

Does Blood Flow Restriction Training Improve Quadriceps Measures After Arthroscopic Knee Surgery? A Critically Appraised Topic

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Introduction

Knee injuries are one of the most prevalent pathologies in sport. It is estimated that 100,000 – 250,000 ACL injuries occur per year³. It is common for patients to struggle with quadriceps strength impairment as high as 18% at two years post ACL repair¹¹. Quadriceps strength is strongly associated with athletic performance and likelihood of re-injury after ACL repair. Quadriceps strength deficits are also documented after other arthroscopic procedures and the presence of knee effusion. Blood flow restriction (BFR) training is an intervention gaining popularity in rehabilitation. BFR can improve strength and hypertrophy measures with loads as low as 20% of 1RM. This makes BFR an ideal intervention when heavier loads are contraindicated.

Research Question

To determine if BFR improves relevant measures of the quadriceps after arthroscopic knee surgery.

Methods

An online search was performed using the following terms; “blood flow restriction,” “knee surgery,” “knee arthroscopy,” “anterior cruciate ligament,” “kaatsu training,” and “occlusion training.”

Results

Five of six articles included in this review support the utilization of BFR to improve post-op quadriceps measures. All five articles demonstrated a significant improvement in at least one quadriceps outcome. All studies consisted of small sample sizes, there was inconsistent initiation of BFR, and little consistency in protocols. There was variability among outcomes measured across the studies.

Conclusion

There is low level evidence that BFR should be included to improve quadriceps following arthroscopic knee surgery. More high quality studies are needed to make stronger recommendations.

Identifying Barriers to Healthcare as Reported by Rural and Medically Underserved Patients in Oklahoma

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Introduction

The Rural Patient Experience Survey seeks to identify barriers to healthcare faced by patients in rural Oklahoma. Through administration of a survey directed toward patients, this study will analyze the current status of healthcare access and usage among rural Oklahoma populations.

Hypothesis

A widely distributed survey to rural and medically underserved patients will identify existing and new barriers to healthcare access.

Study Design

Research will occur in rural communities and Health Professional Shortage Areas in the state of Oklahoma. Medical clinics will be contacted until 15 clinics agree to participate in survey distribution, and two-thirds (67%) of the rural patient population from each participating clinic will be randomly selected for participation.

Methods

The survey sample will be obtained from patient panels of healthcare facilities in partnership with Oklahoma State University's Center for Health Systems Innovation. Facilities that agree to participate will allow access to their patient panel. Patients residing in rural zip codes will be pooled into a randomly sampled population for survey distribution. Responses will be analyzed using summary statistics, descriptive statistics, and significance testing.

Results

Results are pending the distribution of the survey.

Conclusion

As current evaluation of rural healthcare barriers is lacking, this study aims for a unique understanding of rural healthcare access not provided in earlier research by seeking direct insight from rural patients using randomized survey distribution.

Monitoring Among Patients at Risk for Metabolic Syndrome Secondary to Concomitant Antiretroviral and Second-Generation Antipsychotic Therapy in an HIV Patient Population

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Purpose

Second-generation antipsychotics (SGAs) and protease inhibitors (PIs) have significant metabolic side effect profiles. These risks are compounded with concomitant therapy, both due to additive side effects and as a result of the interaction between the classes which can increase serum SGA concentrations. The goal of this study is to explore the prevalence of metabolic syndrome among patients on concurrent SGA and PI therapy compared to SGA use with other antiretroviral therapy (ART) and to evaluate current risk management practices.

Methods to be Conducted

This study has been approved by the Institutional Review Board. Monitoring, incidence of metabolic syndrome, and dosage adjustments among patients taking both SGAs and PIs will be compared to those on concomitant SGA and either integrase inhibitor or non-nucleoside reverse transcriptase inhibitor therapy. A retrospective review of a randomized selection of 100 charts of patients taking both SGAs and ART from September 1, 2017 to September 1, 2018 will be conducted. Monitoring frequency and parameters will be compared to that recommended by the American Diabetes Association for individuals taking SGAs. Our goal is to determine the prevalence of patients at risk for the potential long-term consequences of SGA and PI combination therapy compared to other ART and to evaluate current clinical monitoring and preventative strategies that are in place.

Conclusion

To be determined

A Retrospective, Matched Cohort Study of the Effectiveness of Common COPD Drug Treatments on 30-Day Readmissions

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Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a prevalent lung disease that represents an important public health challenge. Pharmacological treatment of COPD continues to be a challenge in the US, especially in rural areas. Hospitals with high 30-day readmissions may face penalties under HRRP.

Research Question

Are common pharmacological treatments effective in controlling early hospital readmission?

Study Design

Retrospective descriptive matched cohort study

Methods

In this study, we conducted a phase IV drug trial of combination treatments: budesonide/formoterol and fluticasone/salmeterol. We utilized Cerner health facts database to compare 30-day readmission rates among patients prescribed these COPD treatments. Using propensity score matching and chi-square analysis on patient demographics and hospital-associated variables, we tested for differences in readmission rates. Covariates used: drug type, race, marital status, payer type, gender, and hospital location.

Results

Overall there were no significant differences in 30 day readmission rates between treatments. However, the combination of budesonide/formoterol was found to have a lower readmission rate than fluticasone/salmeterol in COPD patients in urban hospital settings, self-payers, Medicare/Medicaid patients, and Caucasians.

Conclusions

Identifying treatments that have lower 30-day readmission among patients could influence clinical decisions as providers make choices regarding patient care such as hospital length of stay and discharge options. However, due to the observational nature we cannot conclude with certainty that medication was the only factor responsible for any differences observed in this study. Further studies are needed which could provide information to guide further research for therapeutics and tools to better patient management post discharge.

Statistical Significance and Sports Medicine Trials

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Objectives

Lowering the threshold for statistical significance in medical research from a P value of .05 to .005 was recently proposed to reduce misinterpretation of study results. What effect this proposal would have on orthopaedic sports medicine literature is currently unclear.

Research Question/Hypothesis

We seek to determine how the newly proposed threshold could affect the interpretation of previously published sports medicine RCTs.

Methods

We searched PubMed from January 01, 2016 to December 31, 2017 for RCTs published in the *American Journal of Sports Medicine*, *Arthroscopy*, and *Knee Surgery, Sports Traumatology, Arthroscopy*. We extracted P value data for primary endpoints, since RCTs are most often powered for these endpoints. We used Google Forms for data extraction and STATA 13.1 for the data analysis.

Results

Of the 159 studies, only 13 (8%) of the studies have endpoints in which all P values are below the new threshold of .005. 40 (25%) of the studies have endpoints in which some would meet the new P value threshold of .005, and some would not meet this new threshold. 106 (67%) of the studies have no endpoints in which the P value(s) was less than .005. Overall, 38% (59/157) of the previously statistically significant primary endpoints were less than .005, while 62% (98/157) would be reclassified as suggestive.

Conclusions

Of statistically significant endpoints in our sample, only 17% (59/350) would maintain their statistical significance with a P value threshold of less than .005, and only 8% of studies would maintain their overall significance with all P values falling below the new threshold.

Systematic Review of the Incidence of Deep SSI Following the Repair of Fractures around the Knee

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Introduction

Managing peri-knee fractures can be challenging and complications may include nonunion, malunion, compartment syndrome, and infection among others. Recent literature indicates that the rate of peri-knee postoperative surgical site infection may range from 2-88% depending on the fracture site.

Research Question/Hypothesis

The purpose of this systematic review is to obtain a more thorough understanding of the incidence of deep SSI following the repair of fractures around the knee.

Methods

For this work, the electronic databases Medline, Embase and Cochrane Controlled Register of Trials were searched from their inception to July 2018. Eligible studies had to specifically report deep infection rates, and needed to study fractures in the distal femur, patella, tibial plateau, or proximal tibia. We also delineate risk factors that increase the risk of deep infection. Comprehensive Meta-analysis software was used for pooling of data.

Results

117 articles were included for this review. Among the 11,432 patients included in our analysis, the incidence of deep infection was 5.71%. The incidence of deep infection among distal femur, patellar, tibial plateau, and proximal tibia fractures was 5.74%, 4.09%, 5.85, and 6.42% respectively. Smoking, diabetes, open fractures, and compartment syndrome all increased the risk of deep infection.

Conclusion

Our results indicate that deep infections occur in nearly 6% of peri-knee fractures; therefore, surgeons managing these injuries are warned to be vigilant when wounds are not pristine, especially in patients with risk factors. Risk factors, such as open fractures, diabetes, smoking, and most importantly, compartment syndrome, should alert the treating surgeon to an increased risk.

Reamer Irrigator Aspirator Intraoperative Ruler Accuracy of Femoral Isthmus Diameter

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Introduction

Over the past two decades, bone graft harvest with the Reamer Irrigator Aspirator (RIA) from the femoral canal has grown in popularity. Intra-operative measurement of the femoral canal is taken with a metallic ruler (RIA ruler) in conjunction with C-arm fluoroscopy.

Research Question/Hypothesis

Our study aims to evaluate the accuracy of the RIA ruler in judging the femoral canal diameter compared to two other measurements.

Study Design

Utilizing 6 fresh frozen human cadavers, each cadaveric femur is imaged in the operative suite in the supine position with C-Arm fluoroscopy. The femoral diameter is then measured with the RIA ruler in AP and lateral plane at all three reference points by multiple surgeons. CT scans of each individual femur were then performed. The cadaveric femurs were then transected at all the guide pins and direct caliper measurements were taken in the AP and Lateral plane.

Results

There was no significant difference in mean AP diameter measured by CT canal measurement and Canal Caliper measurement ($p=0.6276$). Our AP measurements using the RIA ruler were similar to those of both the CT canal and canal caliper (13.000mm vs 12.167mm vs 12.439mm) respectively. Additionally, our lateral measurements were very similar between the RIA ruler and CT canal (14.644mm vs 14.606mm), however lateral RIA ruler measurements were significantly different than the canal caliper method (14.644mm vs 11.947mm).

Conclusion

Our results suggest we are able to reliably estimate the femoral canal size near the isthmus with the RIA ruler on both the AP and Lateral images compared to the CT scan measurements.

Grabbed by the Tail: Phosphorylated CREB in the Tail of the VTA Following Morphine-Prime Reinstatement in Adolescents Sprague Dawley Rats

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Introduction

Morphine leads to phosphorylation of a transcription factor Ca^{2+} and cyclic AMP response element binding protein, CREB. The activated phosphorylated CREB (pCREB) mediates opioid dependence. Recently, it has been demonstrated that the tail of the ventral tegmental area (tVTA) is one of the major targets of opiates. Indeed, selective activation of mu-opioid receptors in tVTA is sufficient for eliciting a real-time place preference. However, the changes in pCREB levels within the tVTA during opioid-retrieval memories in the adolescent brain is unknown.

Hypothesis

Environmental cues and behavioral sensitization will facilitate reactivation of morphine-seeking memories changing pCREB levels of expression in the tVTA and nucleus accumbens (Nacc) of adolescent rats.

Study Design

This study used a mixed variable design. Female and male adolescent Sprague Dawley rats were used (n=24). We explored morphine drug-seeking properties with a CPP paradigm. Between subjects (treatment) and within subject acquisition, post-preference, extinction and reinstatement, individual percentage scores were considered and correlated with cellular expression.

Methods

Morphine-induced conditioned place preference (CPP) was established (5mg/kg/sc) followed by a priming morphine dose (2.5 mg/kg) or saline. The tVTA and Nacc brain slices were used for immunofluorescence targeting parvalbumin and pCREB proteins.

Results

Morphine-primed reinstatement decreased pCREB expression in the tVTA and increased neuronal activation in the Nacc, without observing any significant sex differences.

Conclusion

Morphine-induced seeking memories in the adolescent brain involved changes in the expression of transcription factor CREB in the tVTA affecting dopaminergic activity in the Nacc.

Effects of Aripiprazole on IL-1 β -Induced Chemokine Expression in Normal Human Astrocytes

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Introduction

Neurodegenerative diseases, as well as mood disorders, are a common issue throughout the world, affecting over 200 million people. Research has shown that neuroinflammation plays a key role in these diseases. The induction of inflammation correlates closely with the presence of chemokines at sites of inflammation. Chemokines, signaling proteins secreted by cells, provide an important resource for the immune system as they recruit immune cells to sites of inflammation.

Study design

The cytokine IL-1 β is an important mediator cytokine in the inflammatory response pathway. Additionally, the pro-inflammatory chemokines CXCL-10 is markedly increased at the onset inflammation and can act as a biomarker. The drug Aripiprazole was used to see if it can reduce inflammatory signaling.

Research Question

Determine if Aripiprazole has any effect on the inflammatory response in NHAs and determine whether Aripiprazole is toxic to NHAs.

Methods

We addressed our goal by using an ELISA to detect and measure the levels of CXCL-10 in Normal Human Astrocytes and an MTT Assay to measure cell viability.

Results

Our findings showed that Aripiprazole is relatively non-toxic at concentrations below 20 μ M. We observed that Aripiprazole does not appear to inhibit expression of CXCL10 in Normal Human Astrocytes.

Conclusion

Future studies will focus on determining the extent to which other drugs affect and reduce inflammation in NHAs and Microglia.

Short-term Immobilization versus Functional Treatment of Severe Ankle Sprains: A Critically Appraised Topic

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Introduction

Ankle sprains are one of the most common musculoskeletal injuries in sports and medical care. The most common mechanism of injury of a lateral ankle sprains is supination and adduction (inversion) with the foot in a plantarflexed position. Ankle sprains are graded (1 to 3) based upon their severity, and are currently treated one of three ways: (1) surgical treatment, (2) immobilization (conservative treatment) and (3) functional conservative treatment.

Focused Clinical Question

Does short-term immobilization for a severe ankle sprain provide better functional outcomes compared to conventional functional treatment?

Study Design

Critically Appraised Topic.

Results

An online search was performed using the following terms: “ankle sprain”, “immobilization”, “functional treatment”, “severe”, “pain”, “function”. Eight possible studies were identified. After applying inclusionary and exclusionary criteria, two systematic reviews and two randomized controlled trials were used in the analysis. Collectively, these studies reported that immobilization could be beneficial to recovery for severe ankle sprains over functional treatment.

Conclusions

There is strong (Grade A) evidence that supports that short-term immobilization shows to be more effective in recovery and provides better functional outcomes compared to functional treatment for individuals that suffer from severe ankle sprains.

Free Rides: Patient and Clinic Benefits in a Rural Pediatric Clinic

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Introduction

In rural Oklahoma, lack of transportation is a significant barrier to health care. Rural patients, who are sicker (CDC), face an even higher burden of illness and disease with decreased access to care. Rural clinics, which are frequently financially fragile, in turn bear the brunt of lost productivity and interrupted workflow due to patients without transportation creating no shows, cancellations, rescheduled appointments, and late arrivals.

Methods

The Oklahoma State University Center for Health Systems Innovation (CHSI) partnered with a Rural Oklahoma Network (ROK-Net) pediatric clinic to innovate and implement a rurally viable model for rural clinics to provide transportation to patients who need a ride to scheduled appointments.

Results

Robust data about volume of transportation need, patient benefits and satisfaction, and clinic workflow and financial benefits was gathered. Both patients and the clinic benefited from the program. Transportation need was intermittent and by far greatest for sick patients. While all patients in need of transport had SoonerCare, SoonerCare restrictions such as a three day notice required for ride scheduling left patients, mostly sick patients, and patients with inability to predict their need for ride on the day of appointment without a ride to the clinic. Revenue collected for participant care far exceeded the cost of transporting them, creating a model for rural clinic transportation solutions where the clinic itself provides their patients a free ride.

Global Demethylation Attenuates Glutaminase and Nerve Growth Factor in TNBS-Induced Colitis

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Introduction

One-third of all Americans suffer from inflammatory bowel disease (IBD) leading to inflammatory pain. Many studies have reported the involvement of epigenetic factors in persistent pain. In an effort to combat the inflammatory pain and predisposition for IBD, different epigenetic factors need to be investigated. Cytosine methylation and its binding partner, MeCP2 can act together as either a transcriptional activator or a repressor. Our lab has shown two proteins, glutaminase (GLS) and nerve growth factor (NGF) at the center of inflammatory pain.

Aim

This project was undertaken to determine if these two proteins and their gene expression are modulated by epigenetic factors during colitis.

Methods

Female SD rats were used to induce colitis through intracolonic infusion of 2.5% TNBS in 25% ethanol and pretreated and co-treated with azacytidine (Aza, 50nM) with TNBS. Twenty-four hrs post-treatment, rats were sacrificed and their colon and associated sensory ganglia (L6/S1) were extracted. Genomic DNA, RNA and proteins extracted were used for bisulfite conversion, methylation specific PCR, PCR and WB.

Results

Our data suggest that Aza decreased the TNBS-induced inflammation seen in gross examination. TNBS-induced colitis increased the DNA methylation of GLS and NGF genes. Global demethylation by Aza treatment decreased TNBS-induced GLS and NGF gene expression. Aza also decreased MeCP2 protein expression suggesting reduced interaction of MeCP2 with these gene promoters. Therefore, Aza-induced demethylation can be targeted for therapeutic use to treat inflammatory pain.

Conclusion

Aza can be used to block TNBS-induced methylation and inflammation-induced GLS and NGF alterations.

Ontogeny of Cassowary and Maleo Casques: Differentiating Patterns of Cranial Ornamentation in Birds

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Introduction

Complexly constructed cranial ornaments, consisting of multiple bony partitions (e.g., cranial casques) are common among archosaurs. Yet, the developmental processes and selective regimes that bring about these metabolically expensive and seemingly bizarre structures remains a mystery. Among Aves, this is partially due to contradictory interpretations of cranial osteology, leaving it unclear whether the underlying bones of different casqued birds are arranged in a similar fashion.

Methods

Here we compare the ontogeny of avian casques, independently derived in paleognathous and neognathous birds, to clarify their constituent parts. Flightless cassowaries (paleognaths) and volant birds such as helmeted guinea fowl, magpie geese, curassows, hornbills, and maleos (neognaths) possess casques of varying shapes and relative sizes. Casque bones can grow rapidly and are obscured by keratin sheathing in early ontogeny and sutural fusion in adulthood, rendering them difficult to study. To evaluate the null hypothesis that avian cranial ornaments possess similar anatomical patterns, we compared the skulls of southern cassowaries (*Casuarius*), maleos (*Macrocephalon*) and their non-casques relatives throughout ontogeny using μ CT data. Crucially, sampling neonates and juveniles with incipient casques allowed us to track telescoping elements and measure growth.

Results

Although the neonatal skulls in our sample are broadly similar, our results point towards at least two modes of casque ontogeny: (1) disunited, in which a midline chondrocranial element grows slowly and posteriad to buttresses lateral dermatocranial bones, and (2) geminal, in which a rapidly growing casque is built from anterioposterior right-left dermatocranial constituents only.

Evaluation of Industry Payments and Financial Conflict of Interest Disclosures among Task Force Authors of Endocrine Society Clinical Practice Guidelines

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Introduction

Clinical practice guidelines are considered the gold standard for disease management and treatment. Industry payments to guideline authors may influence their clinical recommendations, potentially resulting in medical and/or financial consequences to patients.

Research Question

Determine the extent Endocrine Society guideline authors receive industry payments and report financial conflicts of interest in adherence to the Physician Payments Sunshine Provision of the Affordable Care Act.

Study Design

Cross-sectional analysis of all clinical practice guidelines published by the Endocrine Society since the Sunshine Provision mandate.

Methods

We searched the Endocrine Society's website for clinical guidelines published between January 2014 and December 2017. Identified guideline authors were independently searched by two investigators on the Open Payments Database. Received payments were extracted and statistically analyzed (excluding food/beverage payments). Payments were cross-referenced with corresponding author disclosure statements.

Results

Of the 57 evaluable guideline authors, 34 authors (59.6%) received at least one industry payment. Of these authors, thirty-three (57.89%) received \geq \$1,000, twenty-six (45.61%) \geq \$10,000, twenty-two (38.60%) \geq \$50,000, and twenty-one (36.84%) \geq \$100,000. Sixteen authors (28.07%) received \geq \$250,000 in industry payments. Median total payments were \$4,060 (interquartile range [IQR] \$0–263,264.23). Twenty-seven (47.37%) financial disclosure statements were inaccurate. Median payment (minus food/beverage) for inaccurate disclosures were \$28,523.93 (IQR \$5,714-94,418.02), with a payment total of \$2,870,485.27.

Conclusion

Industry payments among Endocrine Society clinical practice guideline authors were widespread, with several exceeding \$250,000. Nearly half of author disclosure statements were inaccurate. The Endocrine Society's disclosure policy should be more strictly enforced for future guideline authors.

Is Office-Based Counseling about Media Use, Timeouts, and Firearm Storage Effective? Results from a Cluster-Randomized, Controlled Trial.

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Introduction

The AAP recommends that pediatricians incorporate questions about the presence and availability of firearms into their patient history taking and urge parents who possess guns to prevent access by their children. Studies show that parents who are counseled are more likely to adopt responsible gun storage practices. Implementation of this approach could result in a significant reduction in firearm related injury each year³.

Question

Is OSU Pediatrics performing firearm screening at well child checks?

Design

Randomized retrospective chart review

Methods

Well child checks for children aged 3-17 from January 2016 – December 2016.

Results

Of the 600 charts reviewed, the presence of firearms within the home was asked 71% of the time. Of those, 18.3% stated yes but education regarding AAP recommendations was not documented.

Conclusion

OSU Pediatrics needs further training on firearm screening, safety, and appropriate documentation.

Assessing the Utility of the GA by Comparing ART Regimens and HIV RNA Pre-and Post-GA

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Introduction

Viral resistance testing is a cornerstone for selecting antiretroviral therapy (ART) in patients with HIV. Recommendations regarding regimen switching in the setting of virologic suppression are not standardized, but genotypic assays are frequently utilized in this scenario to help determine an efficacious medication regimen. Currently, only one genotypic assay (GA) is available for patients whose HIV RNA is less than 500 copies/mL. Little data exists for its clinical significance or utility in practice.

Research Question or Hypothesis

This study aims to assess the utility of the GA by comparing ART regimens and HIV RNA pre- and post-GA.

Study Design

This study is a retrospective chart review based on GA reports obtained historically through the Oklahoma State University Internal Medicine Specialty Clinic electronic medical record.

Methods

The information gathered consisted of clinical indications for a GA, mutations on GA results, ART at the time of the archive draw, and ART post-GA results. Demographic and disease related information will also be collected. Other information gathered included reported compliance to therapy, and regimen tolerability.

Results

Data were gathered from 67 patients, primarily male (87%), with an average age of 45. The most common indications for obtaining a GA were baseline testing (29.8%), re-establishing care (25.4%), and history of non-adherence (20.9%). Approximately half (49%) of patients had an undetectable viral load 3 months after switching their ART regimen based on GA results.

Conclusion

This study is ongoing.

Can the Gelatinase Activity of Snake Venom be Inhibited via Enzyme Inhibition as a Potential Treatment Modality/Adjunct in Snake Bite Victims?

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Introduction

Snake envenomation is a serious problem worldwide, with numerous issues limiting treatments, including expense and availability of anti-venom. Enzyme inhibitors as therapeutics may offer a solution. Many American snake venoms show gelatinase activity and were somewhat inhibitable by various protease inhibitors. The snake venoms used for this project are from the species *Agkistrodon contortrix contortrix* (*Acc*), *Crotalus atrox* (*C. atrox*) and *Cerastes cerastes* (*Ccc*).

Research Question

Can the gelatinase activity of snake venom be inhibited via enzyme inhibition as a potential treatment modality/adjunct in snake bite victims?

Study Design

The baseline gelatinase activity of the three venoms, the venom stability over time, the effect of inhibitor on the venoms and the effect of pretreating the venoms with inhibitor were determined.

Methods

Gelatinase activity and inhibition were tested using EnzChek® Gelatinase/Collagenase Kit E12055 in 96 well microplates with a fluoresceinated collagen substrate and the snake venoms being tested. NNGH is the enzyme inhibitor that was used. Data analysis was conducted using Microsoft Excel and the Km values were estimated by nonlinear regression using GraphPad Prism software.

Results

Baseline gelatinase activities were similar for *Acc* and *Ccc*, while *C. atrox* had lower baseline activity. NNGH inhibits the gelatinase activity of *C. atrox* venom more than *Acc* venom. Venom gelatinase activity is not affected by pretreatment with inhibitor.

Conclusion

These results will be useful in understanding reaction kinetics of snake venom enzyme inhibition, which could lead to alternative treatment modalities of envenomation.

Statistical Significance and Orthopaedic Traumatology.

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Purpose of Study

A recent proposal suggests changing the threshold for statistical significance from a P value of .05 to .005 to minimize bias and increase reproducibility of future studies. The present study explores how lowering the P value threshold would affect the interpretation of previously published trauma orthopaedic randomized clinical trials (RCTs) and whether outcomes from these trials would maintain statistical significance under the proposed P value threshold.

Methods

All RCTs published between January 01, 2016 and January 31, 2018 in the *Journal of Orthopaedic Trauma, Injury, and Archives of Orthopaedic and Trauma Surgery* screened by at least 2 authors. Data from included trials were extracted in blinded and duplicate fashion.

Results

Of 75 articles retrieved, 49 were included. We identified 117 primary endpoints from 49 trials: 41 endpoints (35.0%) had a P value less than .05 and 76 (65.0%) had a P value greater than .05. Overall, 41.5% (17/41) of statistically significant primary endpoints were less than .005. Of the 117 primary endpoints, only 17 (14.5%) of the endpoints were less than .005, and would hold significance with the proposed threshold. Only 6.12% (3/49) of the included studies had all primary endpoints that met the new threshold of .005.

Conclusion

Based on our results, adopting a lower threshold of significance would heavily alter the significance of orthopaedic trauma RCTs and should be further evaluated and cautiously considered when viewing the impact it may have on orthopaedic practice.

Computational Analysis of Artiodactyl Carotid Rete Heat Transfer

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Introduction

Cerebral thermoregulatory structures have a high ecologic and conservation potential. Artiodactyls possess anatomical structures that function to cool blood entering the cranial space. These structures form a countercurrent heat exchanger consisting of warm blood from the carotid rete surrounded by cooled blood in the venous sinus. Cooler arterial blood then flows to the hypothalamus, masking the physiological need to evaporatively cool down. Preliminary field-based, *in-vivo* studies do not identify a correlation between cooling and carotid rete height or volume. This contradicts established mathematical countercurrent heat exchange models.

Hypothesis

We hypothesize that there is a positive correlation between the SA to V ratio of the Artiodactyl carotid rete and its cooling effectiveness.

Study Design

We applied computational fluid dynamic analysis to digital vascular datasets to explore the relationship between artiodactyl carotid rete SA and V on heat exchange effectiveness.

Methods

Anatomical data collection included radiopaque latex vascular injection and CT scanning of a domestic goat, followed by 3D modeling in Avizo to build digital models of the carotid rete and its surrounding venous sinus. We then used STAR-CCM+ to simulate countercurrent blood flow for 3 models: the anatomical SA and V and artificially higher and lower SA to V ratio models.

Results

We identify a positive correlation between heat exchange and surface area.

Conclusion

This suggests that other factors, such as adrenergic tone, may be responsible for the lack of correlation seen in field experiments.

Using Simulation Studies to Determine Phylogenetic Effect on the Evolution of Dental Material Properties in Gnathostomes

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Introduction

Sample size and phylogenetic signal are important and related factors in phylogenetic comparative evolutionary analyses; however, methods for assessing minimum taxonomic resolution are currently lacking. Previously, we have measured hardness and elastic modulus values in enamel and orthodontine from a broad sample of Gnathostomata. The distribution of these values demonstrated a lack of phylogenetic signal, potentially due to small sample size given the longevity of the clade.

Methods

Here we tested whether low phylogenetic signal is robust to increased sampling using paired (non-randomized and randomized) simulation studies. In the first simulation, genus-rank sister taxa of represented species were added to the phylogenetic tree and assigned simulated material properties derived from the previously measured values of their congeners. In the second simulation, added taxa were instead assigned material properties randomly from a distribution of the entire materials dataset with bootstrap resampling. Both simulations were performed for 200 iterations, from which phylogenetic signal was estimated.

Results

Analysis of the simulations identified an increase in phylogenetic signal for both hardness and elastic modulus of dental tissues at higher levels of taxonomic representation, suggesting that additional sampling is necessary to elucidate underlying evolutionary processes.

Conclusion

Further analyses should consider the needs of robust sampling to ensure that the relationships between evolutionary relatedness, dental materials, and diets can be meaningfully addressed.

Elucidation of Glial Glutamate Metabolism during Peripheral Inflammation

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Introduction

Glutamine Synthetase (GS) is an enzyme important for the degradation of neurotransmitter glutamate to glutamine. Satellite glial cells (SGCs) surround dorsal root ganglion (DRG) neurons, and have been observed to contain abundant levels of GS. DRG neurons are known to alter concentrations of glutaminase (synthetic enzyme for neurotransmitter glutamate) during peripheral inflammation, but potential complimentary alterations in GS levels are unknown. If GS or SGC function is disrupted, it may lead to aberrant pain processing and sensitization due to dysregulation of glutamate.

Aim

The current study was undertaken to determine if GS mRNA and/or protein levels are altered in rat DRG during peripheral inflammation.

Methods

Peripheral inflammation was induced via injection of Complete Freund's Adjuvant (CFA) in right hindpaw of anesthetized, albino Sprague Dawley rats. Western blot, qPCR, and immunohistochemistry were performed to see expression profile of GS in DRG neurons at 24h and 48h. In addition, glutamate metabolic inhibitors were added to the peripheral injection under the same conditions and compared to CFA-only animals.

Results

Protein results in experimental animals show peak GS levels at day one, and appear to begin to return to baseline at day two.

Conclusion

These data further our understanding of the glutamate/glutamine cycle and of the communication between SGC's and DRG neurons in relation to nociception and inflammation.

Legacy for Children Impact on Medical Home

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Introduction

Legacy for Children has been studied and shown to improve the parent-child relationship and make positive change in parenting practices. This study is a review to determine the program's impact on children's health and family medical compliance.

Hypothesis

We hypothesize that participation in the Legacy for Children program will have a positive impact on a child's health and the family's overall medical compliance.

Study Design and Methods

We used a retrospective patient chart review to evaluate the program's effect on the child's health. Due to limited numbers of participants our numerical measures are statistically insignificant.

Results

Of the charts reviewed there was: (1) 85.4% kept well child checks appointments, (2) 60% received vaccines on schedule, (3) 93% had appropriate growth and met milestones, (4) 20% had a hospitalization (5) 82% underwent appropriate screening at visits, (6) 78% kept appointments with specialists, (7) 27% moved to a new home, (8) 40% changed primary care physicians.

Conclusion

It is unclear whether participation in the Legacy for Children Program has an impact on a patient's medical compliance. This study has a very small sample size. In order to better determine if Legacy has a positive impact on a patient's medical compliance, we would need to have a larger sample size in the program, do comparative studies, or to conduct qualitative studies in either interview or focus group formats. Given the importance of the caregiver/child bond to health and development and the cost of Legacy implementation, further studies are warranted.

Evaluation of a Digital Learning Object (HistoPete©) at OSUCHS

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Introduction

Digital learning objects (DLOs) are units of learning designed for electronic delivery, can be used almost anywhere, can stand alone or be part of a system, and can be used independently or collaboratively. HistoPete© grew out of a computer-based instruction format in 1989, composed of several modules that took the student through the microscopic anatomy of the human body. DLOs can be reviewed or rated according to content quality, learning goal alignment, feedback and adaptation, motivation, presentation design, interaction usability, accessibility, reusability, and standards compliance. MERLOT suggests that an evaluation model for DLOs should include content quality, usability, and effective potential.

Hypotheses

HistoPete© provides an active learning strategy in the histology course, biomedical foundation course, and systems courses.

Study Design

The method of investigation was quantitative.

Methods

Mixed methods were used in the study. Student course evaluations were available from years 1999-2012. Comments from students in classes 2007-2016 were subjected to qualitative analyses using coding and placing in categories.

Results

Results were graphed on a Likert scale for “HistoPete was useful” and a coding of the students comments revealed nine categories of comments.

Conclusion

Students in the old and new curriculum found that HistoPete was useful and that it was an effective learning tool. Students in the old curriculum thought that it was a good preparation for the lab meeting. Students wanted larger images with higher resolution.

Taste Preferences and Body Weight after Soda Consumption in Estrogen-Treated Female Rats

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Introduction

Soda consumption is thought to contribute to obesity due to its high caloric content. However, it is possible that soda consumption leads to obesity by altering preferences for unhealthy sweet and salty foods, thereby increasing their consumption. Obesity typically is greater in women; moreover, estrogen alters taste preferences.

Research Question

The goal of this experiment was to determine whether soda consumption affected rats' preference for salt or sweet tastes and whether estrogen altered any effect of soda on taste preferences.

Study Design/ Methods

One group of bilaterally ovariectomized (OVX) rats (n=5) was given estradiol benzoate (EB) injections and another group (n=5) was given OIL vehicle injections throughout testing. Rats were maintained on standard chow and given access to soda or water for 2-hr/day, alternating weekly. At the end of each week, a 2-bottle preference test was conducted in which rats were given water and either 0.05M sucrose or 0.5M NaCl for 2 hours. Rats were weighed daily, and soda/water intake determined. Taste preferences were calculated as sucrose or NaCl intake/total intake.

Results

Regardless of whether OVX rats were given EB, they consumed similar amounts of soda. However, neither the change in body weight nor preferences for sucrose or NaCl were influenced by soda consumption when rats were maintained on standard chow.

Conclusion

Together, these findings suggest that soda consumption does not alter preferences for salt or sweet *tastes* in females. Rather, the weight gain associated with soda intake may be related to *consumption* of unhealthy foods.

Trend Identification of Community Acquired Infections across Four Regions of the United States: East, South, Midwest, and West.

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Introduction

We have seen an increase in MRSA isolates in staphylococcal infections for the past forty years and the past twenty years we are seeing an increase in community acquired resistant infections.

Study Design

Retrospective longitudinal study

Methods

We performed a retrospective study using data obtained within the Cerner electronic medical record that was made available to OSU CHS. The data collected was between the years of 2000 – 2013 using age, sex, and resistance patterns. Data was then analyzed using descriptive statistics in excel.

Results

The total number of Staphylococcal infections 82,500 adult cases and 15,215 pediatric cases. The trend was a decline in total number of Staphylococcus aureus infections in the resistant and susceptible groups from 2000 -2013. However, the percent of resistant infections in the community population has increased over this time with the highest percentage in the Southern region and within pediatric groups.

Conclusions

Although we have seen a decrease in the total number of reported cases of staphylococcal infections from 200-2013 there has been an increase in the percent of infections that grow out resistant strains of S. aureus. This data shows that the virulence of MRSA is extending from hospitalized patients that we have traditionally thought of as susceptible out into the general population.

Evaluation of Systematic Review Utilization in the Development of OB-GYN Randomized Controlled Trials

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Introduction

The issue of research waste has been raised due to the fact that 85% of funding for biomedical research has been improperly utilized. A prominent issue is the frequency of randomized controlled trials (RCTs) being conducted without prior consultation of existing support, such as systematic reviews (SRs). Meticulous monitoring is necessary to ensure that clinical recommendations are being made with confidence in high-quality biomedical practices. The aim of this study was to survey Obstetric and Gynecology journals to analyze their published articles for citation of SR for justification of conducting the RCT.

Methods

We conducted a search of PubMed for RCTs published between January 1, 2014 and December 31, 2017, in the top ten Obstetric and Gynecology journals. Each included study was evaluated to determine the number of SRs cited within the introduction, methods, and discussion sections. We further analyzed whether the SR was cited verbatim or indirectly, number of participants, type of intervention being studied, funding source, type of trial, and how the outcome was perceived.

Results

Of the 720 articles from our initial search, 458 (63.61%) met inclusion criteria. Of the 458 included studies, 279 (60.92%) cited an SR in the introduction, 34 (7.42%) cited an SR in the methods, and 207 (45.2%) cited an SR in the discussion as justification for conducting the study.

Conclusion

A large portion of the RCTs being published in clinical Obstetrics and Gynecology journals are not citing SRs as justification for conducting their studies, which may be leading to an increase in research waste.

Morphine-Seeking Behavior in Adolescent Rats Calls for Perineuronal Net Remodeling In the Tail of the Ventral Tegmental Area

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Introduction

Neurobiological mechanisms underlying renewed morphine-seeking behavior in adolescents remain unclear. The ventral tegmental area (tVTA) and its GABAergic neurons are important substrates for morphine-seeking effects and are surrounded by perineuronal nets (PNNs) which are net-like structures important for plasticity during adolescent neurodevelopment.

Hypothesis

1a: Environmental cues and behavioral sensitization will facilitate reactivation of drug-seeking memories following long-term extinction of morphine conditioned place preference (CPP) in adolescent rats.

1b: Morphine-primed reinstatement will alter PNN expression within the tVTA.

Study Design

This study used a mixed variable design. Female and male adolescent Sprague Dawley rats were used (n=24). Half of the animals were assigned to the morphine-saline group (drug-paired group) or to control (drug-naïve). We explored morphine drug-seeking properties with a CPP paradigm. Between subjects (treatment) and within subject acquisition, post-preference, extinction and reinstatement, individual percentage scores were considered.

Methods

In drug- or saline-paired compartment, rats received morphine (5mg/kg/sc) or saline alternately for 8 sessions to induce morphine CPP and were then subjected to extinction of conditioning during 10 sessions. This was followed by a priming morphine dose (2.5 mg/kg) or saline. CPP scores were measured.

Results

Morphine-induced CPP was evident for 75% of the opioid treated rats and dissipated following extinction. A priming-morphine dose evoked CPP for the previous drug-paired side.

Remarkably, morphine-primed reinstatement decreased PNN expression, without observing any significant sex differences.

Conclusion

Environmental-cues and sensitization play critical roles in the incentive adolescent morphine-seeking behaviors and PNNs may result in a critical switch underlying opioid-induced plasticity.

Epigenetic Modulation of Glutaminase in Trinitrobenzene Sulfonic Acid-Induced Colitis Using Methylation-Specific PCR.

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Introduction

Ulcerative colitis is a form of inflammatory bowel diseases, which, causes visceral inflammatory pain. We induce colitis in rats by infusing trinitrobenzene sulfonic acid (TNBS) into the colon. TNBS induces inflammatory pain in rats by increasing the expression of enzyme glutaminase (GLS), involved in production of neurotransmitter glutamate. There are various epigenetic factors that modulate ulcerative colitis, one of them being methylation of cytosines that are part of CpG dinucleotide in the DNA sequence.

Research Question

TNBS-induced hypermethylation of GLS promoter can be evaluated by methylation-specific polymerase chain reaction (MSP).

Study Design

Our study uses empirical research using an FDA-approved drug for *GLS* gene-specific research.

Methods

Anesthetized Sprague-Dawley female rats were infused into the colon with either vehicle), TNBS, azacytidine (aza) or combination of Aza and TNBS. Twenty-four hours post-treatment, the rats were euthanized and fresh colon tissue were collected. The DNA was extracted and treated with bisulfite conversion to convert unmethylated cytosines to thymines. From these samples, MSP was performed using *GLS* promoter-specific primers. We also performed gel-based PCR and Western blotting to evaluate the methylated CpG binding protein-MeCP2.

Results

TNBS-induced colitis contributed to hypermethylation in the *GLS* promoter region leading to overexpression of GLS protein while Aza pretreatment reduced TNBS-induced hypermethylation. Aza pretreatment also reduced TNBS-induced inflammation. MSP was successfully used to evaluate TNBS-induced hypermethylation and Aza-induced hypomethylation.

Conclusion

These studies confirm that MSP can be used as a powerful epigenetic technique to evaluate methylation profile of promoter region of any gene.

Effects of Ketamine on IL-1 β -induced Chemokine Expression

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Introduction

In the US approximately 30% of adults suffer from anxiety disorders at some point in their lifetime. Increasing evidence implicates neuroinflammation in the neuropathology of anxiety disorders. Therefore, medications with anti-inflammatory activity may be useful in the treatment of anxiety and other brain disorders involving neuro-inflammation. Ketamine, though typically used to induce anesthesia, has been more recently used as a fast-acting antidepressant and is used to treat suicidal patients. The mechanism by which ketamine exerts antidepressant actions is not fully understood, but may involve modulation of inflammatory signaling.

Research Question

We are particularly interested in characterizing the effects of ketamine on inflammatory signaling in normal human astrocytes (NHA). Astrocytes are the most abundant cells in the brain and are involved in the maintenance and support of neurons. We are testing the hypothesis that ketamine inhibits inflammatory signaling in NHA.

Study Design/Methods

Cells were stimulated *in vitro* with IL-1 β in the presence/absence of ketamine. We then assessed interferon γ -induced protein-10 (CXCL10) production and viability by ELISA and the MTT assay, respectively.

Conclusions

Ketamine had no effect on CXCL10 expression and was cytotoxic at concentrations ≥ 125 μ M.

Hamstring Tendon Autograft versus Tibialis Tendon Allograft for ACL Reconstruction Patients Under Age 35

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Introduction

ACL injuries are extremely common especially in the young and active population. ACL tears require reconstruction surgery with the use of either an autograft or allograft. The purpose of this research is to find whether a hamstring autograft or tibialis allograft provides these patients with longer survivorship

Focused Clinical Question

Does a hamstring tendon autograft or tibialis tendon allograft provide superior outcomes in regards to re-injury rates and subjective functional outcome scores following an ACL tear in patients under the age of 35?

Study Design

Critically Appraised Topic.

Methods

Four relevant studies were chosen based on inclusion and exclusion criteria, three prospective randomized studies and one retrospective clinical study.

Results

Hamstring tendon autografts and tibialis tendon allografts provide similar subjective and functional outcomes. The odds of tearing an ACL graft was significantly higher for the allograft group compared to the autograft group regardless of age.

Conclusion

There is reasonable evidence (Level B) to support that the hamstrings autograft has superior survivorship compared to tibialis allografts.

Peripheral Inhibition of Glutaminase Alters the Expression of Aspartate Aminotransferase and Glutaminase in Rat Dorsal Root Ganglion During Adjuvant Induced Arthritis

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Introduction

Glutamate is a major excitatory neurotransmitter and plays crucial role in peripheral sensitization of nociceptive terminals during the process of inflammation and nociception. Phosphate-activated glutaminase (GLS) and aspartate aminotransferase (AST) are the enzymes responsible for the synthesis of glutamate. Therefore, it is important to know the precise sequence of expression of enzymes leading to biosynthesis of neurotransmitter glutamate. Although AST can provide a net synthesis of glutamate, its precise functional role in sensory neurons during inflammation remains to be established.

Aim

In this study we have evaluated the expression pattern of AST and GLS in dorsal root ganglion (DRG) neurons following peripheral GLS inhibition during adjuvant-induced arthritis (AIA).

Methods

AIA was induced by injecting complete Freund's adjuvant (CFA) into the right hind paw of anesthetized, 8-10 week old male Sprague Dawley rats (200-300gm). 6-Diazo-5-oxo-L-norleucine (DON) (glutaminase inhibitor) was pre- and co-administered to/with CFA in the same paw. L4 and L5 DRG were collected from naive and AIA animals at 24 and 48 hours of inflammation. Messenger RNA and protein expression of AST and GLS in dorsal root ganglion (DRG) was determined by quantitative PCR and immunoblot techniques.

Result & Conclusion

Our findings show alteration in the expression of AST and GLS in the DRG during AIA. DON treatment mitigated some of the inflammation induced changes. Changes in GLS and AST appear to contribute to DRG neurotransmitter changes in response to peripheral inflammation.

Unusual Etiology for a Common Problem

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Introduction

Diagnosing the etiology of iron deficiency anemia can be very challenging.

Hypothesis

Etiology of iron deficiency anemia is not always straightforward

Study design

Case Report

Results

2-year-old female presented with fever, cough, pallor for 4 days. CXR showed diffuse pulmonary opacities. CRP 3.45, ESR 21, WBC 6, platelet of 361, Hgb of 4 gm/dl, MCV 54, developed hemoptysis and was transferred to the PICU with respiratory failure. Bronchiolar lavage and lung biopsy showed extensive hemosiderin-laden macrophages. Iron deficiency anemia, progressive cough, dyspnea, and infiltrates on CXR was consistent with idiopathic pulmonary hemosiderosis. Pneumocystis, HIV, histoplasma, SLE, vasculitides were negative. Patient responded to a burst of steroid with normalization of breathing and Hgb level during follow up. Sixteen (16) y/o female marathon runner with iron deficiency anemia refractory to iron supplementation, Hgb 7.4gm/dl over 6 month period despite taking iron supplements. MVC was 68, ferritin of 2, transferrin/TIBC levels were elevated. Hemocult stool negative. Combination of intense physical exercise, refractory iron deficiency anemia, and lack of GI blood loss led to consideration of march hemoglobinuria. Urinalysis positive for blood, confirming the diagnosis. With IV iron and reduction of intensity of running, Hgb was up to 14.1.

Conclusion

These two cases of uncommon causes of blood loss highlight the importance of considering rare causes for iron deficiency anemia especially when it is not responding to iron supplement. Without treatment of underlying cause, anemia would persist.

Does Public Interest in Specific Injuries Increase When They Occur During Mixed Martial Arts Bouts? A Study of Google Search Patterns

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Introduction

Mixed martial arts (MMA) is a combat sport that combines fighting techniques from many disciplines, such as wrestling, boxing, karate, Muay Thai, and Brazilian Jiu Jitsu. In the early 1990s MMA entered the United States as the Ultimate Fighting Championship (UFC). Both the internet and social media have advanced the popularity of MMA and have increased the public's exposure to fighting injuries. Here we examine injuries from popular UFC bouts and observe whether the volume of Google searches for specific injuries increases after the associated fights.

Research Question

Does public interest in specific injuries increase when they occur during MMA bouts?

Study design

Our sample of injuries was gathered from "Sherdog's Top 10 Worst UFC Injuries" available from www.sherdog.com. Injury information, the injured fighter's name, date of injury, and the popularity of the fighter (measured by number of Twitter followers) were gathered from Google Trends searches.

Results

Searches for the fighter and for the injury (i.e., an alignment) had a co-occurring pattern in 9 of 10 cases. The percent change in search interest for injuries increased in 9 of 10 cases (Mdn = 446%, IQR: 168.75%-1643.75%).

Conclusions

Search interest in fighters and injuries appears to increase shortly after injury occurrence, possibly providing an opportunity for the timely dissemination of evidence-based information.

Venom: Antivenom Immune Complex Binding Assay Using Size-Exclusion High-Performance Liquid Chromatography (SE-HPLC)

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Introduction

The treatment of envenomation with effective snake antivenom immunoglobins has become a critical worldwide health issue. Current methods for testing the effectiveness of new antivenom mixtures in neutralizing venom toxicity/lethality use animal models (e.g. mice). Neutralization of venom toxicity/lethality requires the formation of venom-antivenom immune complexes (though the extent of complex formation *in vivo* is unknown).

Methods

Size-exclusion high-performance liquid chromatography (SE-HPLC) is a reproducible quantitative method to characterize venom-antivenom immune complex formation *in vitro* within a relatively short time.

Results

Changes in SE-HPLC elution profiles due to dose-dependent formation of venom-antivenom immune complexes are presented for 1) *Crotalis atrox* (western diamondback rattlesnake) venom and the current antivenom used clinically in North America [$F_{ab}AV$ (Ovine); CroFab™], and 2) *Bothrops jararaca* venom (Brazil) and Bothropic antivenom [$F(ab')_2AV$ (Equine); Brazil]. Changes in profile region areas were fit to a hyperbolic dose-response function to estimate maximum binding and venom/antivenom concentrations at half-maximum binding.

Exploring the Gastrointestinal Microbiota in an Emerging Preclinical Model, the Prairie Vole

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Introduction

The composition of the gut microbiota has been shown to impact a person's overall health. Accurately examining the microbiota in different sections of the human gastrointestinal (GI) tract remains challenging. Thus, preclinical models provide valuable insights into gut microbial ecology. The highly social prairie vole is an emerging model for studies on the microbiota-gut-brain-behavior axis. We provide the first comparative analysis of the microbial communities throughout the vole GI tract. Additionally, we explore the effects of probiotics and ingested mercury compounds on the gut microbiota.

Hypotheses

We hypothesized that 1) each GI subsection harbors specific microbial communities with some similarities between human and vole microbiotas; and 2) ingestion of probiotics and/or inorganic mercury affects the vole gut microbiota composition.

Study Design: A proof-of-concept study.

Methods

Fecal pellets and intestinal contents from discrete GI tract sections of voles in control and treatment groups were collected for microbial DNA isolation. The DNAs were examined using next-generation sequencing of bacterial 16s rRNA genes. The resulting sequencing reads were used for compositional and diversity analyses as well as for qualitative comparison to human microbiome data.

Results

The microbiota of the vole gastrointestinal sites revealed disparate compositions and diversities; some similarities to equivalent sites in humans were identified. The effects of probiotic and mercury ingestions were subtle and less striking than site specialization.

Conclusion

This proof-of-concept study provides an important basis for further development of the prairie vole as a preclinical model to study the interaction of the gut microbiota with the host.

Indices Methods Will Display Unique Trends According to Vector Density

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Introduction

Describing differences between objects and their environments can be achieved through binary vectors. A binary vector consists of a set of true or false data that has been translated into ones and zeros which describe an object. Binary similarity indices are numerical analysis methods used to compare data involving two binary vectors.

Hypothesis

Indices methods will display unique trends according to vector density.

Study Design

The scope of this project includes comparing 54 binary similarity index methods in relationship to binary vector density using the R programming language. Matrices were created at various vector densities, the matrices were then scrambled to represent random data. The vectors were compared in each of the 54 binary indices methods and then the data was plotted.

Methods

R programming language was used to process the data due to it containing additional packages tailored towards graphing and binary indices analysis. The Simba package was used to compare vectors and the lattice crystal package was used to plot the data.

Results

Numerous unique trends according to indices method were found.

Conclusion

In several methods, a minimal change in vector density resulted in a significant change in the resulting computation. Awareness of these differences is important when selecting an analysis method and in understanding the effects different vector densities can have on the results analysis.

Glutaminase Expression is Regulated by Nerve Growth Factor/Tropomyosin Receptor Kinase a Signaling in Dorsal Root Ganglion Neurons During Peripheral Inflammation

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Introduction

The neurotransmitter, glutamate, and nerve growth factor (NGF) signaling are directly associated with the development of peripheral sensitization of nociceptor terminals during acute and chronic inflammation. We previously reported that the immunoreactivity of an enzyme glutaminase (GLS) which converts glutamine to glutamate is increased in dorsal root ganglion (DRG) neurons during peripheral inflammation. After the initiation of the inflammatory process, the DRG sensory neurons alter the expression of several proteins, mostly attributed to NGF and its high-affinity receptor, tropomyosin kinase A (TrkA). Although under normal conditions, the basal expression of GLS is not regulated by NGF while during the process of inflammation, the role of NGF/TrkA in the regulation of GLS expression needs further evaluation.

Aim

The aim of this study was to evaluate the effect of NGF/TrkA signaling on the expression of GLS in DRG primary afferent neurons during peripheral inflammation.

Methods

Interplantar injections of either complete Freund's adjuvant (CFA) or CFA with a selective TrkA inhibitor were given in the right hind paw of anesthetized rats. Ipsilateral, L4 and L5 DRG were collected after 48 hrs of inflammation and GLS protein and mRNA levels were evaluated by immunohistochemistry, western blot, and quantitative RT-PCR.

Results

The levels of GLS protein and message were significantly increased in CFA treated rats while this increase was significantly attenuated in animals treated with CFA and TrkA inhibitor.

Conclusion

This establishes the role of NGF/TrkA signaling in the regulation of glutamate production by altering GLS expression during the process of inflammation.

(Funding support: NIH-AR047410)

Impact of Heavy Metal/Pesticide Mixtures on Colorectal Cell Function

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Introduction

There may be a causal relationship between environmental factors and the development of colorectal cancer, but this needs further examination. Little data exists examining heavy metal or pesticide effects on colorectal cells. This study is the first to begin systematic examination of cadmium, glyphosate and cadmium-glyphosate mixtures on colorectal cell function.

Hypothesis

Normal colorectal cells exposed to cadmium, glyphosate or mixture will be more severely affected compared to colorectal tumor cells.

Design

An experimental study with controlled experiments using 2-way or a 3-way analysis of variance followed by appropriate posthoc analysis comparing treatment groups to control.

Methods

Tumor (DLD-1) and control (CCD-18Co) colorectal cells were maintained according to ATCC guidelines. Cells were plated (96-well plate) at a density of 10^5 cells/well and allowed to adhere 24 hours prior to assay. Assays for viability and cytotoxicity were performed according to the manufacturer's instructions.

Results

A significant interaction (cell line x treatment) was observed for viability ($F_{5,36}=33.37$; $p<0.0001$) and cell number ($F_{5,36}=186.0$; $p<0.0001$). Both cell lines were robustly affected by cadmium, but CCD-18Co cells were most sensitive to glyphosate. Exposure to subtoxic concentrations of cadmium or glyphosate mixtures resulted in significant reductions in CCD-18Co viability and number compared to control values.

Conclusions

Cadmium exposure exerted similar effects in each cell line, but CCD-18Co cells were more sensitive to the toxic effects of glyphosate and mixtures. Increased sensitivity may increase the susceptibility of normal cells converting to cancerous cells under prolonged exposure.

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Is the Research You Value a Waste of Money?

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Introduction and Hypothesis

Eighty-five percent of health research may be wasted, resulting in \$170 billion annually in wasteful research spending worldwide. Given the increased use of randomized trials and their influence on medicine, one method to combat research waste is to conduct RCTs only when a systematic review (SR) suggests more data are needed or when no previous systematic reviews are identified. Here, we hypothesize SRs would be rarely cited as justification for conducting RCTs.

Study Design

Cross-Sectional

Methods

We analysed RCTs published between 2016 and 2018 in *New England Journal of Medicine*, *Lancet*, and *Journal of the American Medical Association*. We performed duplicate and independent data extraction to ensure the accuracy and validity of our data. For each trial, we extracted whether SRs were cited as justification for conducting the clinical trial.

Results

Our search retrieved 665 records, of which 628 were included. Overall, 706 SR's were cited in these 628 RCTs; of which, 318 were referenced in the introduction, 82 in the methods, and 306 in the discussion. 49 SRs were cited verbatim as justification for conducting the trial. RCTs published in *Lancet* were more likely to cite a SR as justification for conducting the trial.

Conclusion

Very few clinical trials cite systematic reviews as the basis for undertaking the trial. We believe trialists should be required to present relevant systematic reviews to an ethics or peer review committee demonstrating an unmet need prior to initiating a trial. Eliminating research waste is both a scientific and ethical responsibility.

Long Term Consumption of High Fructose and High Salt Diet Did Not Induce Blood Pressure Elevation in Female Mice. Is Estrogen Protective Against Dietary-Induced Hypertension?

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Introduction

High fructose and high salt (HFHS) consumption are linked to hypertension, which is now the leading cause of death worldwide. Results from a previous study showed that the effect of HFHS on blood pressure (BP) is dependent on the concentration and duration of consumption. Sex differences in BP regulation are partially attributed to the effects of sex steroids on key renal sodium transporters.

Hypothesis

We hypothesized that HFHS would induce BP elevation in male and female mice, however, females will have higher expression of renal NCC/NKCC during long-term HFHS diet consumption.

Methods

Four-week-old male and female CD-1 mice (n= 6/group) were placed in metabolic cages and consumed standard chow and water for seven days, followed by 3 months of 4% sodium chloride (NaCl) diet and a drinking solution of 1% NaCl and 20% fructose. Separate mice on the same diet in bins were sacrificed and kidneys extracted at the end of the first week, first and second months, and used for molecular studies.

Results

Females expressed higher mRNA levels of NCC and NKCC throughout the study with fold difference of two or higher. Systolic BP averaged weekly and analyzed via ANOVA showed no sex difference in BP from baseline to the third month. Males showed an increase in BP in the third month compared to baseline (123.6 ± 3.6 mmHg and 106.3 ± 5.4 mmHg, $P < 0.5$ respectively). There were no sex differences in sodium retention.

Conclusion

Females have protection against HFHS induced BP elevation and estrogen may have a protective role.

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The Nociceptin Receptor (NOP) Agonist AT-312 Blocks Acquisition Of Morphine-Induced Conditioned Place Preference And Affects Brain Volume And Connectivity In Adolescent Rats

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Introduction

Nociceptin receptor (NOP) plays a role in the regulation of reward and motivation pathways related to substance abuse. A novel small-molecule NOP ligand AT-312 a high-affinity, selective NOP full agonist showed efficacy blocking ethanol-induced conditioned place preference (CPP) without inducing reward or aversion when administered alone. However, AT-312 effects on morphine rewarding properties are unknown. The ventral tegmental area (VTA) is implicated in morphine reinforcing properties but also plays a role in the modulation of nociception. In addiction medicine, Imaging Techniques and 3D digital reconstruction have become critical tools for evaluating drug-induced changes in gray matter and neural connectivity.

Hypothesis

We hypothesize that AT-312 will reduce morphine priming-induced reinstatement and modify brain-region volume in the adolescent brain.

Study/Design

We explored morphine drug-seeking properties with a CPP paradigm, individual percentage scores were considered and correlated with volumetric and morphological changes that occur in the periaqueductal gray (PAG), and ventral tegmental area (VTA) of adolescent Sprague Dawley rats

Methods

Morphine-induced conditioned place preference (CPP) was established (5mg/kg/sc) followed by a priming morphine dose (2.5 mg/kg) or saline. Followed by Diffused Iodine Contrast Enhanced CT (diceCT) Scanning techniques to build 3D models of the PAG and VTA.

Results

Our results showed that systemic administration of AT-312 in adolescent rats blocked morphine-induced CPP and remarkably reduced drug-primed reinstatement. Also, preliminary sample suggests that morphine-reinstatement affect gray matter quality.

Conclusions

Our results showed that systemic administration of AT-312 in adolescent rats blocked morphine-induced CPP and -induced seeking memories and compromised brain volume and white matter quality.