cells, causing mislocalization in the cytoplasm. To test this hypothesis, MCF-7 cells were transfected with p27 N-terminus mutants truncated at D108 (N108) and D139 (N139) along with a mutant containing a nuclear export sequence (NES). All three of these mutants localized in the cytoplasm while the over-expressed p27 wild type remained nuclear, suggesting that caspase-mediated p27 cleavage leads to cytoplasmic localization. In order to test whether the cleavage of p27 and subsequent cytoplasmic localization promotes resistance to apoptosis, MCF-7 cells were transfected with the truncated N108 and N139 p27 mutants and treated with 500μM hydrogen peroxide for 6 hours. The cells transfected with the N108 and N139 truncated p27 mutants showed an increased resistance to apoptosis compared to p27 wild type and the vector control in our pilot experiment. While more research must be done to determine the extent and mechanism of this anti-apoptotic effect, this is a step towards discovering why chemotherapeutic drugs are ineffective at inducing cell death in breast cancer tumors.

ABSTRACT

Quality Improvement of Ventilator Weaning Protocol in MICU

MATTHEW T. SCHILLING *Texas A&M University* *Class of 2011*

Sponsored by: Brandy J. McKelvy, MD, Department of Internal Medicine – Pulmonary Critical Care and Sleep Medicine Division

Supported by: The University of Texas at Houston Medical School – Summer Research Program

Key Words: Ventilator, weaning

Ventilator associated pneumonia (VAP) is one of the most concerning risks for mechanically ventilated patients. It increases mortality significantly, prolongs time on the ventilator in the intensive care unit (ICU), and increases hospital cost by an estimated $40,000 per patient. A ventilator weaning policy in the MICU at Memorial Herman Hospital –The Medical Center, was established March 3, 2008, but recent data has shown that the weaning process was inadequate (on 60% on weaning protocol). The weaning protocol includes a nightly screen from the respiratory therapist (RT), a sedation holiday driven by medical doctors (MD's) and nurses (RN's) and a spontaneous breathing trial (SBT), in order to access the readiness for patient extubation. A quality improvement study was initiated to increase the efficiency of weaning mechanically ventilated patients, thereby reducing the risk of VAP.
Baseline data collected consisted of 73 ventilated patient days and assessed for RT screening, an MD order for sedation and the completion of SBT. The MD order written for sedation was shown to occur in only 52% of the patient days. The objective of the first intervention, consisting of 79 patient days, was to increase the number of MD orders written for sedation holiday by introducing a sheet detailing weaning parameters and increases MD awareness of the readiness for sedation holiday and extubation. An improvement in sedation holiday orders (65%) was seen, as well as an increase in SBT (from 60% to 70%). In the second intervention, consisting of 117 patient days, a RN driven protocol was created for daily sedation holidays. This has been shown in previous studies to increase overall efficiency. Sedation holidays increased (from 65% to 71%) and SBT occurred more frequently (70% to 78%). An overall increasing trend in RT screen was evident and may have been due to increased awareness of the study. Overall, the interventions showed a successful change in the ventilator weaning process. Further interventions are indicated in the future.

ABSTRACT

Functional Characterization of New Human β-1 sGC Splice Variant

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Sponsored by: Iraida G. Sharina, PhD, Assistant Professor; Center for Cell Signaling
Supported by: The University of Texas at Houston Medical School – Summer Research Program
Key Words: Soluble Guanylyl Cyclase, splicing, expression, Nitric Oxide

Soluble Guanylyl Cyclase (sGC) is a major enzyme of the NO/sGC/cGMP signaling pathway. It is a heterodimeric receptor for nitric oxide (NO) and consists of an α- and β-subunit. The α_1/β_1 heterodimer is the major isoform mediating NO-dependent effects such as vasodilation, neuromediation, etc. We have identified a new splice variant of β_1 sGC named SH-β1 and investigated its expression by RT-PCR analysis. This study demonstrated that SH-β1 is present in different human tissues and cancer cell lines at moderate to high levels. SH-β1 splice form encodes a protein with alterations in heme binding, dimerization, and catalytic domains suggesting that its expression may generate sGC enzyme with changed properties. To characterize enzymatic properties of SH- β_1 /a1 sGC, we generated a shuttle vector for expression in insect Sf9 cells. Presently, we are generating a recombinant baculovirus encoding the SH- β_1 splice form. In conclusion, we identified a new splice variant SH- β_1 sGC, and demonstrated that it is differentially expressed it in human tissues. Our future goals aim to characterize functional properties of SH- β_1 sGC splice variant and to investigate how it may affect the wild type sGC enzyme function.

ABSTRACT

An electrophysiological study on the effects of Methylphenidate sensitization on neuronal activity in Prefrontal cortex and Hippocampus

OFER SHOUVAL *Class of 2012*

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Sponsored by: Nachum Dafny, PhD, Department of Neurobiology and Anatomy

Supported by: The University of Texas at Houston Medical School - Summer Research Program

Key Words: Methylphenidate, Prefrontal cortex, Hippocampus, Electrophisiology

Every year millions of Americans are prescribed Methylphenidate (MPD), otherwise known as Ritalin, to address the symptoms of Attention Deficit Hyperactive Disorder (ADHD). MPD, a drug that is closely related to amphetamine and cocaine, works by inhibiting the transport of dopamine within the brain and is thus considered a dopamine agonist. However the physiology and long-term effects of this process are not well known. For this reason our lab has begun an effort to study the neurophisiological mechanism of MPD action using dose response protocols to record the electrophysiological response of MPD in different brain regions. Using single unit recording techniques, we attempted to measure action potentials evoked by MPD admisitration in the Prefrontal cortex and the Hippocampus of freely moving Sprague Dawley rats, two structures that have been shown to play a role in the dopaminergic reward system. The animals were implanted under general anesthesia with 8 permanent semi microelectrodes. After 3 days of recovery from surgery, the rats were injected with a saline (control), followed by subsequent doses of .6, 2.5, and finally 10 ml/kg of MPD, each dose separated by an hour, while the rats brain activity was recorded. Over the next 5 days they were administered doses of 2.5 mg/kg daily, followed by a washout period of 3 days. On experimental day 10, neuronal recording was resumed identically to experimental day 1. The results from the two recording days would then be compared in order to answer the following questions: First of all, does MPD cause a change in neuronal activity and if so is it an increase or a decrease? Second of all, how long is the latency between the time of injection and the time it begins to affect the neuronal activity in each brain region? And finally, how long does the drug's effect last in each brain region? These results are pending evaluation.

ABSTRACT

Purification technique for the study of the cytoplasmic tail of L-selectin

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Sponsored by: Renhao Li, PhD, Department of Biochemistry and Molecular Biology
Supported by: The University of Texas at Houston Medical School - Summer Research Program
Key Words: L-selectin, ADAM 17, calmodulin, leukocytes, inflammation

L-selectin (CD62L) is a cell adhesion molecule present on the surface of leukocytes. This protein binds to ligands on the face of endothelial cells, slowing the leukocyte as it passes them. The leukocyte then activates its expression of proteins necessary for adhesion and transmigration across the endothelial wall whereupon it initiates inflammatory reactions. After leukocyte activation, L-selectin is cleaved at a membrane-proximal ectodomain site and is shed from the leukocyte [1,3,4]. Proposed pathways for this shedding include interactions of calmodulin and moesin with the 17-residue cytoplasmic tail of L-selectin and eventual cleavage by the transmembrane metalloprotease ADAM17 (or TACE) [1,2,3,4]. In order to characterize these interactions *in vitro,* an efficient and economical process to produce the C-terminal fragment of L-selectin (or cLS) is desired. To make the hydrophobic protein, cLS was attached to either a GST or ubiquitin histidine-tagged fusion protein. A TEV or thrombin cleavage site was also inserted between the cLs and fusion protein. The inserts were ligated into pHUT (for ubiquitin fusion protein) and pHex (for GST fusion protein) vectors and grown in BL21 cells. Because the fusion protein forms inclusion bodies in E. coli, ultracentrifugation was used to fractionally separate the target protein from water-soluble and lipophilic components. After the protein was solubilized by a detergent buffer and identified in one of the supernatant fractions, it was purified by Ni-NTA affinity chromatography. Once the target protein was eluted by imidazole, the protein solution was cleaved by either TEV or thrombin. The target cLS protein was finally purified by HPLC, and will be available for further biophysical and structural characterization.

ABSTRACT

PC-NSAIDs and Their Effect on Spinal Cord Injury Lesion Site

LYNSEY C. SMITH *University of Oklahoma* *Class of 2011*

Sponsored by: Lenard M. Lichtenberger, Ph.D. and Raymond J. Grill, Ph.D., Department of Integrative Biology and Pharmacology

Supported by: The University of Texas at Houston Medical School—Summer Research Program.
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Key Words: NSAID, Omega-3-PC-NSAID

Spinal Cord Injury can leave an organism with motor and sensory deficits that greatly affect function and quality of life. This study was conducted to examine the effects of nonsteroidal anti-inflammatory drugs (NSAIDs) combined with Omega-3-phosphatidylcholine (PC) on injured spinal cord recovery, specifically the lesion site. NSAIDs may have the side effects of intestinal bleeding and ulceration in the GI tract, however when conjugated to PC these side effects are reduced. Omega-3 fatty acids have the ability to inhibit inflammation. It is hypothesized that rats administered Omega-3-PC-NSAIDs will have a reduction in total lesion volume due to a decrease in the following secondary effects of the injury: inflammation; scar formation (inhibiting axonal growth at the lesion site); membrane breakdown; and death of neurons and glial cells. This hypothesis was tested by intragastrically dosing 30 rats with aspirin (25 mg/kg), an equivalent NSAID dose of aspirin-Omega-3-PC (weight ratio 1:1), or saline b.i.d., between days 3 and10 post-injury. After the rats were euthanized the 30 mm of affected cord was removed and cut into 30µm sections via a cryostat. The sections were mounted onto gelatin-coated slides and stained with Cresyl Violet, which dyes the neurons and glial cells bright blue. The next step will be to analyze the samples using Image Pro+ software, an image analysis program. It is our hypothesis that the rats dosed with Asprin-Omega-3-PC will have a smaller lesion site with more tissue surrounding the lesion site, than the rats dosed with saline or aspirin alone. The results from this experiment are to be determined in the following weeks.

ABSTRACT

Impact of p38 MAPK inhibitor SB202190 on ubiquitin-proteasome pathway mediated muscle mass loss in uremic mice

MAHVEEN SOHAIL *Baylor University* *Class of 2011*

Sponsored by: Yi-Ping Li, PhD, Department of Integrative Biology and Pharmacology
Supported by: The University of Texas at Houston Medical School - Summer Research Program
Key Words: ubiquitin-proteasome pathway, p38 MAPK, SB202190, Atrogin-1/MAFbx

Many inflammatory diseases including cancer, diabetes and sepsis exhibit atrophy. Prior research indicates that muscle wasting is caused via the ubiquitin-proteasome pathway (UPP), in which an inflammatory stimulus may activate p38 MAPK, a mediator of ubiquitin ligase Atrogin-1/MAFbx, specifically expressed in muscle, which target muscle protein for rapid breakdown by the 26S proteasome. Additionally, the inhibition of p38 reduces Atrogin-1/MAFbx expression and muscle loss stimulated by LPS. The purpose of the study was to determine the signal mechanisms behind uremia induced atrophy as well as investigate the effect of SB20219 upon muscle loss. Uremia was induced by renal ablation in mice. Expression levels of Atrogin-1/MAFbx were measured within three conditions: a sham operated control (n=9), uremic mice (n=11), and uremic mice treated with 5 mg/kg SB202190 every 24 hours for seven days (n=9). Groups consisting of one mouse of each condition were formed and pair fed to ensure that each mouse per group consumed the same food intake. Afterwards, RNA was extracted from the *Extensor Digitalus Longus* muscle; expression levels of Atrogin-1/MAFbx and MuRF1 were determined by qPCR and compared to control GAPDH expression levels. Although there is evidence of an increase in Atrogin-1/MAFbx expression in uremic mice (±2.51 fold increase) and an inhibitory effect on this expression increase in uremic mice treated with SB202190 inhibitor (±1.08 fold increase), the trend is statistically insignificant due to a large variation in data and limited number of mice. In addition, expression levels of MuRF1, another muscle-enriched ubiquitin ligase, were not conclusively observed as elevated. These results indicate that additional samples are required to conclude the impact of the ubiquitin-proteasome pathway on muscle loss caused by uremia. Investigation of p38 activity and autophagy as an alternative pathway of muscle loss within this animal model is ongoing.

ABSTRACT

Does alcohol use following Ritalin treatment have a liability outcome?

BLAKE R. SONNE *University of Texas at Austin* *Class of 2009*

Sponsored by: Nachum Dafny Ph.D., Department of Neurobiology and Anatomy
Alan Swann M.D., Department of Psychiatry and Behavioral Sciences

Supported by: How and where methylphenidate exerts its effects on the central nervous system, NIHDA R01027222

Key Words: methylphenidate, alcohol, behavior, cross-sensitization, drug interaction, Sprague-dawley rats

Methylphenidate (MPD,) or Ritalin, is a drug prescribed for those affected by Attention Deficit Hyperactivity Disorder (ADHD.) MPD is utilized by many individuals of all ages. Ethanol is known for its intoxicating effects as a drug used widely in social interaction. This study is intended to determine possible interactions (cross-sensitization) between MPD and Ethanol, as many MPD users were reported to also use ethanol. Ethanol (intra-peritoneal injection, 1 mg/kg) was given following eleven days of MPD administration. Behavioral changes were measured before and after MPD and/or alcohol administration. Data was retrieved from recordings via the open field assay. Rats were divided into four groups, control (saline,) 0.6 mg/kg MPD, 2.5 mg/kg MPD, 10.0 mg/kg MPD groups respectively. Rats were placed into recording cages for two hours following I.P. injection of saline, or MPD and/or alcohol. The horizontal activity, total distance, and number of stereotypic movements were evaluated. The data shows dose response characteristics of increased activity with increasing doses of MPD. An evident behavioral sensitization of MPD was induced following six days of administration. Ethanol decreases the ambulatory activity in all of the locomotor indices studied. Additionally, the data shows that rats receiving a high dose of MPD, show a tolerance to the suppressive activity of Ethanol. The simultaneous administration of Ethanol and MPD in rats provides evidence that there is an interaction between these two drugs.

ABSTRACT

Title: Understanding Protein Dynamics Through Computer Simulations

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Sponsored by: Alemayehu A. Gorfe, PhD, Department of Integrative Biology and Pharmacology

Supported by: The University of Texas at Houston Medical School - Summer Research Program

Key Words: Protein dynamics, K-ras

K-ras is a GTP hydrolyzing enzyme that plays an important role in many signal transduction pathways. A mutated K-ras protein increases the possibility of developing a variety of cancers including colon cancer, pancreatic cancer and lung cancer. The purpose of this research is to understand the dynamics of K-ras in water. The techniques used for the study included structural analysis and molecular dynamics simulation. The initial structure of K-ras was taken from the RCSB Protein Data Bank and was displayed and inspected using Visual Molecular Dynamics (VMD). Energy was minimized in the system by reducing the temperature to absolute zero and thus removing the kinetic energy from the system. During the equilibration phase, the protein backbone was constrained to make sure its conformation wouldn't shift as the temperature was raised to 300 K. While the simulation ran for a total of 20 nanoseconds, the last 15.5 nanoseconds were well-equilibrated and used for analysis. Both the alpha helices and beta sheets of the protein remained stable. This contrasted with the random coils, which moved far greater distances during the simulation. Four water molecules stayed in the same position during the simulation; there are two reasons for this surprising result. First, the positively charged magnesium ion in K-ras has a tightly bound hydration shell that requires six negatively charged atoms to surround it. The protein provided 4 of the 6 atoms, and water molecules contributed the rest. Second, two of the water molecules were enclosed by the protein residues. One water molecule was surrounded by hydrophobic residues and was held in place by its hydrogen bonds with 3 backbone atoms. The other water molecule was surrounded by both hydrophobic and hydrophilic residues and was hydrogen bonded with a mixture of backbone and side chain atoms. The results of this study can be used as initial steps in the design of therapeutic drugs against the diseases caused by K-ras mutations.

ABSTRACT

Cortical layer dynamics and behavioral performance in non-human primates

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Sponsored by: Valentin Dragoi, PhD, Department of Neurobiology and Anatomy
Supported by: The University of Texas at Houston Medical School - Summer Research Program
Key Words: visual cortical layers, neural communication

The goal of the project is to examine how communication in local networks across cortical layers impacts behavioral performance. The experiments performed will allow us to assess, for the first time, the relationship between the adaptive changes in neuronal networks involved in stimulus processing and perceptual performance in awake-behaving primates. Electrophysiological recordings were made in the primary visual cortex (area V1) of non-human primates using a system of laminar multielectrodes and single platinum-iridium electrodes. The multielectrode used in the experiments is a 16 contact electrode, with a 100 micron intercontact spacing and 350 micron outer diameter. Electrodes were advanced into a 19 mm recording chamber implanted on the primary visual cortex of a rhesus monkey using a computer controlled NAN microelectrode drive. After reaching the required cortical depth and isolating signals from different neurons, spikes and local field potentials (LFPs) were recorded using a Plexon recording system. Using a combination of laminar multielectrodes and single electrodes allowed us to receive information from different cortical layers while the monkey was performed a behavioral orientation discrimination task. Eye position was monitored using an EyeLinkII eye tracker system. My involvement in the experiments also included monkey preparation and transport, setup and calibration for experiment, and implant cleaning before and after the experiment. Results for the experiments described are pending completion of data analysis.

ABSTRACT

Sprouting of nociceptive sensory axons in the dorsal horn of transgenic ALS mice

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Sponsored by: Raymond J. Grill Ph. D., Department of Integrative Biology & Pharmacology
Supported by: The University of Texas at Houston – Summer Research Program
Key Words: Amyotrophic lateral sclerosis, spinal cord, CGRP, IB4, pain, SOD1

Amyotrophic lateral sclerosis (ALS) is characterized by the progressive loss of motor neurons. Patients afflicted with this disease generally have 3-5 years after diagnosis in which they experience a growing loss of muscle movement, paralysis, and death by asphyxiation. The cause of ALS is currently unclear but has been linked to various environmental and genetic cues. There are several animal models that recreate ALS-like pathology. One such model is the G93A transgenic mouse model. The G93A mouse expresses a mutated form of the human superoxide dismutase (SOD1) gene, a mutation present in about 10% of familial cases of ALS. This mutation produces both oxidative stress and inflammation within the CNS. While the vast majority of studies focus on oxidative stress and inflammation in motoneuron death, we hypothesize that this environment will also promote the plasticity of neurosensory inputs to the spinal cord. Plasticity of nociceptive sensory inputs could result in the development of neuropathic pain.

Nociceptive plasticity was assessed by comparing the density of calcitonin-gene-related peptide (CGRP)- and IB4-immunoreactive sensory axons in the lumbar dorsal horns of G93A mutant or wildtype mice. Quantitative assessment of confocal-generated images demonstrated a statistically significant increase of both markers in the dorsal horns of ALS mice. Our results indicate: 1) that conditions that mimic ALS pathology induce plasticity of nociceptive pathways. 2) the ALS mouse is a good system for assessing the role(s) of oxidative stress and inflammation in regulating the growth of pain-sensitive pathways.

ABSTRACT

Effects of the C-terminus on Adrenal Cytochrome b_{561} Functionality

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Supported by: The University of Texas at Houston Medical School – Summer Research Program
National Institute of Health – General Medicine 080575
Key Words: Adrenal cytochrome b_{561}, C-terminus, Ascorbate interaction

Adrenal cytochrome b_{561} (cyt b_{561}) is a transmembrane protein found in chromaffin granule (CG) membranes in the adrenal glands. Cyt b_{561} contains two heme *b* centers, which, upon reduction by cytoplasmic ascorbate, serve to transport electrons into the CG lumen for neurotransmitter biosynthesis. Mass spectrometric analysis of purified samples of bovine cyt b_{561} expressed in *E.coli* shows that a fraction of the recombinant protein lacks ~10 residues at the C-terminus. None of the residues involved is near either heme in structural models of the cytochrome, and we hypothesized that the C-terminal deletion does not affect cyt b_{561} interaction with ascorbate. To test our hypothesis, we designed cyt b_{561} proteins lacking the last 11 (Δ241) and 24 (Δ228) residues. For each truncated mutant, the cDNA (including codons for a C-terminal hexa-histidine tag) was cloned into the pET43.1a expression vector and used to transform Rosetta Gami *E.coli* cells. The recombinant cyt b_{561} was then expressed and purified using metal ion affinity chromatography. Polyacrylamide gel electrophoresis and Western blotting were used to assess the purity and expression level of recombinant protein, while electronic absorption spectroscopy and equilibrium ascorbate titrations (monitored by an increase in absorbance at 561 nm from the reduction of cytochrome) were used to assess protein functionality. Expression of both Δ228 and Δ241 proteins was comparable to that of wild type cyt b_{561}. Further, the ascorbate titration parameters for the two hemes in both Δ228 and Δ241 truncations were statistically indistinguishable from those in wild type cyt b_{561}. These results indicate that residues 229-252 do not contribute to ascorbate interaction or redox behavior at either heme center in adrenal cyt b_{561}.

ABSTRACT

Relative Accuracy of LaMotte Tracer Fluoride Pocketester for Water Fluoride Measurements

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Sponsored by: Ryan L. Quock, DDS, Department of Restorative Dentistry & Biomaterials
Jarvis T. Chan, DDS, PhD, Department of Integrative Biology and Pharmacology

Supported by: The University of Texas at Houston Medical School - Summer Research Program

Key Words: fluoride, water, dental caries

Appropriate fluoridation of water to decrease the prevalence and severity of dental caries across populations has been well documented. Dentists are advised to know the fluoride content of their patients' drinking water so that appropriate preventive measures can be taken if water fluoride content is too high or low. The purpose of this experiment was to evaluate the Lamotte Tracer Fluoride Pocketester as a viable, convenient, and cost-effective option for fluoride measurement. The experimental Pocketester was compared for relative accuracy with the Thermo Orion 720A+, an accepted standard laboratory apparatus for fluoride measurement. Identical gravimetrically-prepared water solutions ranging from 0.1 to 4.0 ppm fluoride were analyzed for fluoride content by both Pocketester and Thermo Orion units; controlled variables included unit calibration values and solution buffer type. The average difference between the two units' water fluoride measurement for the same solution was 0.030 ppm (SD 0.115). Analysis of the data by t-test showed no statistical difference between measurements taken by the Pocketester and Thermo Orion units. Based on these results, the Pocketester is considered an accurate and practical alternative for dentists to measure water fluoride content for prevention of dental caries.

ABSTRACT

Facial Expression Analysis Using 6D Data: Application to Autism

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Sponsored by: Katherine A. Loveland, PhD, Department of Psychiatry & Behavioral Sciences
Supported by: The University of Texas at Houston Medical School - Summer Research Program
Key Words: Facial Expression Analysis, Autism, Computational Methods

Autism spectrum disorders are characterized by abnormal social-emotional behavior. Facial expressions have been of particular interest for the study of emotion in autism. Facial expressions of emotion often involve subtle, in-depth skin motion such as skin extrusion in the areas of the forehead, the eyebrows, the cheeks, and the chin. These minuscule changes in facial muscles during emotional expression are very difficult to detect and to measure with precision. Recent technology in facial analysis has developed a 6D data analysis system, of which only two exist in the USA. This 6D facial analysis system uses 5D data over time; the 5D data are derived from 3D geometric structures of the face together with 2D texture mapping. Currently, facial expression analysis is most often done manually using facial coding systems that can be slow, labor intensive, and unreliable. The goal of this study is to use this newly developed technology to obtain accurate and robust analysis of dynamic (moving) facial expressions using a personalized annotated face model (AFM). This face model is fitted with low count polygons to produce a high density mesh. Trajectories of points on a face may then be followed and the components of facial expressions distinguished using parameters derived from the facial "action units" in the Facial Action Coding System (FACS). In doing so, precise facial movements may be captured in individuals with autism spectrum or other disorders, allowing for the comparison to typical subjects. The development of this technology may lead to new information about the neurodevelopment of those with autism spectrum disorders. It may also aid in identifying targets for behavioral intervention and for the assessment of specific treatments for those with autism or other disorders. So far, this study has been developing a set of video stimuli that may be used to elicit particular emotions in research participants with and without autism spectrum disorders. Emotion elicitation will be achieved using film clips that have been validated from previous emotion studies. The emotions evoked include: sadness, happiness/amusement, disgust, and neutral. Twenty-five young adult (18-25yrs) participants will be videotaped and their expressions coded using FACS. FACS coders will use the video data to extract features that will allow us to characterize the facial expressions of interest. The same data will also be used with the automated facial analysis system, and the results from the coders will be compared to the computer analysis in order to refine the system. We will then apply the automated system to facial expression data collected from young people with and without autism (12-21yrs). The goal is to make it possible to code dynamic facial expressions rapidly, precisely and accurately in studies of persons with abnormal emotional behavior.

ABSTRACT

Impact of anterior temporal lobectomy on language pathways

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Sponsored by: Nitin Tandon, MD, Department of Neurosurgery
Supported by: The University of Texas at Houston Medical School – Summer Research Program
Key Words: Diffusion tensor imaging, epilepsy

The purpose of this study was to evaluate changes in major sub-cortical white matter tracts in patients undergoing an anterior temporal lobectomy (ATL) for epilepsy. Diffusion tensor imaging allows for the visualization of fiber pathways that correspond to the tracts.

Ten patients with epilepsy (7 males, 3 females, mean age 41.4 years, even numbers of left and right-sided resections) who underwent ATL were studied. Using a Phillips 3T MRI scanner, diffusion weighted imaging (DTI) data were obtained before and after surgery. The uncinate fasciculus (UF), inferior longitudinal fasciculus (ILF), inferior fronto-occipital fasciculus (IFOF), and the arcuate fasciculus (AF) were localized using deterministic tractography techniques (Catani et al. ’02, ’08; Ellmore ’09). Mean fractional anisotropy (FA), mean length, and mean fiber number were calculated for all of the tracts for the group and were compared pre and post operatively.

There was a significant decrease in mean FA of the ipsilateral UF, AF, and IFOF, in mean length of the UF only, and in mean fiber number of the UF, ILF, and IFOF ($p < 0.0125$). There was no significant change in mean FA and mean length contralateral to resection for all four tracts after surgery. The mean fiber number also showed no significant change contra laterally for all fibers except the IFOF. In regards to only pre operative data, the AF showed a significantly lower mean FA value on the ipsilateral side when compared to the contralateral side.

The results of this study show that DTI may be used to quantify post-surgical changes in white matter fiber systems, and represent a promising methodological framework to evaluate the structural basis of functional plasticity and re-mapping. Comparisons with objective measures of language function pre and post resection, obtained via a neuropsychological battery, are underway.

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