

Minneapolis VA Health Care System Research Day 2015



Celebrating 90 Years of VA Research

Abstract List
(alphabetically, by author)

May 14, 2015

1. Oral Presentations – 1st Floor Auditorium (12:00 - 1:00 pm)

☆ **Introductions and Welcome**Hanna E. Bloomfield, MD, MPH, Associate Chief of Staff, Research Service

☆ **2015 Zieve Award Presentation** Hanna Bloomfield (on behalf of James Johnson, MD)

Recipient: Younghoon Kwon, “Sleep Disordered Breathing and Daytime Cardiac Conduction Abnormalities in Older Men”

☆ **Keynote Address**Dimitri Drekonja, MD, MS, FACP, FIDSA

“Fecal transplants for recurrent *Clostridium difficile* infection – the current (and future?) evidence”

☆ *The Minnesota Veterans Medical Research and Education Foundation will be providing Free Box Lunches to the first 120 attendees.*

2. Poster Session – 2nd Floor Flag Atrium (1:00 – 3:00 PM)

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1. VA CSP #592: Efficacy and Safety of ICD Implantation in the Elderly

Adabag, Selcuk^{1,2}; Green, Michele²; Tholakanahalli, Venkat^{1,2}; Singh, Steven³

1. Minneapolis VA Health Care System
2. University of Minnesota
3. Washington DC VA Health Care System

Abstract: Implantable Cardioverter-Defibrillators (ICDs) prevent Sudden Cardiac Death (SCD) by restoring normal rhythm in the event of a life-threatening ventricular tachyarrhythmia. While ICD therapy is a proven preventer of SCD in younger patients, its benefit to older patients is unclear. ICD therapy is an under-utilized treatment option. The proportion of potentially eligible veterans implanted with an ICD peaks at age 67 and declines continuously thereafter. No randomized clinical trials have focused solely on an older population. The objective of CSP 592 is to study the safety and efficacy of ICD implantation as a primary prevention strategy of SCD in patients aged 70 years and older. Participants will be randomized (1:1 ratio) to ICD + Optimal Medical Therapy (OMT), or OMT alone, stratified by participating site and co-morbidity level (Charlson score < 3 versus > 3). We postulate that ICD + OMT will result in a 25% reduction in the hazard for all-cause mortality.

Research Topic: Heart Disease

Funding Agencies: CSR&D; HSR&D

Grant Support: Department of Veterans Affairs, Office of Research & Development

2. Trends in the Use of Cardio-reno-protective Drugs after In-Hospital Acute Kidney

Akkina, Sunil¹; Solid, Craig²; Collins, Alan²; Ishani, Areef³

1. University of Minnesota
2. Center for Chronic Disease Outcomes Research
3. Minneapolis VA Health Care System

Abstract: Acute kidney injury (AKI) in hospitalized patients confers significant short- and long-term morbidity and mortality. Cardio-reno-protective agents such as ACEi and ARBs are frequently discontinued for transient in-hospital AKI. The rates of reinitiation have not been previously studied. The presence of AKI was ascertained from the 5% Medicare cohort of hospitalized patients from March 2009 to December 2009. At 100 days after hospital discharge, the cumulative probabilities of reinitiation were 55% for all patients with AKI and with CHF, and 60% for patients with CKD and diabetes. Rates of initiation among patients with no prior ACEi/ARBs use were 10-15%. Hazards ratio for reinitiating ACEi/ARB therapy following AKI in sub-groups were as follows: CHF (0.95 (0.89-1.01, p<0.11)), CKD (0.79 (0.7 to 0.89 vs. no CKD; p=0.0001)), and diabetes (1.11 (1.05-1.17, p<0.0001)). In this study, we found lower rates of ACEi/ARB therapy resumption even among patients with CHF, CKD, and diabetes.

Research Topic: Kidney Disorders

Funding Agencies: None

Grant Support: None

3. Men with Urinary Tract Infections & Sub-Study about Bacterial Resistance to Antibiotics

Amundson, Carla¹; Drekonja, Dimitri^{1,2}

1. Minneapolis VA Health Care System

2. University of Minnesota

Abstract: Current guidelines suggest 7-14 days of antibiotics for men with urinary tract infections (UTI). This study is for men with UTI prescribed at least 7 but not more than 14 days of either ciprofloxacin or trimethoprim/sulfamethoxazole. Patients are randomized to 7 or 14 days of antibiotics, and followed for 1 month to determine if UTI symptoms resolve without recurrence. There is a sub-study of bacterial resistance, a potential harm of antibiotic use. This involves testing 2 stool samples for antibiotic-resistant bacteria. As of March 2015, 37 patients have been enrolled; this is significantly less than anticipated. We have identified common barriers to enrollment (time constraints, aversion to research, medical issues, and travel) and are developing strategies to improve recruitment. Optimal treatment duration for men with UTI is unknown, and in need of high-quality evidence. Efforts to improve recruitment rates are ongoing, and raising awareness of this study is a high priority.

Research Topic: Infectious Diseases

Funding Agencies: CSR&D

Grant Support: VA Merit Review

4. The Effect of treatment with Resiniferatoxin and Capsaicin on Dynamic Weight Bearing Measures and Evoked Pain Responses in a Chronic Inflammatory Arthritis Murine Model

Bert, Joseph¹; Krug, Hollis^{1,2}; Mahowald, Maren^{1,2}; Frizelle, Sandra²; Dorman, Christopher²; Funkenbusch, Sonia²

1. University of Minnesota Medical School

2. Minneapolis VA Health Care System

Abstract: Background: We examined whether Capsaicin and Resiniferatoxin (vanilloid receptor agonists) might benefit a chronic Complete Freund's Adjuvant induced inflammatory arthritis. Methods: Chronic Inflammatory arthritis was produced by intra-articular (IA) injection of 30 µl of Complete Freund's Adjuvant (CFA) into the left knee of C57BL6 male mice 3 weeks prior to pain behavior testing. Groups of mice were injected with IA RTX (10µl of 0.001% or 10µl of 0.003%) or IA CAP (10µl of 0.01%) 7 days prior to testing. Evoked pain behavior was measured by tallying fights and vocalizations per one minute with repeated palpation of the knee at 1100 gf/cm². ADWB (weight and time on each limb) was measured using an Automated Dynamic Weight Bearing apparatus. Results: Treatment with IA CAP or IA RTX did not result in improvement in EPS and ADWB measurements when compared to the chronic inflammatory arthritis model. Conclusion: IA CAP and IA RTX did not result in analgesia in CFA induced arthritis.

Research Topic: Autoimmune, Allergic & Hematopoietic Disorders

Funding Agencies: RR&D

Grant Support: 510 IRX000379-03

5. A multidisciplinary, iterative approach to developing a mobile app for Veterans in a self-medication program

Bjella, Jessie¹; Cooper, Carolyn¹; Dao, Vinh¹; Larson, Mary¹; Litynski, Heather¹; Kent, Derek¹; Schreffler, Colleen¹; Ferguson, John^{1,2}; MacLennan, Don¹

1. Minneapolis VA Health Care System
2. University of Minnesota

Abstract: For Veterans in the VA Polytrauma Transitional Rehabilitation Program (PTRP), self-management of medications is a crucial step towards functional independence. Mobile apps have the potential to be useful tools for Veterans to learn and practice medication self-management skills. However, many mobile health apps are developed without input from the people that will be using them, often resulting in a disconnect between design and implementation. In this project, we utilized an iterative approach to develop a mobile health app for medication self-management using qualitative feedback from patients and providers in speech-language pathology, nursing, pharmacy, and occupational therapy. The result was a mobile health app that responded to the individual needs of Veterans with brain injury while demonstrating the importance of involving relevant stakeholders early in the development process.

Research Topic: Acute & Traumatic Injury

Funding Agencies: HSR&D; RR&D

Grant Support: Polytrauma and Blast-Related Injuries (PT/BRI) QUERI Locally Initiated Project

6. Effectiveness and Harms of Pharmacist-led Patient Care Compared to Usual Care - A Systematic Review

Bolduc, Jennifer¹; Geurkink, Eric¹; Rector, Thomas²; Olson, Kimberly³; Greer, Nancy²; Koeller, Eva²; MacDonald, Roderick²; Wilt, Timothy²

1. Department of Pharmacy, Minneapolis VA Health Care System
2. Center for Chronic Disease Outcomes Research, Minneapolis VA Health Care System
3. General Internal Medicine, Minneapolis VA Health Care System

Abstract: Background: Pharmaceutical care is collaboration of pharmacist with health team members to optimize therapeutic outcomes by identifying, resolving, and preventing drug therapy problems. Increased involvement of pharmacists may improve patient access and care. VA clinical pharmacy specialists have an expanded scope of practice including independent prescribing, disease management, patient medication counseling, and education. Purpose: Conduct a systematic review of effectiveness and harms of pharmacist-led patient education and chronic disease and comprehensive medication management for community-dwelling adults with chronic diseases. Methods: Search MEDLINE, CINAHL, and Cochrane database and International Pharmaceutical Abstracts and relevant citations/systematic reviews for comparative, US studies. Preliminary Results: 63 studies included; few studies report important policy-relevant or patient-centered outcomes; most reported intermediate outcomes specific to the disease condition

Research Topic: Health Systems

Funding Agencies: HSR&D

Grant Support: Department of Veterans Affairs, Veterans Health Administration, Office of Research and Development, Quality Enhancement Research Initiative (QUERI)

7. Identification and structural characterization of heparin-binding hotspots in Gremlin1

Buelt-Gebhardt, Melissa¹; Shekels, Laurie¹; Curry, James¹; Nelson, Matthew¹; Klein, Mark²; Sham, Yuk³; Gupta, Pankaj²

1. Research Service, Minneapolis VA Health Care System
2. Hematology/Oncology Section, Minneapolis VA Health Care System
3. Center for Drug Design, University of Minnesota

Abstract: Gremlin1 is a multi-functional, heparin/heparan sulfate (HS) binding protein that plays a pathogenetic role in diverse malignancies and diseases of the lungs, kidneys, eyes and bones. However, there are no drugs that target this molecule. Binding interactions with HS are essential for critical pathophysiological effects of Gremlin1, e.g. on angiogenesis. Inhibiting Gremlin1-HS interactions may be of broad therapeutic value. We elucidated structural features of heparin/HS-binding domains in Gremlin1. Site directed mutagenesis identified a previously unrecognized heparin-binding site ("A") in Gremlin1. Molecular dynamics simulation analysis identified a 2nd site predicted to interact with heparin. Both sites are involved in each of 2 possible complexes that can form between Gremlin1 and heparin. Our characterization of heparin/HS-binding domains of Gremlin1 may provide a basis for structure-based design of novel pharmacologics that target this pathogenic protein.

Research Topic: Cancer

Funding Agencies: BLR&D

Grant Support: Heparan sulfate proteoglycans in human hematopoiesis

8. VA providers beliefs about racial disparities in healthcare

Burgess, Diana^{1,2}; Gollust, Sarah²; Bokhour, Barbara³; Cunningham, Brooke²; Gordon, Howard^{4,5}; Jones, Dina²; Saha, Somnath^{6,7}; Do, Tam¹; Pope, Charlene⁸

1. Center for Chronic Disease Outcomes Research, Minneapolis VA Health Care System
2. University of Minnesota
3. Center for Healthcare Organization and Implementation Research, Boston University
4. Jesse Brown VA Medical Center, Center of Innovation in Complex Chronic Healthcare
5. University of Illinois at Chicago
6. Center to Improve Veteran Involvement in Care, VA Portland Health Care System
7. Oregon Health & Science University
8. COIN/Health Equity & Research Outreach Innovation Center (HEROIC), Ralph H. Johnson VA Medical Center

Abstract: Objectives: Provide guidance for the development of disparity-reduction strategies by examining VA providers' beliefs about healthcare disparities. Methods: Individual semi-structured interviews with 53 providers in 3 VA facilities Results: Some providers believed disparities were rare or non-existent in VA, due in part to viewing disparities as primarily due to lack of health insurance/limited access to care; viewing disparities in terms of overt rather than unconscious and subtle bias that can be difficult to detect; and seeing racism as historical rather than a present day problem. Lack of time and other system factors were seen as barriers to providing equitable care. Providers frequently focused on solutions to improve healthcare quality overall rather than those targeted specifically towards disparities reduction. Impacts: Healthcare system level changes and targeted training approaches are needed to successfully engage providers in disparity-reduction efforts.

Research Topic: Access & Disparities in Care

Funding Agencies: HSR&D

Grant Support: None

9. T1-rho and T2-rho relaxometry in Multiple Sclerosis

Carpenter, Adam¹; Mangia, Silvia²; Tyan, Andrew²; Garwood, Michael²; Michaeli, Shalom²

1. Brain Sciences Center, Minneapolis VA Health Care System
2. Center for Magnetic Resonance Research, University of Minnesota

Abstract: Background: Quantitative MRI techniques can provide more specific measures of relevant pathologic processes in MS (such as demyelination, neurodegeneration, and iron deposition) than conventional MRI methods. Adiabatic T1-rho and T2-rho utilize rotating frame relaxations to provide enhanced sensitivity to molecular motion and generate novel MRI contrasts. Methods: We investigated T1-rho and T2-rho relaxometry in eight relapsing-remitting MS (RRMS) patients and eight age- and gender-matched controls, using a 4-Tesla magnet. Regions of interest including T2 lesions (T2L) and normal-appearing white matter (NAWM) were identified from T2-weighted images from the MS subjects, and the corresponding regions were compared on the R1-rho and R2-rho maps from MS patients and controls. Results: T1-rho was significantly longer in MS patients vs controls, in both T2L and NAWM, suggesting that these novel MRI methods may improve our ability to detect focal and diffuse pathologic processes in MS.

Research Topic: Central Nervous System Injuries & Associated Disorders

Funding Agencies: UMN

Grant Support: Academic Health Center Seed Grant from the University of Minnesota Medical School (Carpenter)

10. Diagnosis of Posttraumatic Stress Disorder (PTSD) Based on Correlations of Prewhitened fMRI Data

Christova, Peka¹; James, Lisa¹; Engdahl, Brian¹; Lewis, Scott¹; Georgopoulos, Apostolos¹

1. Brain Sciences Center, Minneapolis VA Health Care System

Abstract: Successful diagnosis of posttraumatic stress disorder (PTSD), a disabling condition resulting from exposure to traumatic events, has previously been shown using neural correlations of prewhitened magnetoencephalographic time series (Georgopoulos et al. 2010, James et al. 2014). Here we show that highly successful classification of PTSD versus control subjects is also possible using neural correlations of prewhitened resting-state functional magnetic resonance imaging (fMRI) data. Fifteen veterans with a primary diagnosis of PTSD and 21 healthy control veterans participated in the study. Participants completed diagnostic interviews and then underwent an fMRI. One-thousand bootstraps showed that all but one control (20/21) and all but one PTSD (14/15) subject were correctly classified. In contrast, correlations of the same data without prewhitening yielded only chance-level classifications. We conclude that suitably processed fMRI could aid significantly in PTSD diagnosis.

Research Topic: Acute & Traumatic Injury

Funding Agencies: CSR&D

Grant Support: Evaluation of MEG Synchronous Neural Interactions (SNI) Test for PTSD

11. Brain Connectivity, Cognition, and Mental Health in Early-Career National Guard SoldiersDavenport, Nicholas^{1,2}; Kielbasa, Alicia¹

1. Minneapolis VA Health Care System
2. University of Minnesota

Abstract: Mild traumatic brain injury (mTBI; concussion) is common among military members. While most people with mTBI recover within 3 months, some report lasting changes in mood, concentration, or physical health. Prior research has shown associations among mTBI, brain connectivity, mental health, and symptom reports, but these relationships are difficult to fully characterize without pre-injury information. We have assessed a broad range of clinical, cognitive, and neuroimaging measures on more than 35 Minnesota National Guard service members prior to Basic Training, with a target of N=240. All participants will be given the opportunity to provide information about their training upon returning, and a subset will be invited back for additional in-person procedures. Approximately one third of the sample reported a potential head injury event, and nearly half reported a traumatic experience. However, lasting effects were rare, and overall baseline mental and physical health were excellent.

Research Topic: Mental Illness

Funding Agencies: RR&D

Grant Support: CDA-2 RX-000709-01A3

12. A Novel Pager Coverage System to Enhance Morning ReportDrake, Tyler¹; Ercan-Fang, Nacide¹

1. Minneapolis VA Health Care System

Abstract: Residents attending morning report frequently receive pages, missing significant educational time. Beginning in July 2014, a chief resident covered all of the pagers of residents on the medicine service at the Minneapolis VA Health Care System during the morning report conferences. The chief resident returned pages and took messages; if there was an urgent clinical matter the chief resident would ask the resident to attend to the issue. There have been 272 pages received during 140 morning reports. Of these, only 8% required the resident to step out of morning report. The total number of pages per resident during morning report has also decreased, from 0.38 pages/resident to 0.25 pages/resident. A chief resident pager coverage system during educational conferences was easily instituted and dramatically reduced the number of residents who are paged out of morning report, enhancing their educational value and improving resident satisfaction. This system also appears to be reducing the total number of pages.

Research Topic: Health Systems

Funding Agencies: None

Grant Support: None

13. Role of orexin A signaling in dietary saturated fatty acid activated microglial cells

Duffy, Cayla M.^{1,2}; Yuan, Ce²; Wisdorf, Lauren E.²; Billington, Charles J.^{1,3,4}; Kotz, Catherine M.^{1,2,4}; Nixon, Joshua P.^{1,2}; Butterick, Tammy A.^{1,2}

1. Veterans Administration Medical Center, Minneapolis, MN
2. Department of Food Science and Nutrition, University of Minnesota, St Paul, MN
3. Department of Medicine, University of Minnesota, Minneapolis, MN
4. Minnesota Obesity Center, St Paul, MN

Abstract: Dietary saturated fats such as palmitic acid (PA) contribute to hypothalamic inflammation, metabolic dysregulation, and obesity. In rats, PA activates microglia, increasing central expression of pro-inflammatory cytokines TNF α and IL-6. Orexin A reduces inflammation and prevents neurodegeneration via a microglia-mediated pathway. We hypothesize that OXA reduces PA-induced inflammation in immortalized murine microglial cells (BV2). BV2 cells were pretreated with 300nM OXA for 1h and treated \pm 0.1mM PA for 4 h. Cell mRNA was analyzed using qRT-PCR; supernatant was analyzed by ELISA. PA exposure increased expression of orexin-1 but not orexin-2 receptor. OXA pretreatment reduced PA-induced pro-inflammatory cytokines TNF- α and IL-6. This is the first report demonstrating OXA acts as an immunomodulator in response to PA. Our results provide insight into mechanisms by which dietary fatty acids provoke inflammatory responses, and how OXA functions as a central immunomodulator.

Research Topic: Central Nervous System Injuries & Associated Disorders

Funding agencies: BLR&D; RR&D; NIH; UMN;

Grant Support: BLR&D BX001686 (TAB), RR&D RX000441 (CMK), NIDDK R01 DX100281 (CMK), University of Minnesota Healthy Foods, Healthy Lives Institute (CMD)

14. Vermal cerebellar lesions as a mouse model of autism

Dziobek, Derek¹; Koob, Michael²; Ashe, James^{3,4}

1. University of Minnesota Graduate Program in Neuroscience
2. University of Minnesota Department of Laboratory Medicine and Pathology
3. University of Minnesota Department of Neuroscience
4. Minneapolis VA Health Care System

Abstract: Autism is a disorder characterized primarily by deficits in social interactions, and its pathology and etiology remain unclear. This project attempts to develop a mouse model of autism by recreating the most common pathology seen in autistic humans, in particular the loss of Purkinje cells in lobules VI and VII of the cerebellar vermis. We have designed a system that will provide the necessary spatial and temporal control of Purkinje cell death via inducible tissue-specific expression of Diphtheria toxin. After cell loss, the mice will be screened for behavioral abnormalities commonly associated with autism spectrum disorders. This project provides a unique look at the cerebellum's role in cognition, as well as furthering our understanding of this debilitating disorder.

Research Topic: Mental Illness

Funding Agencies: None

Grant Support: None

15. Combined Impact of Mobility and Cognition on Risks of Hospitalization and Mortality in Women in Late Life

Ensrud, Kristine^{1,2}; Lui, Li-Yung³; Paudel, Misti²; Schousboe, John²; Kats, Allyson⁴; Cauley, Jane⁵; McCulloch, Charles³; Yaffe, Kristine⁶; Cawthon, Peggy³; Hillier, Teresa⁷, Taylor, Brent^{1,2}

1. Minneapolis VA Health Care System
2. University of Minnesota
3. California Pacific Medical Center Research Institute
4. Chronic Disease Research Group (Minnesota Medical Research Foundation)
5. University of Pittsburgh
6. University of California, San Francisco
7. Kaiser Permanente Northwest

Abstract: Combined effects of mobility and cognition on risk of hospitalization and mortality in late life are uncertain. We studied 371 women (avg age 87.7 yrs) participating in the Year 20 (Y20) examination of a prospective cohort study with assessment of cognition and mobility who were linked to their Medicare claims data. During the 12 months after Y20, 31.4% were hospitalized. After consideration of traditional prognostic indicators including prior hospitalization and comorbidity burden, women with low mobility/cognitive impairment compared to those with high mobility/normal cognition had a 3-fold higher odds of hospitalization and a 5-fold greater rate of inpatient days. During an average follow-up of 4.9 years, 44.7% died. The adjusted mortality risk was 2-fold higher among women with low mobility/cognitive impairment compared to those with high mobility/normal cognition. These findings have implications for developing health care policies for growing population of adults aged ≥ 85 yrs.

Research Topic: Aging

Funding Agencies: NIH; UMN

Grant Support: R01 AG005407, R01 AR35582, R01 AR35583, R01 AR35584, R01 AG005394, R01 AG027574, and R01 AG027576.

16. A pilot trial of VA-CRAFT: Online training to enhance family well-being and Veteran mental health service use

Erbes, Christopher^{1,2}; Kuhn, Eric³; Gifford, Elizabeth⁴; Spont, Michele^{1,5}; Meis, Laura⁵; Polusny, Melissa^{1,2}; Oleson, Heather¹; Taylor, Brent^{1,5}; Hagel-Campbell, Emily¹; Wright, Jillian⁶

1. Center for Chronic Disease Outcomes Research
2. University of Minnesota Psychiatry
3. National Center for PTSD (NC-PTSD), Palo Alto
4. Center for Healthcare Evaluation (CHCE), Palo Alto
5. University of Minnesota
6. Minneapolis VA Health Care System

Abstract: This pilot project examined the acceptability and effect of VA-CRAFT, an online adaptation of an empirically supported family-focused outreach program, (Community Reinforcement and Family Training), on Veteran mental health and substance abuse service utilization and family member well-being. Family members of Veterans who screened positive for PTSD or alcohol use disorders and were not engaged in mental health services were randomly assigned to complete the VA-CRAFT online training (n = 34) or a wait-list condition (n = 32) over 90 days. Family members in the VA-CRAFT group had a significantly greater decrease in reports of caregiver burden on the Caregiver Burden Scale than family members in the control group. There was no statistically significant difference between the two groups on Veteran mental health service utilization. Further enhancements may be needed for this promising intervention to aid family in encouraging Veterans to engage in care.

Research Topic: Mental Illness

Funding Agencies: HSR&D

Grant Support: CRE-12-024

17. Sensor Based Control of a Bimodal Ankle-Foot Prosthesis with a Smartphone Interface

Fairhurst, Stuart^{1,2}; Lin, Xiaobin²; Nickel, Eric³; Hansen, Andrew^{2,3}; Ferguson, John^{2,3}

1. Minnesota Veterans Medical Research & Education Foundation
2. University of Minnesota
3. Minneapolis VA Health Care System

Abstract: Our research group has previously developed a bimodal ankle-foot prosthesis which allows persons with lower limb amputations to switch between standing and walking modes using a wireless key fob. In this project, we designed a new control system that uses an accelerometer and gyroscope to detect user activity and to switch to the most useful mode automatically. We also developed a smartphone application that gives the user control over the walking and standing modes when automatic switching is not desired.

Research Topic: (Not Provided)

Funding Agencies: RR&D; MVMREF

Grant Support: VA RR&D A1531R - Bimodal Prosthetic Ankle-Foot System for Improved Balance and Mobility

18. Development of a Manual Wheelchair For Improved Shoulder Biomechanics

Fairhurst, Stuart^{1,2}; Nickel, Eric³; Morin, Steve⁴; Goldish, Gary^{5,6}; Hansen, Andrew^{5,6}

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2. University of Minnesota
3. Minneapolis VA Health Care System
4. Biomedical Engineering, Minneapolis VA Health Care System
5. EC&R, Minneapolis VA Health Care System
6. PM&R Department, University of Minnesota

Abstract: Conventional manual wheelchairs have hand rims attached to the drive wheels at the rear of the chair. This configuration introduces problems for users. First, users propel the chair with the shoulders in an extended position, increasing overuse injuries such as rotator cuff damage. Second, the wheelchair user's hands make frequent incidental contact with the wheels themselves, leaving the hands dirty. In a hospital environment this can facilitate the transmission of hospital-acquired infections. We developed a prototype wheelchair with a chain drive system that separates the hand rims from the drive wheels, reducing shoulder extension during propulsion and eliminating hand contact with the drive wheels. The chain drive also permits manipulation of the gear ratio to support users who have reduced arm or shoulder function but who wish to remain in a manual wheelchair. This system also permits unobstructed lateral transfers when the hand rims are removed.

Research Topic: Central Nervous System Injuries & Associated Disorders

Funding Agencies: RR&D; MVMREF

Grant Support: This project is supported by the Mike Utley Foundation.

19. Portable Wireless Visuotemporal Cue Device for Gait Therapy

Fairhurst, Stuart^{1,2}; Simone, Amanda³; Ferguson, John^{2,3}; Hansen, Andrew^{2,3}

1. Minnesota Veterans Medical Research & Education Foundation
2. University of Minnesota
3. Minneapolis VA Health Care System

Abstract: Recent studies have shown that the use of visuotemporal cue devices during gait therapy resulted in positive gait outcomes. However, existing devices were not practical to use in a clinical setting as they had moving parts, took up too much floor space, and required too much time and effort to use. Researchers and clinicians from the VA collaborated to develop a portable, lightweight, and inexpensive visuotemporal cue device using sequentially illuminating lights in a compact housing. The new design is user-friendly, easy to set up, and provides a motivational tool that therapists can use to measure improvements in gait speed. It can be placed across the end of parallel bars and the visuotemporal speed can be remotely adjusted to suit individual patient needs. The prototype device is currently available for use by clinicians at the Minneapolis VA.

Research Topic: Central Nervous System Injuries & Associated Disorders

Funding Agencies: RR&D; MVMREF

Grant Support: None

20. Skeletal Site of, and Risk Factors for Clinical Fractures in Older Men by Baseline BMD Category: the Osteoporotic Fractures in Men (MrOS) Study.

Fink, HA¹; Blackwell, TL²; Taylor, BC³; Orwoll, ES⁴; Ensrud, KE³

1. Geriatric Research Education & Clinical Center, VA Health Care System, Minneapolis, MN
2. California Pacific Medical Center, San Francisco, CA
3. Center for Chronic Disease Outcomes Research, VA Health Care System, Minneapolis, MN
4. Oregon Health Sciences University, Portland, OR

Abstract: Low BMD increases fracture (fx) risk, but most men who fx are not osteoporotic. We examined if sites & risk factors for incident fx differ in older men by BMD category. Baseline BMD (female ref) was used to categorize 5984 men as normal ($T \geq -1$ all sites), low bone mass ($-2.5 > T > -1$ all sites), or osteoporotic ($T \leq -2.5$ any site). Self-reported incident fx were collected every 4 mo. & centrally confirmed. Participant characteristics with age-adj associations with incident fx ($p < 0.05$) were assessed for age-adj, BMD-stratified associations with major osteoporotic fx (MOF=hip, wrist, proximal humerus, or clinical spine), and associations were tested for interaction by BMD category. Over 10.5+/-3.6y, >80% of men with MOF were not osteoporotic (28% had normal BMD, 56% low bone mass, 17% osteoporosis). Of men with clinical fx, 34%, 52%, & 68% were at MOF sites in those with normal BMD, low bone mass, & osteoporosis, respectively. Associations of risk factors for MOF appeared similar across BMD categories. Results suggest interventions to address modifiable non-BMD risk factors may be needed to reduce the population burden of fx in older men.

Research Topic: Acute & Traumatic Injury

Funding Agencies: NIH

Grant Support: U01 AG027810, U01 AG042124, U01 AG042139, U01 AG042140, U01 AG042143, U01 AG042145, U01 AG042168, U01 AR066160, and UL1 TR000128.

21. Two-Port Totally Extraperitoneal Inguinal Hernia Repair: A 10-Year ExperienceFuglestad, Matthew¹; Waisbren, Steven²

1. University of Minnesota Medical School, UNMC
2. University of Minnesota Medical School, Minneapolis VA

Abstract: Purpose: To evaluate laparoscopic two-port totally extraperitoneal (TP-TEP) inguinal hernia repair. Methods: A 10-year retrospective analysis from 2004–2013 of patients undergoing TP-TEP. Results: 336 consecutive patients underwent TP-TEP repairing 478 hernias. 315 patients were male and 21 were female. Mean age \pm SD was 47 ± 14 years and mean body mass index \pm SD was 28.0 ± 4.7 kg/m². Indications for surgery included primary repair (303), recurrence from open repair (28), and incarceration (5). 194 cases were unilateral and 142 were bilateral. Operative time \pm SD was 38.7 ± 14.9 mins for unilateral repair and 43.4 ± 17.6 mins for bilateral repair. TP-TEP was successful in 316 (94.0%). 20 cases required an additional port. 2 cases were converted to open repair. Mean follow up time \pm SD was 5.4 ± 2.7 yrs. Postoperative complications included urinary retention (5), seroma (7), hematoma (1), surgical site infection (4), and chronic inguinal pain (3). 11 (2.3%) hernias recurred. Conclusion: TP-TEP appears to be a feasible, safe, and effective method for inguinal hernia repair and should be considered a viable, less invasive alternative to conventional techniques.

Research Topic: Acute & Traumatic Injury

Funding Agencies: UMN

Grant Support: None

22. Deficits in Visual System Functional Connectivity after Blast-Related Mild TBI are Associated with Injury Severity and Executive DysfunctionGilmore, Casey^{1,2}; Camchong, Jazmin³; Sponheim, Scott^{2,3}; Kardon, Randy^{4,5}; Lim, Kelvin^{1,2,3}

1. Defense and Veterans Brain Injury Center
2. Minneapolis VA Health Care System

Abstract: Visual processing problems and cognitive dysfunction are common complaints after blast TBI. Understanding functional relationships between visual pathways and higher order brain regions could serve as a foundation for treating these visual and cognitive symptoms. 131 OEF/OIF veterans underwent eyes-closed resting-state fMRI scans. Regression analyses revealed 1) functional connectivity (FC) between four visual system seeds – lateral geniculate nucleus, primary visual cortex, lateral occipital gyrus, and fusiform gyrus – and regions in occipital, parietal, and frontal cortex, and 2) negative correlation between severity of veterans' blast TBI and the magnitude of resting FC. Further, higher FC between visual and frontal regions was correlated with better performance on two cognitive tasks. Identification of visual-frontal neural network deficits associated with blast-TBI severity highlights the detrimental relationship between TBI and integration of visual input and executive processes.

Research Topic: Acute & Traumatic Injury

Funding Agencies: MVMREF

Grant Support: Minnesota Veterans Medical Research & Education Foundation (MVMREF) and the Congressionally Directed Medical Research Program (W81XWH-08-2-0038) to Scott R. Sponheim.

23. Enhancing cognitive control using transcranial direct current stimulation

Gilmore, Casey^{1,2}; Gentz, Carolyn^{1,2}; Clancy, Doris^{1,2}; Gierke, Molly^{1,2}; Dickmann, Patricia^{2,3}; Lamberty, Greg^{2,3}; Armstrong, Michael²; Lim, Kelvin^{1,2,3}

1. Defense and Veterans Brain Injury Center
2. Minneapolis VA Health Care System
3. University of Minnesota

Abstract: Impulsivity is a multidimensional construct that includes impaired cognitive control, commonly manifested by excessive risk-taking. Transcranial direct current stimulation (tDCS) applied over dorsolateral prefrontal cortex has been shown to induce a decrease on tasks measuring risk-taking. This study will explore effects of tDCS on risk-taking in veterans who exhibit impulsivity. Subjects complete two tDCS sessions per day for five days, and two monthly followup sessions. Subjects complete questionnaires of impulsivity and pre- and post-intervention behavioral measures of risk-taking. Preliminary results on two subjects showed risk-taking behavior decreased an average of 7% and 20% in two risk-taking tasks from the first to last day of tDCS treatment. This study measures change on outcome tasks from pre- to post-intervention, and stability of these effects over time. This study could have application as a non-invasive clinical intervention for veterans with decreased cognitive control.

Research Topic: Mental Illness

Funding Agencies: DOD

Grant Support: Defense and Veterans Brain Injury Center (DVBIC)

24. Increased Postural Sway in Veterans with Mild Traumatic Brain Injury Measured with a Force Platform

Gilmore, Casey^{1,2}; Nelson, Brent^{2,3}; Gentz, Carolyn^{1,2}; Clancy, Doris^{1,2}; Gierke, Molly^{1,2}; Lim, Kelvin^{1,2,3}

1. Defense and Veterans Brain Injury Center
2. Minneapolis VA Health Care System
3. University of Minnesota

Abstract: Postural sway problems can indicate sensorimotor neurological dysfunction. This study uses an inexpensive force platform, the Nintendo Wii Balance Board, to assess postural sway in veterans with mild TBI. 44 veterans with mTBI and 10 without were assessed by standing motionless on the Wii board for 60 seconds with eyes: 1) closed 2) open, or 3) open, searching text on a paper on the wall for a particular letter. Sway was measured as the average absolute distance traveled in anterior-posterior (AP) and medial-lateral (ML) directions. In the AP direction, veterans with mTBI had significantly greater postural sway than Controls in the eyes closed condition. There were no ML differences between mTBI and Controls. Current findings indicate that objective assessment of postural sway in mTBI may be helpful in identifying individuals at increased risk of fall. This balance assessment could be an important tool in guiding rehabilitation of mTBI patients.

Research Topic: Acute & Traumatic Injury

Funding Agencies: DOD

Grant Support: Defense and Veterans Brain Injury Center (DVBIC)

25. Here's to Safety! Dedicated Rounds Improve Event Reporting

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1. University of Minnesota
2. Minneapolis VA Health Care System Department of Medicine
3. Minneapolis VA Health Care System Patient Safety Office

Abstract: Medical errors and safety events occur frequently, but are rarely discussed formally. Among graduating internal medicine residents last year, only 10% had ever reported a safety event. We aimed to have 100% of internal medicine residents report at least 1 event by May 2015. To improve reporting, we implemented morning reports focused on quality improvement (QI) and biweekly chief resident rounds with inpatient teams during which safety events were elicited and discussed. Control charts assessed change in event reports. Monthly surveys evaluated individual-level reporting. Total and medication-related safety event reports significantly increased since July 2014. Residents reporting at least 1 error increased from 10% to 55%. Rounds and subsequent feedback required 3-3.5 hours of physician time. Significant improvements in event reporting can be achieved efficiently, though additional work remains. Reporting changes have resulted in multiple improvements in clinical care processes.

Research Topic: Health Systems

Funding Agencies: None

Grant Support: None

26. Minneapolis VA Evidence-based Synthesis Program (ESP)

Greer, Nancy¹; MacDonald, Roderick¹; Koeller, Eva¹; Wilt, Timothy¹

1. Center for Chronic Disease Outcomes Research, Minneapolis VA Health Care System

Abstract: Objective: Provide timely and accurate evidence syntheses on topics of particular importance to VA managers and policymakers to improve health and care of Veterans; final reports posted on VA HSR&D website and disseminated including VA Management Briefs and Cyberseminars. Results: 2014 Reviews – 1) Effects of Shared Decision Making on Cancer Screening; 2) Fecal Microbiota Transplantation for C. diff Infection; 3) Comparative Effectiveness of Home-based vs In-Center Kidney Dialysis; 4) Colonoscopy Outcomes by Duration of NPO Status Prior to Colonoscopy. 2015 Topics – 1) Effectiveness and Harms of Pharmacist-led Patient Care Compared to Usual Care; 2) Benefits and Harms of the Mediterranean Diet Compared to Other Dietary Interventions; 3) Prevalence and Epidemiology of Combat Blast Injuries from the Military Cohort 2001-2014. Summary: VA ESP reports inform clinical policy, lead to implementation of effective services to improve patient outcomes, and give direction to future research to address knowledge gaps

Research Topic: Health Systems

Funding Agencies: HSR&D

Grant Support: Department of Veterans Affairs, Veterans Health Administration, Office of Research and Development, Quality Enhancement Research Initiative (QUERI)

27. Differential function of Ag-specific CD4 T cells after sepsis-induced lymphopenia is influenced by gut microbiota

Griffith, Thomas^{1,2}; Cabrera-Perez, Javier²; Babcock, Jeffrey²; Badovinac, Vladimir³

1. Minneapolis VA Health Care System
2. University of Minnesota
3. University of Iowa

Abstract: Sepsis changes the composition and function of the naïve CD4 T cell repertoire, but the mechanism(s) that control such changes are unknown. We posited that the constituents of the gut flora define the responsiveness of CD4 T cell populations specific for Ag present in the commensal bacterial species that establish polymicrobial sepsis after cecal-ligation and puncture (CLP) versus those CD4 T cells undergoing sepsis-induced Ag-independent homeostatic proliferation. We tracked the loss/recovery and function of CD4 T cells specific for an Ag present in segmented filamentous bacteria (SFB) in mice containing or devoid of this bacteria in their gut. SFB-specific CD4 T cells underwent Ag-driven proliferation in CLP-treated SFB+ mice, but not in SFB- mice. This correlated with their functional ability after secondary infection with SFB Ag-expressing *Listeria*. Our data suggest the extent of recovery and function of a particular Ag-specific T cell population during sepsis can be determined by the

Research Topic: Infectious Diseases

Funding Agencies: BLR&D

Grant Support: None

28. The effect of blood and blood breakdown products on the arachnoid blood-CSF-barrier

Hansen, Eric¹; Lam, Cornelius^{1,2}; Hubel, Allison²; Yuan, Ching²; Norby, Kiersten²

1. Minneapolis VA Health Care System
2. University of Minnesota

Abstract: Introduction: Blood and blood products are present in the setting of brain injury. They are cleared from the central nervous system by a number of means including bulk flow of cerebrospinal fluid. This study investigates the effect of blood and blood products on the arachnoid egress gateway. Method: Immortalized rat arachnoid cells were plated on 3.0 University of Minnesota membranes of the Transwell© system and incubated for 3-5 days until confluency. Arachnoid cells were treated with whole blood, lysed blood, cell membranes, hemoglobin, bilirubin, and biliverdin, placed either in the apical or basal compartments and compared to negative controls. Results: Arachnoid cells subjected to hemoglobin, whole blood (in the basal chamber), bilirubin and biliverdin had significantly increased permeabilities unless the blood or blood products themselves obstructed transport. Conclusion: Blood and blood products can overwhelm and obstruct the transport mechanism of arachnoid cells.

Research Topic: Acute & Traumatic Injury

Funding Agencies: BLR&D

Grant Support: VA Merit Review grant

29. Prediction Model for Risk of Adenoma at Screening Colonoscopy

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2. Division of Internal Medicine, University of Minnesota
3. Masonic Cancer Center, University of Minnesota
4. Section of Gastroenterology, Minneapolis VA Health Care System

Abstract: Background: No clinical tool exists to predict the probability of adenoma at time of screening colonoscopy. A prediction tool would identify patients at greatest risk and allow prioritized screening. Our aim was to identify a clinical prediction tool. Methods: We extracted demographic data, risk factors, colonoscopy and histopathology results from individuals who underwent a screening colonoscopy between 2007 and 2012. Results: 3000 veterans were included. Median age of this population was 61. Adenomas were found in 35%. Risk factors for adenoma included age, male sex and smoking. Variables included in the final model were age, sex, BMI, race, use of aspirin, smoking history, and family history of CRC. The adjusted AUROC for the cohort was 0.532. Conclusion: We identified risk factors and developed a prediction model for estimating the risk of adenoma at time of screening colonoscopy. This model may be useful in prioritizing individuals for screening colonoscopy.

Research Topic: Digestive Diseases

Funding Agencies: BLR&D

Grant Support: VA CDA-2 (I01 CX000245)

30. Incidental Melanomas Detected in Veterans Referred to Dermatology

Hanson, Jamie^{1,2}; Kingsley-Loso, Jaime¹; Grey, Katie¹; Raju, Srihari²; Bershow, Andrea^{2,3}; Warshaw, Erin^{2,3}

1. University of Minnesota Medical School
2. Minneapolis VA Health Care System
3. University of Minnesota Medical School Department of Dermatology

Abstract: Objective: To characterize and compare incidental versus consult melanomas detected in veterans referred to the Minneapolis VA Health Care System dermatology clinic. Methods: Retrospective chart review of consults from 01/2004-03/2012. Results: Of the 28,405 consults sent during the study period, 17,174 met inclusion criteria. 231 melanomas were identified in 221 patients. 144 melanomas were identified on the consult and 87 melanomas were discovered incidentally. The incidental melanoma detection rate was 0.5% (84/17,174). Consult melanomas were more likely to be invasive than incidental melanomas (RR 1.51, 95% CI 1.23-1.86, p<0.0001) and less likely to have a Breslow depth of less than 1.00mm (RR 0.73, 95% CI 0.61-0.88, p=0.0036). Incidental melanomas were smaller than consult melanomas (mean diameter: 0.98 cm vs 1.3 cm) and thinner (mean Breslow depth: 0.64 mm vs 1.74 mm). Conclusion: Melanomas detected during an in-person skin exam by a dermatologist are detected at an earlier stage of disease.

Research Topic: Cancer

Funding Agencies: None

Grant Support: None

31. Prediction of Changes in Self-Stigma Among Veterans Participating in Partial Psychiatric Hospitalization: The Role of Disability Status and Military Cohort

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1. Minneapolis VA Health Care System
2. Anderson University
3. San Francisco VA Medical Center
4. VISN 5 MIRECC, Baltimore

Abstract: Information was provided by 235 veterans attending a partial psychiatric hospitalization program, regarding their levels of internalized stigma on admission and discharge from a 3-week program that included interventions targeting internalized stigma. Upon discharge, veterans receiving disability benefits demonstrated less reduction in internalized stigma than those not receiving disability benefits. Time of service moderated the relationship between disability status and change in internalized stigma, such that veterans serving in the more recent Operation Enduring Freedom/Operation Iraqi Freedom/Operation New Dawn (OEF/OIF/OND) cohort who received disability benefits had a more difficult time resolving internalized stigma. Further analyses suggested that OEF/OIF/OND cohort veterans receiving disability benefits have more difficulty developing effective stigma resistance than other veterans.

Research Topic: Mental Illness

Funding Agencies: None

Grant Support: None

32. VA Cooperative Study #578: Prevention of Serious Adverse Events Following Angiography (PRESERVE)

Herrmann, Rebekah¹; Williams, Hattie¹; Burg, Matthew¹; McFalls, Edward¹; Adabag, Selcuk¹; Garcia, Santiago¹

1. Minneapolis VA Health Care System

Abstract: The intravascular administration of iodinated contrast media for diagnostic imaging is a common cause of acute kidney injury and a leading cause of iatrogenic renal disease. Multiple studies have demonstrated that contrast-induced AKI (CIAKI) is associated with increased short-term mortality, prolonged hospitalization, increased medical resource utilization, and adverse long-term outcomes. Intravenous (IV) isotonic fluid is the principal intervention for the prevention of CIAKI. Recently, clinical trials have focused on the comparative effectiveness of IV sodium bicarbonate vs sodium chloride. Another preventive intervention for CIAKI is N-acetylcysteine (NAC). This multicenter, randomized clinical trial is designed to assess the comparative effectiveness of these interventions for the prevention of clinically important, adverse outcomes in high-risk Veterans undergoing cardiac and non-cardiac angiography.

Research Topic: Kidney Disorders

Funding Agencies: None

Grant Support: Department of Veterans Affairs Cooperative Study Program

33. Recovery and Contractile Reserve on Cardiac MRI in Hibernating Myocardium Post-CABG

Hocum Stone, Laura¹; Holley, Christopher¹; Crampton, Melanie¹; Kelly, Rosemary¹; McFalls, Edward²

1. Cardiothoracic Surgery, University of Minnesota
2. Cardiology, Minneapolis VA Health Care System

Abstract: Clinical studies have suggested that functional recovery of hibernating myocardium may not occur following coronary artery bypass graft (CABG) surgery. Using a swine model of hibernating hearts and MRI estimates of circumferential strain (ECC), we tested whether contractile reserve within hibernating hearts is present post-CABG. 10 pigs underwent thoracotomy with placement of a constrictor around the LAD artery. At 12 weeks, they underwent MRI imaging prior to off-pump revascularization with a LIMA graft to the LAD artery. At 4 weeks post-CABG, MRI studies were repeated at baseline and during an infusion of dobutamine. Following CABG, CT angiography confirmed a patent LIMA graft. MRI studies post-CABG showed that baseline circumferential strain in the Hibernating (LAD) Region was lower than the Remote Region ($P < 0.01$). Despite reduced basal function, contractile reserve was present in the Hibernating Region, which suggests that recovery may occur.

Research Topic: Heart Disease

Funding Agencies: RR&D; NIH

Grant Support: Department of Veterans Affairs (RR&D Merit Review-RK) and National Institutes of Health (NHLBI-RO1 HL089307-EM)

34. PPAR- γ . Stimulation Increases Mitochondrial Antioxidants in Chronically Ischemic Pig Hearts

Holley, Christopher¹; Hocum Stone, Laura¹; Duffy, Cayla²; Butterick, Tammy²; Ward, Herbert¹; Kelly, Rosemary¹; McFalls, Edward³

1. Cardiothoracic Surgery, University of Minnesota
2. Minneapolis VA Health Care System Research Division
3. Cardiology, Minneapolis VA Health Care System

Abstract: We hypothesized that chronic administration of the PPAR γ agent pioglitazone (PIO) would increase the expression of mitochondrial anti-oxidant proteins in chronically ischemic heart. 18 pigs underwent thoracotomy with placement of a constrictor around the LAD artery. 8-weeks later, they were given daily PIO (3 mg/kg) or placebo for 4 weeks. Regional function by ECHO was measured at baseline. Regional blood flow was determined at baseline and during high-dose dobutamine. Mitochondria from the LAD region were isolated to determine protein content of PGC-1 α in nuclear fractions (Westerns) and antioxidant proteins (iTRAQ). In all pigs, baseline regional wall thickening was lower in the LAD versus Remote region ($P < 0.05$). LAD blood flow was $83 \pm 5\%$ at baseline and $64 \pm 7\%$ during dobutamine, characteristic of chronic ischemic myocardium. PIO animals had higher content of mitochondrial anti-oxidant peptides and PGC-1 α , suggesting that PIO may enhance these peptides via increased PGC-1 α signaling.

Research Topic: Heart Disease

Funding Agencies: RR&D; NIH

Grant Support: Department of Veterans Affairs (RR&D Merit Review-RK) and National Institutes of Health (NHLBI-RO1 HL089307-EM)

35. Mitochondrial Fusion Proteins are Increased in Hibernating Myocardium Following CABG

Holley, Christopher¹; Hocum Stone, Laura¹; Duffy, Cayla²; Butterick, Tammy²; Ward, Herbert¹; McFalls, Edward³; Kelly, Rosemary¹

1. Cardiothoracic Surgery, University of Minnesota
2. Minneapolis VA Health Care System Research Division
3. Cardiology, Minneapolis VA Health Care System

Abstract: Expression of mitochondrial proteins within the ETC of hibernating swine hearts does not normalize at 4-weeks following bypass surgery (CABG). We hypothesized that mitochondrial fusion proteins are increased at this time as a result of enhanced PGC-1 α signaling. 12 pigs underwent thoracotomy with placement of a constrictor around the LAD artery and had reduced regional function 12 weeks later. 6 pigs then underwent sternotomy and off-pump revascularization with a LIMA graft to the LAD. Patency was confirmed by CTA at 4 weeks post-CABG. 5 pigs underwent a SHAM operation. In the hibernating regions that underwent CABG, maximal blood flow during dobutamine was lower than control (P<0.05). The content of both fusion proteins and PGC-1 α signaling was significantly increased in Hibernating hearts that had undergone CABG. These changes suggest that the mitochondrial proteome may require delayed biogenesis following revascularization, to favorably support higher energetics in hibernating hearts.

Research Topic: Heart Disease

Funding Agencies: RR&D; NIH

Grant Support: Department of Veterans Affairs (RR&D Merit Review-RK) and National Institutes of Health (NHLBI-RO1 HL089307-EM)

36. Immediate Discharge from Post Anesthesia Care Unit to Home Following Laparoscopic Appendectomy for Acute Non-Perforated Appendicitis

Hrad, Valery¹; Waisbren, Steven^{2,3}

1. University of North Dakota
2. Minneapolis VA Health Care System Research Division
3. University of Minnesota

Abstract: Purpose: Examine the efficacy and safety of immediate discharge from the post-anesthesia care unit following laparoscopic appendectomy for patients with acute non-perforated appendicitis. Methods: Retrospective study of 114 laparoscopic appendectomy cases. 74 patients met inclusion criteria of having uncomplicated acute appendicitis. Patient demographics, operative times, length of postoperative stay, and complication rates were analyzed. Results: 3 of the 74 patients failed to be discharged immediately. Mean post-op discharge time was 130.5 minutes with 86% of patients leaving within 3 hours. Delay in voiding was the most common cause of stays longer than 4 hours. Six of the 74 patients (8%) returned to the ER with no inpatient re-admissions. No complications were attributed to early discharge. Conclusion: Immediate discharge from the post anesthesia care unit for patients with acute non-perforated appendicitis appears safe and effective in the community hospital setting. .

Research Topic: Digestive Diseases

Funding Agencies: None

Grant Support: None

37. Blood Biomarkers of Chronic Inflammation in Gulf War Illness

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1. Minneapolis VA Health Care System
2. University of Minnesota

Abstract: Gulf War Illness (GWI) is a chronic disorder of 1990-91 Gulf War veterans defined by symptoms in 2 or 3 categories - fatigue, mood-cognition, musculoskeletal pain. No objective diagnostic criteria exist. Objectives: 1) To evaluate inflammation in GWI; 2) To identify objective criteria for diagnosis Methods: Subjects: 57 veterans with GWI (GWI+) and 28 without (GWI-). Assays: 1) CBC; 2) Multi-Analyte (MAP) analysis of 89 inflammation-related blood proteins. Analyses: 1) Univariate analysis; 2) Multivariate analysis; 3) Discrimination (C statistic). Results: Compared to GWI- veterans GWI+ veterans had significantly 1) Higher CBC, neut., mono., lymph., and platelet counts; 2) Differences in 6 inflammation-related proteins including CRP and leptin; 3) Model-based, predicted probability above 0.70 had a predictive value of 90%. Conclusions: 1) Inflammation exists in GWI; 2) Cell counts and protein assays provide diagnostic criteria to aid GWI diagnosis.

Research Topic: Gulf War Veterans Illness

Funding Agencies: CSR&D; DOD

Grant Support: Congressional Directed Medical Research Programs: Biomarkers of Gulf War Veteran's Illnesses: Tissue Factor, Coagulation, & Inflammation (DoD); Gulf War-Associated Chronic Coagulopathies: Tissue Factor, Coagulation, & Immune System Activation (VA); Tissue Factor and Gulf War-Associated Chronic Coagulopathies (VA)

38. A longitudinal analysis of pseudohyperkalemia in patients with chronic lymphocytic leukemia (CLL)

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2. Center for Chronic Disease Outcomes Research, Minneapolis VA Health Care System
3. Nephrology Section, Minneapolis VA Health Care System
4. Nephrology Division, Department of Medicine, University of Minnesota
5. Hematology/Oncology Section, Minneapolis VA Health Care System
6. Hematology/Oncology Division, Department of Medicine, University of Minnesota

Abstract: Pseudohyperkalemia in CLL patients with leukocytosis has led to inappropriate potassium (K)-lowering interventions in case studies, but none provide guidance for clinical decision-making when interpreting K. We identified 310 patients with CLL (1997-2014) from the Minneapolis VA Health Care System Tumor Registry and analyzed 57 eligible patients (49-95 yrs, WBC \geq 50.0x10⁹/L during their disease) by extracting 1,119 paired WBC counts and plasma K, and using longitudinal fixed effects linear regression to test for a relationship between them. Overall, 19% of K values >ULN. For each increase in 100 x 10⁹ WBC/L, K increased by 0.5 mmol/L (avg). For each increase in 10 x 10⁹ WBC/L, the adjusted odds of K>ULN increased by 1.4. When WBC \leq 50 x 10⁹/L, 1.7% of K >ULN; when WBC \geq 100 x 10⁹/L, 8.1% of K>ULN. WBC variation explained only part of the K variation, likely because numerous factors other than WBC influence K. Thus, a correction factor cannot be created, and interpretation requires clinical judgment.

Research Topic: Cancer

Funding Agencies: UMN

Grant Support: None

39. VA CSP 588 Randomized Endo Vein Graft Prospective (REGROUP) Trial

Kelly, Rosemary^{1,2}; McFalls, Edward^{1,2}; Ward, Herb^{1,2}; Shumway, Sara^{1,2}; Loor, Gabriel^{1,2}; Marsh, Bonnie²; Bruetzman, Gayle²; Thompson, Katie²

1. University of Minnesota
2. Minneapolis VA Health Care System

Abstract: CABG is the most common major surgical procedure in the U.S. and the VAMC Health System, and typically requires vein from the leg to be used to bypass around critically blocked coronary arteries. While EVH has become the preferred method for harvesting the vein because it provides a minimally invasive approach, more recent investigations indicate potential for reduced long-term bypass graft patency and worse clinical outcomes with EVH. In order to offer the safest and most durable revascularization strategy for veterans requiring CABG surgery, it is imperative to provide definitive evidence on the long-term clinical outcomes of EVH in order to minimize harvest site morbidity while preserving long-term clinical outcomes. REGROUP is a national study that randomizes eligible, interested patients undergoing CABG to either open or endoscopic vein harvesting and tracks outcomes for six years.

Research Topic: Heart Disease

Funding Agencies: HSR&D

Grant Support: None

40. Evidence of dyskinesia as predictive of schizophrenia rather than unexpressed genetic liability: A family study of motor control through digitized handwriting assessment

Kent, Jerilyn^{1,2}; Skorheim, Mallory³; Lano, Timothy¹; Caligiuri, Michael⁴; Sponheim, Scott^{1,5}

1. Minneapolis VA Health Care System
2. Indiana University
3. Midwestern University
4. University of California, San Diego
5. University of Minnesota

Abstract: Motor deficits are reported in schizophrenia (SZ) and at-risk populations. Dyskinesia, thought to reflect regulatory disinhibition within the basal ganglia, is found in prodromal individuals and is predictive of outcome. We assessed dyskinesia in 1st degree relatives (REL), who carry unexpressed genetic liability for the development of SZ. Handwriting samples were obtained from 51 SZ, 32 REL and 62 controls (CN). Average normalized jerk (ANJ), which examines changes in handwriting acceleration within a stroke (i.e. dyskinesia proxy) was calculated. The group effect was significant; SZ had significantly more ANJ than CN or REL (no significant difference between CN and REL). ANJ was not significantly correlated with antipsychotic dose. Lack of dyskinesia in REL is consistent with retrospective studies wherein abnormal movements differentiate those who eventually develop SZ from their non-affected siblings. Dyskinesia may be a marker for risk of conversion to SZ, not genetic liability.

Research Topic: Mental Illness

Funding Agencies: CSR&D

Grant Support: Merit Review Grant (VHA CSR&D I01CX000227-01) to Scott Sponheim.

41. Evaluation of p16INK4A-Derived Peptides in Mesothelioma

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2. University of Minnesota
3. Center for Drug Design, University of Minnesota

Abstract: Introduction: Mesothelioma is a highly fatal disease with few therapeutic options. Low expression of p16INK4A, an endogenous tumor suppressor acting as a CDK4/CDK6 inhibitor, has been demonstrated in 50-90% of mesothelioma tumors. Truncated peptides derived from the 3rd anykyrin repeat of p16INK4A have been shown to exhibit similar activity to the full-length protein. Hypothesis: Amino-acid substitutions will affect the structure and function of p16INK4A-derived peptides. Results and Discussion: We have conducted molecular dynamics simulations of alanine-substituted p16INK4A-derived peptides based on the 10mer and 20mer peptides. For the 10mer peptide, alanine substitution has significant effects on the alpha helicity of the native solution structure. For the larger 20mer peptide, similar substitutions showed a slightly different effect on the predicted conformation population. We anticipate that molecular dynamics studies will inform the design of stabilized peptide candidates.

Research Topic: Cancer

Funding Agencies: DOD

Grant Support: Peer-Reviewed Cancer Research Program Career Development Award, American Cancer Society Institutional Research Grant

42. Taxonomy of Health Care Overuse Literature

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1. Minneapolis VA Health Care System
2. University of Minnesota

Abstract: Background: Overuse is the provision of care in which the benefits don't justify the harms or costs. Reducing healthcare overuse will improve patient outcomes and reduce costs. The literature is poorly described making research to reduce overuse hard. Objective: To review and categorize the literature on overuse in order to gain a clearer understanding of the state of overuse practice and research. Methods: We searched Ovid using a strategy adapted from other studies of overuse. Samples of abstracts were categorized first by subject and then again by specific topic. Results: We identified 2,843 abstracts. Of 918 abstracts reviewed there were 295 on overtreatment, 162 on methods to avoid overuse and 53 on overdiagnosis. Half of the abstracts were reviewed again. 88 were on strategies to avoid overuse, 83 on drivers of overuse, 57 on prevalence and 6 on barriers to reducing overuse. Conclusions: Categorizing the literature on overuse is difficult but will help guide future research.

Research Topic: (Not Provided)

Funding Agencies: HSR&D

Grant Support: Department of Veterans Affairs, Veterans Health Administration, Office of Research and Development, Quality Enhancement Research Initiative (QUERI) and the Under Secretary of Health Award for Health Services Research

43. Sleep Disordered Breathing and Daytime Cardiac Conduction Abnormalities in Older Men

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1. Minneapolis VA Health Care System
2. University of Minnesota
3. Brigham & Women's Hospital
4. Harvard Medical School
5. California Pacific Medical Center Research Institute
6. Case Western Reserve University

Abstract: The relationship between sleep-disordered breathing (SDB) and ECG parameters is uncertain. We postulate that greater SDB severity is associated with a higher odds of ECG abnormalities in older men. We examined 475 men aged ≥ 67 years from the MrOS Sleep study who had overnight polysomnography and a standard resting 12-lead ECG performed. SDB severity was categorized by percent of total sleep time with oxygen saturation $< 90\%$ (% time $\text{SpO}_2 < 90\%$) and apnea hypopnea index (AHI). ECGs were reviewed by 3 physicians blinded to SDB status. After adjusting for multiple confounders, men with % time $\text{SpO}_2 < 90\% \geq 3.5$ (hypoxemia) compared with those with % time $\text{SpO}_2 < 90\% < 1.0$ had a 5-fold higher odds of having a pacemaker present. While men with $\text{AHI} \geq 15$ (sleep apnea) compared to those with $\text{AHI} < 5$ appeared twice as likely to have pacemaker present, this association was not significant. Greater hypoxemia was also associated with a lower odds of sinus bradycardia. Future studies are warranted.

Research Topic: Other Chronic Diseases

Funding Agencies: NIH; UMN

Grant Support: U01 AG027810, U01 AG042124, U01 AG042139, U01 AG042140, U01 AG042143, U01 AG042145, U01 AG042168, U01 AR066160, and UL1 TR000128. R01 HL071194, R01 HL070848, R01 HL070847, R01 HL070842, R01 HL070841, R01 HL070837, R01 HL070838, and R01 HL070839.

44. Million Veteran Program (MVP)

Lederle, Frank¹

1. Minneapolis VA Health Care System

Abstract: Objectives: To establish a national, representative longitudinal cohort of 1 million Veterans for future genetic and other observational research, to include the collection of new data from survey instruments (demographic and lifestyle questionnaires), blood specimen collection, electronic health information from multiple VA and non-VA resources and ancillary data collection efforts, with the ultimate goal of improving Veterans' healthcare. VA researchers are conducting genetic studies to better understand the relationships between genetic characteristics, behaviors and environmental factors, and Veterans' health. Research Plan and Methods: Consented participants will provide a blood sample that will be stored at a VA Central Biorepository. Information collected about Veterans' health, disease characteristics, and lifestyle will be stored in the VA Central Research Database.

Research Topic: Personalized Medicine & Genomics

Funding Agencies: HSR&D

Grant Support: Department of Veterans Affairs Office of Research & Development

45. Network of Dedicated Enrollment Sites (NODES) Pilot ProgramLederle, Frank¹

1. Minneapolis VA Health Care System

Abstract: The Network of Dedicated Enrolled Sites (NODES) initiative is a pilot program that was developed from a response to support the VA Cooperative Studies program (VA CSP). The specific aims of the initiative include; enhancing study performance and enrollment rates; provide a more consistent and comprehensive approach to CSP study management, quality and regulatory compliance at the VA Medical Centers; obtain center-level perspectives in the design and execution of studies; and provide opportunities for research personnel interested in supporting the VA CSP research mission. The following achievements reflect cumulative data from the NODES sites: 1. Established cross-coverage on CSP studies; 2. NODES staffing incorporated as part of local CSP study teams; 3. Created procedures for CBOC recruitment; 4. Work stream meetings on improving study design & procedures; 5. Beta testing Case Report Forms; 6. Enhanced recruitment; 7. Development of Research/HR Management Proposal.

Research Topic: Health Systems**Funding Agencies:** HSR&D**Grant Support:** Department of Veterans Affairs Office of Research & Development

46. Effects of age on brain network interactions and properties, measured by magnetoencephalography (MEG) in the resting state.Mahan, Margaret^{1,2}; Loe, Maren³; Leuthold, Arthur^{1,4}; Georgopoulos, Apostolos^{1,4,5}

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2. Graduate Program in Biomedical Informatics and Computational Biology, University of Minnesota, Minneapolis, MN

3. Undergraduate Program in Department of Mathematics, University of Chicago, Chicago, IL

4. Department of Neuroscience, University of Minnesota Medical School, Minneapolis, MN

5. Graduate Program in Biomedical Informatics and Computational Biology, University of Minnesota, Minneapolis, MN

Abstract: A central effort of our research is focused on investigating brain function across the lifespan. Here, we investigated the age-dependent changes in lagged crosscorrelations (CCs). For that purpose, we use magnetoencephalography to record resting-state brain activity. This yields 248 sensors x 60,000 ms matrix of neural activity recorded simultaneously from the cerebral cortex. To estimate the magnitude of neural interactions, we calculate pairwise CCs between the prewhitened sensor time series for ± 50 ms lags. This yielded 101 CCs for each one of the 30,628 sensor pairs. The strength, sign, and lag of each CC were noted and more general patterns were quantified. We then regressed each of these measures against the age of 133 brain-healthy women veterans. We discovered highly significant associations between CC attributes and subject age. These served as the basis to construct a model of how brain communication patterns change with age, in such a way that brain function remains healthy.

Research Topic: Aging**Funding Agencies:** UMN**Grant Support:** American Legion Brain Sciences Chair

47. Percutaneous Endoscopic Gastrostomy Tube Placement in Veterans Treated with Concurrent Chemotherapy and Radiation for Head and Neck Cancer

Mariash, Evan^{1,2}; Rector, Thomas¹; Klein, Mark^{1,2}

1. Minneapolis VA Health Care System
2. University of Minnesota

Abstract: Background: Percutaneous endoscopic gastrostomy (PEG) tubes are used to provide head and neck cancer patients nutrition; however, there is no consensus as to the most appropriate time to place a PEG tube. Hypothesis: Patients who receive PEG tubes prophylactically will have less weight loss and nutritional compromise compared to patients with reactively placed PEG tubes or no PEG tubes. Results and Discussion: Patients were retrospectively identified and stratified into 3 groups: those who did not receive a PEG tube, those who received a PEG tube prophylactically, and those that received a PEG tube in a reactive manner. The mean decline in weight for patients at 6 weeks was 24.4 pounds in patients not receiving a PEG tube, 15.0 pounds in patients receiving a prophylactic PEG tube, and 20.6 pounds in patients receiving a PEG tube reactively (p=0.03). Albumin levels did not differ between groups. A prospective study of PEG tube placement is needed to evaluate this common practice.

Research Topic: Cancer

Funding Agencies: None

Grant Support: Minneapolis VA Health Care System Support

48. Molecular Characterization of Environmental Escherichia coli Isolates from Public Restrooms in the Minneapolis-St. Paul Area

Mohamed, Muhanad^{1,2}; Owens, Kris^{2,3}; Gajewski, Abby^{2,3}; Clabots, Connie²; Thuras, Paul²; Kuskowski, Michael²; Johnston, Brian²; Johnson, James^{1,2}

1. University of Minnesota
2. Veterans Affairs Medical Center
3. Ecolab
4. Hologic

Abstract: We previously reported our recovery of 26 E. coli isolates from 1120 samples, from 56 public restrooms (PR) in the Mpls-St. Paul area. Here, PCR, DNA sequencing, and pulsed-field gel electrophoresis (PFGE) were used to further characterize these isolates as to major E. coli phylogenetic group, virulence gene (VG) profile, ExPEC status, sequence type (ST), and pulsotype. Overall, the 26 E. coli isolates were from phylogenetic group, B2 (27%), D (27%), A (23%), and B1 (23%). 8 isolates (35%) qualified as ExPEC. Compared with the 17 non-ExPEC isolates, the 9 ExPEC isolates were more commonly from group B2 (56%, vs. 12%), had higher VG scores (median, 10 vs. 2). Two isolates represented the classic ExPEC lineages ST95 and ST69. The ST95 strain's PFGE profile matched those of multiple ST95 clinical isolates in a large private database. PRs are contaminated with ExPEC, some of which exhibit extensive VG profiles, represent human-associated STs, and closely resemble known human pathogens.

Research Topic: Infectious Diseases

Funding Agencies: CSR&D; MVMREF

Grant Support: VA CSR&D Grants I01 CX000192-01 and I01 CX000920-01

49. Transcranial Current Stimulation for the Treatment of Medication Refractory Auditory Hallucinations

Nelson, Brent¹; Jasberg, Suzanne¹; Gentz, Carolyn²; Gierke, Molly²; Otopalik, Ben¹; Gilmore, Casey²; Camchong, Jazmin¹; Cullen, Kathryn¹; Schulz, S. Charles¹; Lim, Kelvin^{1,2,3}

1. University of Minnesota
2. Defense and Veterans Brain Injury Center
3. Minneapolis VA Health Care System

Abstract: Auditory hallucinations in schizophrenia are medication refractory in 30% of patients. Transcranial current stimulation is promising and involves applying weak electrical current to the scalp. This study includes two arms (tDCS and sham; DLPFC and temporal parietal junction). Two treatment sessions/day for 5 days. Assessments include Positive and Negative Symptoms (PANSS) and Auditory Hallucination Rating (AHRs) scales at 1, 3, 6, 9, and 12 months. During a piloting phase, 3 subjects completed through 6 months. Subject 1: AHRs inc in frequency and salience, dec in length and loudness and PANSS total dec of 2. Subject 2: AHRs dec in all domains and PANSS total dec of 26. Subject 3: AHRs inc in distress but dec in salience, frequency, and loudness and PANSS total dec of 2. Our data suggests subjects respond differently, possibly due to hallucination type. Loudness decreased in all subjects, thus specific sub symptoms may be identified.

Research Topic: Mental Illness

Funding Agencies: MVMREF

Grant Support: Minnesota Veterans Medical Research and Education Foundation and NARSAD Young Investigator Grant.

50. Repeated tDCS Administration as an Adjunct to Working Memory Training: Preliminary Findings from a Randomized, Single-blind Control Trial

Nienow, Tasha^{1,2}; MacDonald, Angus^{1,3}; Dahl, Carly¹; Wang, Yuanyuan¹; Landrum, Christina¹; Marggraf, Matthew¹; Yang, Kalia¹; Lupo, Joe¹; Lim, Kelvin^{1,2}

1. Minneapolis VA Health Care System
2. University of Minnesota, Psychiatry
3. University of Minnesota, Psychology

Abstract: The aim of this proof of principle study was to examine whether cognitive training was more efficacious when combined with tDCS. To explore this hypothesis, working memory training was offered to a sample of 15 outpatients with schizophrenia who were randomized to receive it with either tDCS or sham stimulation. Working memory training consisted of 48 1-hour sessions in which participants completed adaptive, computer-based tasks that targeted working memory processes. Beginning in the third week of the protocol, working memory training was augmented with 20 minutes of stimulation (1 mA tDCS/sham) twice a week. Participants received a total of 28 sessions of working memory training combined with tDCS or sham stimulation. Efficacy of the intervention was assessed with performance on trained (N-back) and untrained working memory tasks. Results of this study suggest that pairing tDCS with working memory training produces a more effective learning experience.

Research Topic: Mental Illness

Funding Agencies: RR&D

Grant Support: VA Rehabilitation Merit Grant D6981R

51. Brain-derived neurotrophic factor (BDNF) attenuates high fat diet-induced apoptosis of hypothalamus

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1. Department of Food Science and Nutrition, University of Minnesota
2. Minneapolis VA Health Care System
3. Department of Medicine, University of Minnesota

Abstract: Background: High fat diet (HFD) contributes to obesity and apoptosis of hypothalamus (Hyp), and BDNF may antagonize the HFD-induced disorders. Methods: Male rats were given HFD or control diet (CD), and cannulated in Hyp. HFD rats were sub-grouped and injected (every other d for 20d) with aCSF (HF-C), BDNF (HF-B), or aCSF pair-fed isocaloric to HF-B rats (HF-PF). CD rats were given aCSF (CD-C). Behavioral and cellular response was evaluated. Results: HF-C rats had increased adiposity vs. CD-C ($P<.05$). HF-B rats reduced energy intake (vs. HF-C; $P<.05$), and body weight, fat mass and visceral fat (vs. HF-C & HF-PF; $P<.05$). In neuronal change, HF-C rats had increased caspase-3+ POMC cells and neurons, and Fluoro-Jade B (FJB)+ POMC cells ($P<.05$) vs. CD-C; but HF-B rats had reduced Hyp caspase-3 and FJB staining ($P<.05$) vs. HF-C and HF-PF. BDNF also increased new cell growth in Hyp. Conclusion: BDNF reduces HFD-induced obesity and Hyp apoptosis, which is independent of reduced energy intake.

Research Topic: Other Chronic Diseases

Funding Agencies: NIH

Grant Support: R01DK080782

52. Liver Injury and NAFLD in Patients with Spondyloarthropathy after Initiation of TNF- α Inhibitors: A Case Series

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1. University of Minnesota Internal Medicine
2. Minneapolis VA Health Care System

Abstract: Biologic therapy has been increasingly used to inhibit tumor necrosis factor-alpha (TNF- α) in patients with spondyloarthritis. While TNF- α inhibitors have been associated with liver toxicity in patients with TNF- α inhibitor treated spondyloarthritis, the development of nonalcoholic fatty liver disease (NAFLD) after TNF- α inhibition is just being described. Herein, we report a case series of 6 patients with spondyloarthritis who developed elevated LFTs and NAFLD after initiating TNF- α inhibitors. The mean BMI change was 4.8 kg/m², mean max normalized ALT was 3.13x ULN, mean time to max ALT was 2.99 yrs. Liver injury and the increasing incidence of NAFLD are important clinically and have potential serious complications ranging from cirrhosis to hepatocellular carcinoma. With increasing use of TNF- α inhibitors in spondyloarthritis, it is important to recognize that NAFLD may be an unintended consequence of these therapies and may impact future choice of therapeutic modalities.

Research Topic: Autoimmune, Allergic & Hematopoietic Disorders

Funding Agencies: UMN

Grant Support: None

53. Spontaneous physical activity (SPA) following optogenetic manipulation of lateral hypothalamic orexin neurons is dependent on the circadian cycle

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2. Department of Food Science and Nutrition, University of Minnesota, St. Paul, MN
3. Minneapolis VA Health Care System, Minneapolis, MN, USA
4. Center for Integrative Medicine and Innovative Science, Universidad Andres Bello, Santiago, Chile

Abstract: The neuropeptide orexin-A (OXA) has been shown to mediate behaviors including energy homeostasis, arousal, reward, feeding, and spontaneous physical activity (SPA). The following studies examined the effects of optogenetic manipulation of OXA neurons and the role the circadian cycle has on this activity. Results indicate that optogenetic activation of the OXA neurons significantly increased SPA in mice expressing ChR2 only within the dark phase of the circadian cycle. Additionally, optogenetic inhibition of orexin neurons reduced SPA in mice expressing eNpHR3.0 within the early phase of the dark cycle. These data suggest that selective activation/inhibition of lateral hypothalamic OXA neurons can be sufficient to affect SPA, but is dependent on the circadian cycle.

Research Topic: Other Chronic Diseases

Funding Agencies: NIH

Grant Support: NIH/NIDDK NORC Grant Number P30 DK050456

54. Readiness and Resilience in National Guard Soldiers (RINGS-CAM): Longitudinal Mixed Method Study of Chronic Pain, PTSD & CAM in OEF/OIF Veterans

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1. Center for Chronic Disease Outcomes Research, Minneapolis VA Health Care System
2. University of Minnesota
3. Minneapolis VA Health Care System

Abstract: This study will identify factors that contribute to the development of chronic pain and utilization of pain management strategies among OEF/OIF Veterans as well as their preferences and attitudes towards pain management approaches. We will collect self-report data utilizing an existing sample of 3,458 National Guard Soldiers enrolled in an ongoing prospective, longitudinal study (the RINGS study). Surveys will assess participants' experiences with chronic pain, pain and health-related beliefs, mental health symptoms, substance abuse, quality of life, exposure to deployment stressors, and pain-related health services utilization. A subsample of Veterans with chronic pain (n=64) will also be invited to complete an in-depth interview about their perspectives on the use of CAM and other non-pharmacological approaches. The study will inform prevention and treatment development efforts to encourage Veterans' use of evidence-based non-pharmacological approaches to pain management.

Research Topic: Other Chronic Diseases

Funding Agencies: NIH

Grant Support: R01AT008387-01 National Center for Complementary and Integrative Health (NCCIH)

55. The Lung Tissue Microbiota of Mild and Moderate Chronic Obstructive Pulmonary Disease

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1. University of Minnesota
2. Minneapolis VA Health Care System

Abstract: The chronic obstructive pulmonary disease lung microbiota contains oral taxa, either due to aspiration or oral contamination of the specimen. Our objective was to determine the COPD lung microbiota without oral contamination. We studied 9 subjects with COPD undergoing lung lobectomy. After lobectomy, the mouth, nose, bronchi, and lung tissue were sampled. 16S rDNA amplicons were sequenced using Illumina MiSeq. Data analysis was performed using QIIME and SourceTracker. Alpha diversity was greater in the oral samples (mean 203 ± SD 50) than in the nasal samples (102 ± 50), bronchial samples (70 ± 89), and lung samples (85 ± 75) (ANOVA p=0.001). Principal coordinate analysis revealed 3 clusters: oral samples, nasal samples, and combined bronchial and lung samples. SourceTracker determined that the lung tissue microbiota sources were 29% (mean) oral microbiota, 18% nasal microbiota, and 53% unknown. Our work suggests that aspiration is a source of the COPD lung microbiota.

Research Topic: Lung Disorders

Funding Agencies: NIH; MVMREF

Grant Support: 5KL2TR113 from the University of Minnesota CTSI (8UL1TR000114) to AAP; 5T32AI055433 to AAP; MN Veterans Medical Research and Education Foundation to CHW.

56. Cognitive Training Changes Thalamocortical Connectivity in Schizophrenia: A Placebo-Controlled Trial

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1. Minneapolis VA Health Care System
2. University of Minnesota, Psychology
3. University of Minnesota, Psychiatry

Abstract: Thalamic projections to the prefrontal cortex are critical for cognition and may be disrupted in schizophrenia. This study examined whether thalamocortical connections were plastic in response to cognitive remediation therapy (CRT) and whether neural change related to cognitive improvement. 26 patients were randomized to a working memory-focused CRT (N=14) or a placebo control condition (N=12). Before and after treatment, patients underwent resting state fMRI and neurocognitive testing. Analyses examined intrinsic functional connections between the thalamus and the anterior cingulate cortex (ACC) and middle frontal gyrus (MFG). Change in connectivity was related to change in performance on the MATRICS Battery (MCCB). Connectivity changes were observed in the right MFG and ACC for the CRT but not the placebo group. Increases in connectivity in the right MFG correlated with improvements on the MCCB. Last, baseline MCCB inversely related to connectivity in the right MFG and ACC.

Research Topic: Mental Illness

Funding Agencies: RR&D; MVMREF

Grant Support: MVMREF, VA RR&D Merit Grant (D6981R), Institutional Center Cores for Advanced Neuroimaging Grant #1P30 NS076408 NIMH F31 National Research Service Award Grant #1F31MH106080-01 (Ramsay)

57. Comparative Effectiveness Research In Veterans With PTSD

Scheel, Allison¹; Curry, Kyle¹; Wright, Jillian¹; Schnurr, Paula²; Chard, Kathleen³; Ruzek, Josef⁴

1. Minneapolis VA Health Care System
2. White River Junction VA Medical Center
3. Cincinnati VA Medical Center
4. VA Palo Alto Health Care System

Abstract: Comparative Effectiveness Research in Veterans with PTSD (CERV-PTSD) is designed to compare efficacy of prolonged exposure (PE) and cognitive processing therapy (CPT). CERV-PTSD is the first direct comparison of these treatments. Seventeen VA hospitals will aim to randomize 900 Veterans. A screening process will determine eligibility. Once eligible, participants will be randomized to PE or CPT. Research visits will occur during and after treatment. Compensation for research visits is given. Recruitment has begun at the Minneapolis VA Health Care System. Eligible participants must have PTSD due to a military event, receive PTSD treatment in the study alone, and be on a stable regimen of medications for at least 2 months. Exclusionary conditions apply. Referrals are being accepted. Interested providers or Veterans can contact Jillian Wright Site Coordinator at 612-467-2184 for more information.

Research Topic: Mental Illness

Funding Agencies: HSR&D

Grant Support: Cooperative Studies Program

58. Proactive Smoking Cessation Treatment For Minnesota Priority Populations: "OPT-IN"

Fu, Steve¹; van Ryn, Michelle²; Burgess, Diana¹; Thomas, Janet¹; Nelson, David¹; Clothier, Barbara¹; Saul, Jessie³; Nyman, John⁴; McAlpine, Donna⁴; Joseph, Anne⁵

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2. Mayo Clinic, Division of Health Care Policy & Research
3. North American Quitline Consortium
4. University of Minnesota School of Public Health, Division of Health Policy and Management
5. University of Minnesota Medical School, Department of Medicine

Abstract: Background: Smoking prevalence and tobacco-related disease burden are high in low-income populations. Low-income smokers are less likely to use evidenced-based cessation treatments. Methods: A randomized controlled trial examined the effects of a proactive intervention on abstinence and treatment use in low-income smokers. We randomized 2406 smokers enrolled in Minnesota Health Care Programs (MHCP) to proactive outreach or usual care. The intervention contacted smokers and provided free NRT and telephone counseling. One year post-randomization data were collected for all randomized individuals. The primary outcome was six-month prolonged abstinence at one year. Secondary outcomes were short-term abstinence and treatment use. Results: In proactive outreach, 24% engaged in telephone counseling. The prolonged abstinence rate was 16.5% in outreach and 12.1% in usual care (aOR=1.47, p=.006). Conclusions: Results suggest dissemination of proactive treatment approaches for low-income smokers.

Research Topic: Access & Disparities in Care

Funding Agencies: HSR&D; NIH

Grant Support: National Cancer Institute (1R01CA141527-01), National Institutes of Health.

59. Telemedicine for Postoperative Visits at the Minneapolis VA Health Care SystemStypulkowski, Katie¹; Uppaluri, Sarika²; Waisbren, Steven^{1,3}

1. Minneapolis VA Health Care System
2. Case Western Reserve University
3. University of Minnesota

Abstract: Purpose: Examine potential benefits of telemedicine (electronic communication technologies to provide health care) for remote postoperative visits at MVAMC. Methods: Survey of 346 veterans. Results: Half of the patients preferred face-to-face follow-up while the other half preferred telemedicine. The mean + SD distance to the MVAMC was 118 + 119.1 miles with 2.8 + 1.9 hours of travel time. Patients reported use of 18 different community based outpatient clinics (CBOC) with a mean distance of 51 + 47.23 miles and 1.4 + 0.76 hours of travel time to these clinics. Travel costs to Minneapolis were \$64.62 + 66.11 with travel costs to the CBOC \$27.88 + 26.07. About 20% of patients needed assistance in reaching the VA and 28% used a VA-supplied van. Conclusion: These results suggest a demand for remote postop visits using telemedicine and that such visits would have substantial cost, time, and convenience benefits for patients that have to travel long distances.

Research Topic: Access & Disparities in Care

Funding Agencies: None

Grant Support: None

60. Targeting CK2 in MelanomaTrembley, Janeen^{1,2}; Dodd, Erin²; Abedin, Md^{1,2}; Ahmed, Khalil^{1,2}; Ahmed-Saucedo, Rehana²

1. Minneapolis VA Health Care System
2. University of Minnesota

Abstract: Metastatic melanoma is an aggressive form of skin cancer which is resistant to current therapies. Long-term survival remains poor. CK2 is a constitutively active kinase that protects cells from cell death. We evaluated the potential for targeting CK2 in melanoma. CK2 α protein expression was detected in normal skin and in melanoma. We examined the effects on cell viability following loss of CK2 activity. Cells demonstrated decreased viability post-treatment with a CK2 inhibitor. Whole cell lysates were processed 24 and 48 h after treatment, and immunoblot analysis was used to examine key cell signaling proteins. Cells demonstrated decreased levels of pro-proliferative regulators, including NF κ B p65 p-S529, AKT p-S129 and cyclin D1. Furthermore, detection of cleaved caspase-3 and lamin A/C proteins indicated activation of apoptosis. Reduction of CK2 protein expression by siRNA transfection also reduced cell viability and induced death. These findings support targeting of CK2 in melanoma.

Research Topic: Cancer

Funding Agencies: BLR&D; UMN

Grant Support: Women's Dermatologic Society Academic Research Award (Ahmed-Saucedo); Merit Award 11O1B001731 (Ahmed); R01 CA150182 NCI, NIH, Department of Health and Human Services (Ahmed)

61. Accuracy of ICD-9 Codes for Clinically Significant Acute Heart Failure Hospitalizations

Turner, Matthew¹; Huang, Hans¹; Lederle, Frank²

1. University of Minnesota
2. Minneapolis VA Health Care System

Abstract: Hospitalization for acute decompensated heart failure (ADHF) is a commonly measured outcome in clinical trials but is challenging to accurately identify. This study aimed to assess the accuracy of principal ICD-9 discharge codes in identifying hospitalizations for ADHF and to construct a final strategy that would accurately identify these hospitalizations. A total of 1,467 hospitalizations from 2009 to 2014 at the Minneapolis VA Health Care System were abstracted for adjudication. Of these, 446 were adjudicated. Using electronic medical records, two independent reviewers (MT, HH) classified each case as probably ADHF, probably not ADHF, or cannot be determined. Agreement between the reviewers was considered to represent a true outcome (i.e. true positive or true negative). ADHF hospitalizations were most accurately defined by the following strategy: 402.91 + 404.x + 428.x. This strategy resulted in a sensitivity of 97.7% and PPV of 90.9%.

Research Topic: Heart Disease

Funding Agencies: UMN

Grant Support: None

62. Brain oscillations synchrony is modulated during movement planning

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2. Department of Neuroscience, University of Minnesota,
2. College of Biological Sciences, University of Minnesota

Abstract: Understanding brain processing during the preparation of a motor response can help the development of brain-machine interfaces for controlling artificial limbs. To this effect, we investigated the synchrony of brain oscillations during the preparation of a response with varying degrees of uncertainty about the location of the upcoming target. Ten healthy volunteers performed this task while brain activity was recorded with a 248 channel MEG scanner. A measure of synchrony of brain oscillations, the Phase Lock Index (PLI), was computed for 2 frequency bands (alpha, beta) using seed voxels in the motor cortex. The results show that brain oscillations synchrony was reduced during motor planning and that the reduction was modulated by the degree of uncertainty regarding the upcoming target to reach. These results provide new insights regarding the dynamics of neural processes during motor planning.

Research Topic: Central Nervous System Injuries & Associated Disorders

Funding Agencies: CSR&D; UMN; MVMREF

Grant Support: Brain Mechanisms of Cognitive-Motor Processes (CSR&D), Undergraduate Research Scholarship (University of Minnesota), Evaluation of ECoG for Decoding Reaching and Grasping Movements (MVMREF)

63. VA Augmentation and Switching Treatments for Improving Depression Outcomes Study (VAST-D)

Westermeyer, Joseph¹; Dickmann, Patty¹; Warwick, Marion¹

1. Minneapolis VA Health Care System

Abstract: Purpose: The goal is to learn more about treatment resistant depression. Approximately 14% of Veterans are diagnosed with depression, and that is considered to be an under-diagnosed figure. VAST-D is a study aiming to improve treatment for Veterans whose depressive symptoms are not improving even though they are taking an Anti-depressant medication. The VAST-D study aims to improve prognosis for those who are in need of a next step in treatment. Methods: Participation involves: 1. Meeting with study staff regularly over the course of 3 months (and potentially up to 9 months). 2. Adherence to medication regiment that follows study protocol. 3. Willingness to have vital signs taken every visit, as well as scheduled blood draws to monitor bloodwork. 4. Completing different questionnaires asking about psychiatric symptoms, medications, general well-being, and quality of life.

Research Topic: Mental Illness

Funding Agencies: HSR&D

Grant Support: Office of Research and Development

64. Minneapolis VA High Value Care (HiVAC) Initiative

Wilt, Timothy^{1,2}; Partin, Melissa¹; Koeller, Eva¹; Velasquez, Tina¹; Greer, Nancy¹; Lillie, Sarah¹; Danan, Elisheva¹; Taylor, Brent¹

1. Minneapolis VA Health Care System

2. University of Minnesota

Abstract: High value care is healthcare that justifies its benefits, harms and costs. The HiVAC initiative's goal is to bring together an interdisciplinary team to improve the implementation of healthcare by defining, discovering and delivering high value care and reducing low value care. Results: Our VA Evidence Synthesis Program identified the harms and lack of evidence for benefit of routine screening pelvic exams in asymptomatic women, leading the American College of Physicians to recommend against this practice. We defined a "Value Framework" to deliver high value cancer screening, according to intensity, and developed best practice advice for high value screening. Members also created shared decision-making tools to improve prostate cancer screening decisions. Conclusion: The Minneapolis VA HiVAC initiative is engaged in research, education and policy to help Veterans and their clinicians choose wisely about health care options and increase the delivery of high value healthcare.

Research Topic: (Not Provided)

Funding Agencies: HSR&D

Grant Support: Department of Veterans Affairs, Veterans Health Administration, Office of Research and Development, Quality Enhancement Research Initiative (QUERI) and the Under Secretary of Health Award for Health Services Research.

65. Orexin neuron stimulation in mice protects against high fat diet-induced weight gain.

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1. University of Minnesota Graduate Program in Neuroscience
2. Minneapolis VA Health Care System
3. University of Minnesota Department of Medicine
4. University of Minnesota Department of Food Science & Nutrition

Abstract: Spontaneous physical activity (SPA) is a promising therapeutic target for improving multiple clinical outcomes in obesity. Low levels of the neuropeptide, orexin, are correlated with reduced SPA and obesity in humans and animals. We used a pharmacosynthetic approach (Designer Receptors Exclusively Activated by Designer Drugs; DREADDs) to activate orexin neurons in a mouse model of diet-induced-obesity. DREADD-containing viruses were injected into the lateral hypothalamic area of mice expressing the DNA-recombinase, Cre, in orexin neurons. In the presence of Cre, viruses expressed the excitatory, Gq-coupled DREADD. A single systemic dose of the Designer Drug, Clozapine-N-Oxide (CNO; 5mg/kg; IP), activated DREADD-containing orexin neurons and increased SPA three-fold 2hrs post-injection. When fed a high fat diet (HFD), all animals gained weight and adiposity. Five daily injections of CNO (once per day) induced weight loss such that body weights on day 5 had returned to pre-HFD levels.

Research Topic: Other Chronic Diseases

Funding Agencies: RR&D; NIH; UMN

Grant Support: MN Obesity Center P30 DK50456; Veterans Affairs RR&D 1I01RX000441; NIH T32 GM008471; NIDA T32 DA07234; NIDDK DK100281; and the 3M Graduate Fellowship.