–Minneapolis VA Health Care System–

VA Research Day 2017

Program and Abstract List

(alphabetically, by author)

May 3, 2017

VA

U.S. Department of Veterans Affairs

Veterans Health Administration

Office of Research and Development

☆Program☆

1. Oral Presentations – 1st Floor Auditorium (12:30 - 1:30 pm)

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

☆**2017 Zieve Award Presentation** .....James Johnson, MD

Recipient:
Theresa Fox, MD
"Predictive characteristics of methicillin-resistant* Staphylococcus aureus *(MRSA) nasal swab for MRSA positive culture in hospitalized Veterans"

☆**Keynote Address**.....Erin Krebs, MD, MPH
Women's Health Medical Director, Minneapolis VAHCS

"Research to Improve Chronic Pain Care"

☆ *The Minnesota Veterans Medical Research and Education Foundation will be providing Free Box Lunches to the first 200 attendees.*

2. Poster and Exposition Session – 2nd Floor Flag Atrium (1:30 – 3:30 PM)

☆ *Research Findings and Innovations from the Minneapolis VA Health Care System*

☆ *Popcorn provided by the Minneapolis VA Research Office*

Author Index *(first author only)*

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

Adabag, Selcuk [1-2]; Buelt-Gebhardt, Melissa [1]; Tholakanahalli, Venkat [1-2]; Florea, Viorel [1-2]; Singh, Steven [3]

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

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 ability to reduce all-cause mortality in those with advanced age is unclear. ICD therapy is considered to be an under-utilized treatment option despite widely recognized safety and efficacy. Age bias is a particularly prominent theory in the effort to explain under-utilization of ICD. In major clinical trials of patients receiving ICDs over the past 15 to 20 years, the mean and median age of study populations range from 50 to 65 years of age. The proportion of potentially eligible VA patients implanted with an ICD peaks at approximately 67 years of age and declines continuously thereafter. No randomized clinical trials have focused solely on an older population. The overall aim of CSP #592 is to study the safety and efficacy of ICD implantation as a primary prevention strategy of Sudden Cardiac Death (SCD) in patients 70 years of age and older. In particular, this study is designed to compare the effectiveness of ICD, in addition to Optimal Medical Therapy (OMT), on all-cause mortality versus OMT alone. OMT includes standard intervention for chronic heart failure patients, such as disease management with neurohormonal blockade, adoption of healthy diet, and exercise. One particularly important secondary objective is to assess treatment efficacy under the conditions of high versus low co-morbidity burden. In the study, participants are 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). Follow-up will occur every 6 months until study close. 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; MVMREF
Grant support: Cooperative Studies Program

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

Amundson, Carla [1]; Drekonja, Dimitri [1-2]

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

Abstract: Background: Current guidelines suggest that men should be treated with 7 to 14 days of antibiotics for a urinary tract infection (UTI). This is based on prior research demonstrating that 3 days of antibiotics did not work as well as 14 days, but that 14 days worked as well as 28 days. In the VA, 9 out of 10 men are treated with the recommended 7 to 14 days of antibiotics. A recent study suggested that those receiving more than 7 days of treatment did no better than those receiving less than 7 days of treatment, but did have a higher risk of complications related to antibiotics. Specifically, those getting longer treatment had a recurrence of their UTI at the same rate as those getting shorter, and also had an increase in Clostridium difficile infection. Methods: This study is for men that have a UTI and are prescribed at least 7 but not more than 14 days of either ciprofloxacin or trimethoprim/sulfamethoxazole. Patients are randomly assigned to either 7 or 14 days of antimicrobial treatment, and followed for 1 month to determine if the UTI symptoms resolve and no not recur. The entire study can be completed via telephone and overnight mail, minimizing inconvenience and demands on patient time. There is also a sub-study exploring bacterial resistance to antibiotics. This study is being conducted to investigate the potential harms of antibiotic use. One of the potential harms is that some of the bacteria normally carried in the colon become resistant to antibiotics. These bacteria form the normal colonic microbiota and serve many useful purposes, but they can also be a source of future infections. Colonic carriage of antibiotic-resistant bacteria makes it more likely that any future infection is more difficult to treat. We are interested in studying whether longer-duration antibiotic treatment leads to increased carriage of resistant bacteria. To study this, we are conducting a voluntary sub-study that involves taking 2 stool or rectal samples, during and after treatment, and sending them to a lab here at the Minneapolis VA Medical Center. Conclusion: This study, conducted entirely at the Minneapolis VA Medical Center, will help to ensure that Veterans receive the optimal treatment for this common condition, and help to define the potential harms of antibiotics. As of 4/5/2017, 118 patients have enrolled, with 97 opting to participate in the sub-study on antimicrobial resistance. We look forward to presenting our results at a future Research Day.

Research Topic: Infectious Diseases
Funding agencies: CSR&D
Grant support: VA Merit Review; 1I01CX000830-01A2

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3. Allergenic Ingredients in Facial Wet Wipes

Aschenbeck, Kelly [1-3]; Warshaw, Erin [1,3]

1. University of Minnesota Medical School
2. Minneapolis VA Health Care System
3. Hennepin County Medical Center Parkside Occupational and Contact Dermatitis Clinic

Abstract: Background: Facial dermatitis is one of the most common locations of allergic contact dermatitis (ACD). Facial cleansing wipes may be an under-recognized source of allergens. Objective: To determine the frequency of potentially allergenic ingredients in facial wet wipes. Methods: Ingredient lists from name brand and generic facial wipes from four large retailers were recorded. Results: In the 178 facial wipes examined, a total of 485 ingredients were identified, with an average of 16.7 ingredients per facial wipe. Excluding botanicals, the most common potentially allergenic ingredients were glycerin (64.0%), fragrance (63.5%), phenoxyethanol (53.9%), citric acid (51.1%), disodium EDTA (44.4%), sorbic acid derivatives (38.8%), tocopherol derivatives (38.8%), polyethylene glycol derivatives (32.6%), glyceryl stearate (31.5%), sodium citrate (29.8%), glucosides (27.5%), cetearyl alcohol (25.8%), and propylene glycol (25.3%). Of note, methylisothiazolinone (2.2%) and methylchloroisothiazolinone (1.1%) were uncommon. The top 12 potential allergens of botanical origin were Aloe barbadensis (41.0%), chamomile extracts (27.0%), tea extracts (21.3%), Cucumis sativus (20.2%), and Hamamelis virginiana (10.7%). Conclusions: Many potential allergens are present in facial wipes including fragrances, preservatives, glucosides and propylene glycol.

Research Topic: None indicated
Funding agencies: N/A
Grant support: N/A

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4. Allergenic Ingredients in Hand Wet Wipes

Aschenbeck, Kelly [1-3]; Warshaw, Erin [1,3]

1. University of Minnesota Medical School
2. Minneapolis VA Health Care System
3. Hennepin County Medical Center Parkside Occupational and Contact Dermatitis Clinic

Abstract: Background: Hand dermatitis is a common location for allergic contact dermatitis (ACD). Wet wipes may be an important allergen source. Objective: To evaluate potential allergenic ingredients in hand wipes. Methods: Ingredient lists from name brand and generic hand wipes from 4 large retailers were recorded to create a database of hand wipe ingredients. Results: In the 34 hand wipes evaluated, a total of 87 ingredients were identified, with an average of 9 ingredients per hand wipe. The most common potentially allergenic ingredients were Aloe barbadensis (85.3%), tocopherol derivatives (61.8%), citric acid (55.9%), fragrance (55.9%), alcohol (52.9%), benzalkonium chloride (52.9%), glycerin (47.1%), disodium EDTA (41.2%), phenoxyethanol (35.3%), sorbic acid derivatives (35.3%), disodium cocoamphodiacetate (29.4%), parabens (23.5%), propylene glycol (20.6%), methylchloroisothiazolinone (17.6%), methylisothiazolinone (17.6%), chamomile extracts (14.7%), glucosides (11.8%), and lavender extracts (11.8%). Conclusions: Many potential allergens are present in hand wipes, especially fragrance and preservatives.

Research Topic: None indicated
Funding agencies: N/A
Grant support: N/A

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5. Allergenic Ingredients in Personal Hygiene Wet Wipes

Aschenbeck, Kelly [1-3]; Warshaw, Erin [1,3]

1. University of Minnesota Medical School
2. Minneapolis VA Health Care System
3. Hennepin County Medical Center Parkside Occupational and Contact Dermatitis Clinic

Abstract: Background: Personal hygiene wipes are a significant allergen source for anogenital allergic contact dermatitis (ACD). Objective: To determine the frequency of potentially allergenic ingredients in personal hygiene wipes. Methods: Ingredient lists from name brand and generic personal hygiene wipes from four large retailers were recorded. Results: In the 54 personal hygiene wipes evaluated, a total of 132 ingredients were identified, with an average of 12 ingredients per personal hygiene wipe. The most common potentially allergenic ingredients were Aloe barbadensis (77.8%), citric acid (77.8%), fragrance (72.2%), sorbic acid derivatives (63.0%), tocopherol derivatives (63.0%), glycerin (59.3%), phenoxyethanol (55.6%), disodium cocoamphodiacetate (53.7%), disodium EDTA (42.6%), propylene glycol (42.6%), iodopropynyl butylcarbamate (40.7%), chamomile extracts (38.9%), sodium benzoate (35.2%), bronopol (22.2%), sodium citrate (22.2%), lanolin derivatives (20.4%), parabens (20.4%), polyethylene glycol derivatives (18.5%), disodium phosphate (16.7%), DMDM hydantoin

(14.8%), and cocamidopropyl PG-dimonium chloride phosphate (11.1%). Conclusions: Many potential allergens are present in personal hygiene wipes, especially fragrance and preservatives.

Research Topic: None indicated
Funding agencies: N/A
Grant support: N/A

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6. Piercings and Metal Sensitivity: Extended Analysis of the North American Contact Dermatitis Group Data, 2007-2014

Aschenbeck, Kelly [1-3]; Warshaw, Erin [1,3]; NACDG Members [4]

1. University of Minnesota Medical School
2. Minneapolis VA Health Care System
3. Hennepin County Medical Center Parkside Occupational and Contact Dermatitis Clinic
4. North American Contact Dermatitis Group

Abstract: Background: Body piercing is a cultural and aesthetic practice that provides a unique route of metal exposure. Nickel, a notorious metal in the field of contact dermatitis, is one of the most common contact allergens associated with piercing jewelry. Objective: To update previous analyses using NACDG data comparing demographics and positive reaction rates to metals (nickel, cobalt, chromate) by pierced status and number of piercings. Methods: Retrospective cross-sectional analysis of 17,912 patients patch tested by the North American Contact Dermatitis Group from 2007-2014, for which piercing data was available. Results: The pierced population was significantly more likely ($p < 0.003$, Bonferroni correction) to be female, > 18 years old and atopic. Nickel allergy (defined by positive patch test reaction to nickel) was statistically associated with = 1 piercings ($p < 0.0001$, RR 2.54). The reaction rate for nickel also increased with the number of piercings (14.3% with 1 piercing to 34.0% with = 5 piercings). Chromium allergy was negatively correlated with piercings ($p < 0.0001$, RR 0.56) and cobalt allergy was not associated with pierced status once stratified analysis was applied. Further analysis of nickel allergy revealed that both males and females were more likely to have nickel allergy if pierced ($p < 0.0001$, both), though the association was stronger for males (RR 2.21) than females (RR 1.47). Males with piercings ages 30-39 years and 40-49 years were significantly more likely to have nickel allergy ($p = 0.002$, RR 2.01; $p = 0.002$, RR 2.30, respectively). No significant associations were found for other age groups by gender. Conclusions: Individuals with at least 1 piercing were significantly more likely to have a positive patch test reaction to nickel, but not other metals. The number of piercings positively correlated with the nickel reaction rate. Nickel allergy was significantly more common among pierced males and females, but this association was stronger in males.

Research Topic: None indicated
Funding agencies: N/A
Grant support: N/A

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7. Wet Wipe Allergens: Retrospective Cross-sectional Analysis of North American Contact Dermatitis Group (NACDG) Data 2011-2014

Aschenbeck, Kelly [1-3]; Warshaw, Erin [1,3]; NACDG Members [4]

1. University of Minnesota Medical School
2. Minneapolis VA Health Care System
3. Hennepin County Medical Center Parkside Occupational and Contact Dermatitis Clinic
4. North American Contact Dermatitis Group

Abstract: Background: Wet wipes are a relatively new source of allergic contact dermatitis (ACD). Objective: To determine the prevalence of wet wipes as a source of ACD and identify associated allergens. Methods: Retrospective cross-sectional analysis of data collected from 2011-2014 by the NACDG. Results: Of the 9,037 patients patch tested during the study period, 79 (0.9%) had a positive patch test reaction to an allergen associated with a wet wipe source. Most were adults (96.2%). There were no statistically significant differences in age, gender, atopic markers, or race between individuals with a wet wipe source of allergens and those without. Anogenital dermatitis was 15 times more likely (RR 15.3, CI 9.79-23.93, $P < 0.0001$) in those with wet wipe allergy. The most common category of associated allergens was preservatives: methylisothiazolinone (59.0%), methylchloroisothiazolinone/methylisothiazolinone (35.6%), bronopol (27.4%) and iodopropynyl butylcarbamate (12.3%). Fragrance materials were the second most common category (12.3%). Over 92% of patients with wipe-associated ACD were detected by the NACDG screening series. Conclusions: Wet wipes are an important source of ACD. Preservatives, especially isothiazolinones, and fragrance are the most commonly associated allergens.

Research Topic: None indicated
Funding agencies: N/A
Grant support: N/A

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8. Blood Biomarkers of Chronic Inflammation in Gulf War Illness

Bach, Ronald [1-2]; Johnson, Gerhard [1-2]; Slater, Billie [1]; Leis, Linda [1]; Rector, Thomas [1-2]

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

Abstract: Background: Many U.S military personnel who served in the 1990-91 Gulf War suffer from an unexplained chronic multi-system disorder known as Gulf War Illness (GWI). GWI symptoms include chronic fatigue, musculoskeletal pain, memory problems, depression, insomnia, gastrointestinal disorders, and skin rashes. Goals: Translational research going from bench to bedside in 3 steps: 1) DISCOVER blood biomarkers of GWI using proteomics and cellomics; 2) IDENTIFY a therapeutic target from the blood biomarker fingerprint; 3) TEST an evidence-based intervention in a clinical trial. Methods: Surveillance study of 85 Gulf War Veterans. 57 GWI+ and 28 GWI- subjects by CDC 10 criteria (Fukuda case definition). Peripheral blood counts and immunoassays of 61 plasma proteins. Statistical analyses: Mann-Whitney rank sum test to compare biomarker distributions and stepwise logistic regression to formulate a diagnostic model. Results: Lymphocytes, monocytes, neutrophils, and platelets elevated in GWI+ subjects. Four plasma proteins higher (C-reactive protein, leptin, brain-derived neurotropic factor, matrix metalloproteinase-9) and two lower (metalloproteinase-2 and fatty acid binding protein 3) in GWI+ subjects. A diagnostic model of three biomarkers—lymphocytes, monocytes, and C-reactive protein had a predicted probability of 90% (CI 76-90%) for diagnosing GWI when the probability of having GWI was above 70%. Conclusions: Quantification of inflammation-related plasma proteins and cellular enumeration provide objective criteria for the diagnosis of GWI. GWI biomarker fingerprint (all 11 elements) points to chronic inflammation as the underlying cause of GWI symptoms and an evidence-based therapeutic target. Conducting a clinical trial (Gulf War Illness Inflammation Reduction Trial, ClinicalTrials.gov #NCT02506192) to determine if reducing inflammation with delayed-release prednisone is an effective treatment for GWI. Key Words: Gulf War Illness, Biomarkers, Chronic Inflammation

Research Topic: Gulf War Veterans Illness
Funding agencies: DOD
Grant support: Department of Defense, Congressionally Directed Medical Research Program, GWI Research Program Awards GW080080 and GW130025

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9. Automated segmentation to optimize subdural hemorrhage evacuation reveals that posterior drain placement is superior to central positioning

Bin Zahid, Abdullah [1]; Balser, David [1]; Ahmadi, Aliya [2]; Moosa, Zahra [2]; Juma, Sana [2]; Hubbard, Molly [1]; Samadani, Uzma [1]

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

Abstract: Introduction: A subdural hematoma (SDH) is a bleed on the surface of the brain, resulting in significant neurological morbidity and mortality. Veterans are at tenfold higher risk of subdural hematoma than the civilian population. SDH drainage improves neurological outcome and reduces mortality but is associated with the complications and cost of an invasive neurosurgical operation. Twist drill craniostomy (TDC) is a common and minimally invasive procedure used for the drainage of subdural hematoma (SDH). It is unknown if drain placement at the centroid of the hematoma or its thickest portion optimizes drainage. The purpose of this study was to assess the optimal location of drain placement based on post-hoc analysis of CT images. Methods: We analyzed the pre and post procedure scans for 23 male patients (mean age (years) = 75.7 S.D. 10.8) who underwent subdural evacuation using TDC in a VA hospital. Pre and post TDC scans were superimposed using intensity based coregistration. Hematoma volume was calculated on both pre and post scans. The drain location was identified on the post-TDC scan and projected onto the pre-TDC scan. The centroid of the hematoma was identified on the pre-TDC scan. Finally, the distance from the drain location to the centroid and along the anterior-posterior (AP) plane were correlated with residual hematoma volume expressed as a percent of the initial SDH (rSDH%). Results: Pre and post-drain scans in the 23 patients were on average 31 hours apart (range 4 - 144). The initial mean hematoma volume was 112 ml (range: 25 - 194 ml), and the residual hematoma was 70 ml (range: 7 - 132 ml), with 42 ml drained on average (range: -10 to 132). The mean residual hematoma was 66% of the initial hematoma (range: 20-123%). The distance of the TDC site from the 3D centroid of the hematoma did not correlate with rSDH% (linear regression, $R = 0.111$, $p = 0.613$). The anteroposterior distance of the drain from the plane of the glabella inversely correlated with rSDH% (linear regression, $R = 0.570$, $p = 0.005$). Conclusion: In this study, placement of the drain closer to the centroid of the hematoma did not impact the volume of hematoma drained. However, posterior placement of TDC drains was associated with decreased residual hematoma volume. Placing TDC drains closer to the back of the skull may increase the fraction of hematoma drained and improve procedure effectiveness.

Research Topic: Acute & Traumatic Injury
Funding agencies: CSR&D
Grant support: CX000887-01: Cerebral Atrophy, Anticoagulants, and the Risk for Chronic Subdural Hematoma

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10. Differential Responsiveness to Orexin-Mediated Changes in Spontaneous Physical Activity and Memory in Aged Mice

Bunney, Patricia [1-2]; Zink, Anastasia [3]; Billington, Charles [4-6]; Kotz, Catherine [2,5,7]

1. Minnesota Obesity Prevention Training Program, University of Minnesota
2. Geriatric Research Education and Clinical Center, Minneapolis VA Health Care System
3. Medical Devices Center, University of Minnesota
4. Department of Medicine, University of Minnesota
5. Minnesota Obesity Center, University of Minnesota
6. Endocrinology section, Minneapolis VA Health Care System
7. Department of Integrative Biology and Physiology, University of Minnesota Health Care System

Abstract: Aging is associated with increased weight gain, decreased physical activity and energy expenditure, and cognitive decline. Levels of physical activity and cognition are correlated during aging, and it has been shown that reduced cognitive function predicts declines in physical activity, and vice versa. The neuropeptide orexin (hypocretin) is produced by neurons in the lateral hypothalamus (LH4), and drives spontaneous physical activity (SPA). Orexin neurons also project to the hippocampus and mediate long-term potentiation. As individuals age, the number of orexin neurons produced decreases by 23% from infancy to later adulthood. Previous research has shown a strong relationship between reductions in orexin producing neurons and decreases in physical activity, and it is likely that age-related cognitive decline is associated with reduced numbers of orexin neurons. It is unknown to what extent the loss of orexin neurons may be overcome through orexin supplementation to counteract obesity. We hypothesized that activation of the orexin system via Designer Receptors Exclusively Activated by Designer Drugs (DREADDs) would produce reduced increases in SPA and fail to improve memory in aged mice. Ten male and 10 female Orexin-Cre mice (18-months) were injected bilaterally with a Cre-dependent AAV vector containing an excitatory DREADD into the caudal lateral hypothalamus (orexin neuronal field). Following acclimation, injections of 1, 3, or 5mg/kg clozapine n-oxide (CNO) or saline were administered every other day and changes in time spent moving were assessed within 4 h post-injection. Then, animals were trained in the Barnes Maze for four days. Following the final training session, mice were injected with 5 mg/kg CNO, and tested 24 h later. In contrast to our previous studies, which showed that 5 mg/kg CNO increases SPA, there was no significant effect of any CNO dose on SPA in aged mice ($F(3,48)=1.2$; ns), yet this dose enhanced memory in the Barnes Maze ($t(18)=3.0$; $p < 0.01$). These results suggest a divergence in effects of orexin stimulation across the lifespan, with a functional preservation of pathways important to memory processing.

Research Topic: Aging
Funding agencies: NIH
Grant support: This work was supported by the Department of Veterans Affairs (5I01RX000441-04 to CK and CB), the National Institute of Health (5R01DK100281-03 to CK and CB) and the Minnesota Obesity Center (5R01DK100281-03 to CB), and by Award Number T32DK083250 from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK; to CK and PB).

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11. What Causes Racial Disparities in Health Care? A Mixed-Methods Study of Providers Negotiating Uncertainty in Attributing Blame and Responsibility

Burgess, Diana [1-2]; Gollust, Sarah [3]; Cunningham, Brooke [4]; Bokhour, Barbara [5-6]; Gordon, Howard [7-8]; Pope, Charlene [9-10]; Saha, Somnath [11-12]; Jones, Dina [13]; Do, Tam [1]

1. Center for Chronic Disease Outcomes Research (CCDOR), Minneapolis VA Health Care System
2. Department of Medicine, University of Minnesota
3. Division of Health Policy and Management, School of Public Health, University of Minnesota
4. Department of Family Medicine and Community Health, University of Minnesota
5. Center for Health Care Organization and Implementation Research, ENRM VA Medical Center
6. Department of Health Law, Policy & Management, School of Public Health, Boston University
7. Center of Innovation for Complex Chronic Health Care, Jesse Brown VA Medical Center
8. Section of Academic Internal Medicine and Geriatrics, Department of Medicine, University of Illinois at Chicago
9. Health Equity & Research Outreach Innovation Center (HEROIC), Ralph H. Johnson VA Medical Center
10. College of Nursing, Medical University of South Carolina
11. Center to Improve Veteran Involvement in Care (CIVIC), VA Portland Healthcare System
12. Public Health & Preventative Medicine, Medical Informatics & Clinical Epidemiology, Oregon Health & Science University (OHSU)
13. Tobacco Center of Regulatory Science (TCORS), School of Public Health, Georgia State University

Abstract: Purpose: To understand how VHA providers make attributions about causes of racial health care disparities. Methods: Fifty-three providers completed a survey assessing their perceptions of the causes of racial health care disparities and subsequently participated in a semi-structured qualitative interview. We explored how causal attributions differed based on providers' prior categorization (from survey data) as to the extent they believed that provider factors contributed to health care disparities: Low Provider Attribution (LPA) versus High Provider Attribution (HPA). Results: Survey data demonstrate that providers attributed more responsibility for reducing health care disparities to the health care system (mean = 4.5) and providers (4.3) compared to patients (2.9) and that attributions differed based on providers' beliefs about the causes of disparities, with HPA participants attributing greater responsibility to the health care system and providers than to patient factors. In-depth qualitative analysis revealed important distinctions in how providers talked about causal attributions and negotiated uncertainty. In particular, providers classified as HPA demonstrated facility at holding more than one causal story at the same time and

navigating ambiguity. For instance, while all providers described patient causal attributions for disparities in care, the HPA group also endorsed structural factors. Similarly, LPA participants expressed more certainty in their claims that a particular cause was not race, instead invoking patient behaviors, patient socioeconomic status, language, or health literacy. Less than half of LPA participants discussed interpersonal or structural racism, while three-quarters of HPA participants did. All participants discussed access to care as important determinants of racial health care disparities. Conclusions: This study reveals the importance of qualitative data in understanding providers' attributions for racial health care disparities, since providers differ not only in their assessment of causes and attributions of responsibility but also in how they talk and reason about these issues. This study provides a foundation for understanding how to engage providers, with varying predisposing beliefs, in efforts to reduce health care inequality.

Research Topic: Access & Disparities in Care
Funding agencies: HSR&D
Grant support: VA HSR&D IIR 11-328

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12. Catheter management of neurogenic bladder after spinal cord injury

Chrouser, Kristin [1-2]; Lane, Giulia [1-2]; Tawfik, Kyrollos [3]; Driscoll, Amy [1]

1. Minneapolis VA Health Care System
2. University of Minnesota
3. University of Tennessee Health Science Center

Abstract: AIMS: This cross-sectional study describes the catheter management of neurogenic bladder (NGB) in patients with traumatic spinal cord injury (tSCI) with emphasis on the motivations behind transitions between intermittent (IC) and indwelling catheters. Methods: Patients at the Minneapolis VA with history of tSCI who utilized either intermittent catheterization (IC), urethral (UC) or suprapubic (SP) catheters, participated in a voluntary, anonymous survey regarding their bladder management strategies. Results: 100 patients participated, 94% were male and 90% Caucasian with median age of 61 years. Patients with current UC or SP were older than those utilizing IC ($p = 0.002$). The median age at injury and years since SCI were 32 years and 20.5 years, respectively. The median time with current modality was 11 years. 27% of all patients reported at least one transition between catheter type. 14 of 54 patients using IC had prior use of UC or SP, while 12/25 patients using SP and 10/21 patients using UC had prior use of IC. The most common reasons to stop IC included inconvenience, physician recommendation, and dislike of IC. 53% of patients currently using UC or SP reported never using IC. Patients currently using SP were more content with their current catheterization method than those using UC or IC ($p = 0.046$). ConclusionS: Among patients using catheters for NGB, intermittent catheterization was the most common modality utilized and the transition between intermittent and indwelling catheter was most often influenced by patient preferences and clinician recommendations.

Research Topic: Central Nervous System Injuries & Associated Disorders
Funding agencies: N/A
Grant support: N/A

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13. Noninvasively Measured Human Brain Glutathione and Ascorbate Concentrations in Healthy Aging and in Alzheimer's Disease

Crocker, Jillian [1]; Terpstra, Melissa [2-3]; McCarten, J. Riley [1,4]; Hodges, James [5]; Hemmy, Laura [1,6]; Grant, Andrea [7]; Deelchand, Dinesh [3,8]; Marjanska, Malgorzata [3,8]

1. Geriatric Research, Education and Clinical Center, Minneapolis VA Health Care System
2. Center for Magnetic Resonance Research, University of Minnesota
3. Department of Radiology, University of Minnesota
4. Department of Neurology, University of Minnesota
5. Division of Biostatistics, School of Public Health
6. Department of Psychiatry, University of Minnesota
7. Department of Neuroscience, University of Minnesota
8. Center for Magnetic Resonance Research, University of Minnesota

Abstract: Numerous studies have found lower levels of antioxidants in the blood and cerebrospinal fluid of elderly adults. Oxidative stress is involved in Alzheimer's disease (AD) pathogenesis and progression. Increased sensitivity of magnetic resonance technology has made it possible to noninvasively quantify concentrations of the antioxidants glutathione (GSH) and ascorbate (Asc) in intact human brain. The brain's occipital lobe (OCC) shows little evidence of change anatomically with age or Alzheimer's disease (AD). Conversely, the posterior cingulate changes early in the course of AD. Differences between these two areas of brain may reveal important changes in normal vs. pathological aging. Ultra-high field magnetic resonance spectroscopy (MRS) was used to measure concentrations of GSH and ascorbate in the occipital cortex (OCC) and posterior cingulate cortex (PCC) of seventeen young adults, twenty-five cognitively normal older adults, and eleven patients with AD. For the first time, the concentration of GSH was found to be lower ($p = 0.05$) in the OCC of the elderly in a way that is not contingent upon the transverse relaxation rate. Healthy aging tended to impact neurochemicals associated with excitotoxicity (i.e. N-acetylaspartate) in the OCC, whereas those more closely linked to reactive astrogliosis (i.e., myo-inositol, creatine and choline) were impacted in the PCC. The

concentration of Asc was higher (p = 0.005) in the PCC of the patients with AD than in the healthy older adults. This is the first time human brain Asc has been studied noninvasively in patients with AD. In patients, one of the neurochemicals associated with reactive astrogliosis (myo-inositol) was higher in the OCC and two were higher in the PCC (i.e., myo-inositol and choline). Taken together, these outcomes show that both aging and AD impact brain regions differentially. These findings fill part of the gap in understanding how the brain deteriorates throughout aging and AD. Ultra-high field ultra-short-echo-time MRS supplies hitherto missing steps along the pathway to preventing and treating cognitive decline, i.e. means to identify which antioxidant is compromised, in which brain region, in whom, and whether intervention can achieve normalization.

Research Topic: Aging
Funding agencies: NIH
Grant support: N/A

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14. VA Traumatic Brain Injury Model System: 2017 Update

Crocker, Jillian [1]; Finn, Jacob [1-2]; Lamberty, Gregory [1-2]

1. Polytrauma Rehabilitation Center, Minneapolis VA Health Care System
2. Department of Psychiatry, University of Minnesota

Abstract: The Traumatic Brain Injury Model System (TBIMS) is a prospective, 20-year longitudinal, multi-center study which examines TBI recovery and outcomes following coordinated acute medical care and inpatient rehabilitation. In 2008, the Department of Veterans Affairs Polytrauma Rehabilitation Centers (VAPRCs) joined TBIMS and has enrolled over 1,000 Veterans nationwide. The Minneapolis VA PRC site has enrolled 133 Veterans, and currently reaching Veteran's for year 5 follow-ups. Individuals who are admitted to the Minneapolis VA PRC or Polytrauma Transitional Rehabilitation Program (PTRP) for inpatient rehabilitation following a mild, moderate, or severe TBI are eligible for study participation. Vehicle accident is the most frequent cause of injury in the Minneapolis TBIMS study sample. Preliminary data analyses from the 2015 "Improved Understanding of Medical And Psychological Needs (I-MaP)" has been progressing. The Rehabilitation Needs Survey has identified several needs post-injury including help with managing daily stressors and sequelae of brain injury. Chronic TBI remains an issue in both civilian and Veteran populations. Identifying longitudinal effects will contribute to rehabilitation interventions and practice guidelines in VA PRC's.

Research Topic: Acute & Traumatic Injury
Funding agencies: DOD; MVMREF
Grant support: N/A

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15. The Contributions of Cochrane Urology in Guiding Evidence-Based Patient Care

Dahm, Philipp [1-2]; Miller, Alea [1]; Jung, Jae Hung [3]

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Abstract: Introduction: Cochrane Urology is based at the Minneapolis Veterans Administration Medical Center with the mission to conduct and disseminate high-quality systematic reviews related to urological diseases. It was initially founded at this institution in 1996 as the Prostatic Diseases Urological Cancers Group and renamed in 2015 to reflect a broader scope that includes urology-related stone disease. Methods: We assessed the current organizational structure of Cochrane Urology as well as its past and ongoing contributions to the mission of VA healthcare to provide high-quality care to its patients and train future generations of healthcare providers to provide evidence-based medical care. Results: The Cochrane Urology portfolio includes a total of 49 published reviews of interventions in the diagnosis, prevention, treatment and rehabilitation of benign and malignant prostate conditions (i.e. benign prostatic hyperplasia, prostate cancer, prostatitis), male sexual dysfunction (i.e. erectile dysfunction, undescended testes, Peyronie's disease), benign and malignant urology-related renal topics (renal cancer, stones), and other urological cancers (i.e. bladder, testicular, penile, urethral). Three additional reviews are currently in press. We have 12 published protocols as well as 40 ongoing review at various draft stages. The development of comprehensive search strategies is supported through a network of 14 information specialists at six different institutions. The editorial process is overseen by an international network of seven contact editors in six countries, a managing editor and a coordinating editor. We collaborate closely with the VA Evidence Synthesis Program and the University of Minnesota Evidence-Based Practice Center. We provide training research opportunities for medical students, residents and fellows and participate in biannual training workshops for guideline developers on the GRADE approach for rating the quality of evidence and developing evidence-based recommendation by the US GRADE Network. Ongoing challenges relate to the training of review authors, the timeliness of review completion and the acquisition of extramural funding. Conclusion: Systematic reviews of high-quality evidence are important tools to help patients and health care providers make decisions with the best available evidence. Cochrane Urology is dedicated to providing high-quality, accessible publications of systematic reviews to aid decision-making to support the VA's mission.

Research Topic: Personalized Medicine & Genomics
Funding agencies: UMN
Grant support: N/A

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16. The Fragility of Statistically Significant Findings from Randomized Controlled Trials in the Urologic Literature

Dahm, Philipp [1-2]; Gandhi, Shreyas [3]; Chrouser, Kristin [1-2]; Evaniew, Nathan [4]; Narayan, Vikram [1-2]

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Abstract: Introduction. Randomized controlled trials (RCTs) have the potential of providing high quality evidence to inform clinical practice. This quality relies not only on safeguards against bias, but also on statistical power. In this study, we determined the Fragility Index of urological RCTs as a novel metric (Walsh M et al, JCE 2014) to assess the robustness of statistically significant results. Methods: Statistical significance implies that an observed event is unlikely to occur by chance alone. The fragility index is defined as the minimum number of patients in an arm of a trial whose status would have to change from "non-event" to "event" in order to turn a statistically significant result into a non-significant one. All RCTs published in the 4 major urology journals between 2011-2015 were identified. We excluded studies not reporting dichotomous outcomes, as well as those with non-significant results and non-parallel designs. We applied the Fisher exact test to determine fragility index values. Results: 332 RCTs were identified, and 42 studies met inclusion criteria. Median sample size (IQR) was 99 (65, 179), while median event rate per study outcome was 38 (24, 65). The median fragility index was 3 (1, 4.5), indicating that an addition of only three alternate events to an arm of the average trial would have eliminated its statistical significance. There was statistically significant correlation between the fragility index and events per study ($\rho = 0.552$, $p = 0.01$) as well as sample size ($\rho = 0.493$, $p = 0.01$). In 27/40 cases (67.5% of cases), the number of patients lost to follow-up was larger than its fragility index. Conclusions: Statistically significant results in urology RCTs are often fragile, with significance hinging on few events. This is of particular concern in studies that may have large loss to follow-up numbers. Urologists should therefore interpret RCTs cautiously. There may be a role for reporting fragility index values routinely alongside the p-value to provide additional guidance as to the statistical robustness of findings.

Research Topic: Personalized Medicine & Genomics
Funding agencies: N/A
Grant support: N/A

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17. The Reporting Quality of Diagnostic Accuracy Studies in the Urologic Literature

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Abstract: Introduction: Transparent study reporting is a critical aspect of high quality research. For studies of diagnostic accuracy, the Standards for Reporting of Diagnostic Accuracy Studies (STARD) statement that was initially developed in 2003 and updated in 2015, describes the minimal requirement for reporting such studies. We conducted the first systematic assessment of the reporting quality for diagnostic accuracy studies for the urological literature. Methods: A PubMed Clinical Category search was performed of four major urology journals (JU, Eur Urol, BJU Intern and Urology) for studies published from January through December 2015 relating to questions of diagnostic accuracy. Two independent reviewers performed study selection and data abstraction in duplicate. We performed descriptive statistical analysis using SPSS version 23. Results: The search yielded 818 studies of which 67 were reviewed in full-text with 63 studies meeting inclusion criteria. Studies performed well with regards to explaining the study background (100%), defining the study hypothesis (93.7%) and explaining on what basis patients were enrolled (93.7%). Poor performance was noted in following patient flow via a diagram (20.6%), and less than 15% of studies did not define an intended sample size. Conclusion: While many STARD criteria are well reported, there remains room for improvement. To minimize the risk of bias, urologic investigators should utilize STARD in the design, implementation, and reporting of diagnostic studies.

Research Topic: Personalized Medicine & Genomics
Funding agencies: N/A
Grant support: N/A

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18. An Evidence Map of the Women Veterans' Health Research Literature (2008 – 2015)

Danan, Elisheva [1-2]; Krebs, Erin [1-2]; Ensrud, Kristine [1-2]; Koeller, Eva [1]; MacDonald, Roderick [1]; Velasquez, Tina [1]; Greer, Nancy [1]; Wilt, Timothy [1-2]

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2. University of Minnesota Medical School

Abstract: Background: Women comprise a growing proportion of Veterans seeking care at Veterans Affairs (VA) healthcare facilities. In recent years, multiple VA initiatives have accelerated changes in services for female Veterans, yet the corresponding literature has not been systematically reviewed since 2008. In 2015, VA Women's Health Services and the VA Women's Health Research Network jointly requested an updated literature review to facilitate future policy and research planning. Methods: The VA Evidence-based Synthesis Program performed a systematic search of research related to female Veterans' health published from January 2008 to December 2015. We extracted study characteristics including healthcare topic, design, sample size and proportion female, research setting and funding source. We created an evidence map by organizing and presenting results via visual representation and text summary within and across healthcare topics, and describing patterns, strengths and gaps. Results: We identified 2,276 abstracts and independently assessed them for relevance. We excluded over 350 studies that included female Veterans because authors did not stratify results by sex. Of 437 eligible articles, nearly half were related to mental health (k = 207, 47%), particularly post-traumatic stress disorder (k = 71), military sexual trauma (k = 36), and substance abuse (k = 20). The number of studies addressing VA priority topic areas increased over time, including reproductive health, healthcare organization and delivery, access and utilization, and post-deployment health. Few studies addressed common chronic diseases such as diabetes (k = 3), hypertension (k = 0), depression (k = 3), or anxiety (k = 1). Nearly all (k = 396, 91%) studies used an observational design. Less than 2% (k = 8) were randomized trials. Conclusions: Female Veterans' health and healthcare literature grew substantially from 2008 to 2015. Observational studies in mental health make up the majority of research, though additional priority areas demonstrate progress. Methodologic and health topic gaps remain. This evidence map can inform clinical, research, and policy initiatives.

Research Topic: Women's Health
Funding agencies: HSR&D
Grant support: VA ESP Project #09-009

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19. Gender Differences in the Influence of Social Support on Post-Traumatic Stress Disorder Symptoms in National Guard Service Members

Decker, Ellie [1]; Keacher, Lisa [1]; Polusny, Melissa [1-2]; Davenport, Nicholas [1-2]

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

Abstract: Social support is associated with decreased Post Traumatic Stress Disorder (PTSD) symptoms in military populations; however differences between men and women are less clear. Further understanding the role of social support in response to periods of prolonged stress may inform short-term and long-term outcomes for service members following training and deployment. We have assessed reported levels of perceived stress and PTSD symptoms in 39 Minnesota Army National Guard service members at three time periods: shortly before shipping to Basic Training, shortly after returning from training, and several months after returning from training. Social support levels were assessed at the middle time point. We utilized these reports to test the hypothesis that higher self-reported levels of military and civilian social support during training are associated with lower levels of perceived stress and PTSD symptoms immediately following and months after training. Perceived stress and PTSD symptoms increased soon after training, relative to pre-training baseline, followed by subsequent decreases in both domains at the final time point. Gender differences in perceived stressed and PTSD symptoms were observed. Military and civilian social support was not significantly associated with PTSD symptoms in women. In men, higher levels of military support were associated with lower levels of PTSD symptoms shortly after training and several months after returning from training. This association suggests that military social support may be an important protective factor against the development of PTSD symptoms.

Research Topic: Special Populations
Funding agencies: RR&D
Grant support: Career Development Award to Dr. Davenport from the US Department of Veterans Affairs, Rehabilitation Research and Development

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20. Narrow Pedicle Transposition Flap: A Novel Reconstructive Technique

Demer, Addison [1]; Becker, Lauren [1]; Aakhus, Angela [1]; Reich, Hilary [1]; Lee, Peter [1]

1. University of Minnesota Dermatology Department

Abstract: The Narrow Pedicle Transposition Flap is a novel reconstructive technique that is best employed for closure of large Mohs micrographic (MMS) surgical defects and for skin cancers in challenging anatomic sites. By utilizing tissue that would otherwise be sacrificed in the standing cones of traditional closure techniques, this method minimizes tissue loss and subsequently leads to shortened, low tension defects, with cosmetically acceptable results. The narrow pedicle design allows for successful defect closure in areas within tight anatomical confines, while the generous subcutaneous pedicle provides adequate vascular supply and ensures flap survival. After creation of a round or ovoid surgical defect, a traditional Burow's triangle is designed. With the exception of a narrow cutaneous pedicle proximal to the surgical defect, the entire triangle is dissected to the layer of the deep fat. The resulting flap is subsequently transposed and rotated 90 degrees, draped over the defect, shaped to fit exactly, and carefully sutured in place to minimize tissue redundancy of the proximal flap. In a series of thirteen patients treated with the Narrow Pedicle Transposition Flap technique there was no incidence of flap necrosis, and no revision surgeries were required. In three cases, post-operative intralesional triamcinolone was successfully utilized for pedicle flattening. No additional complications were observed, and all results were deemed cosmetically acceptable. The Narrow Pedicle Transposition Flap technique, which is a modification of a rhombic flap, makes use of tissue that would otherwise be discarded. It has been used with success to repair defects on challenging anatomic sites including the medial canthus, nose, and ear, as well as for closure of large defects of more forgiving sites such as the cheek. In areas where maximizing pedicle size is difficult, using this narrow cutaneous pedicle with a robust subcutaneous pedicle can allow for successful defect closure, while ensuring excellent flap survival rates. Use is limited by defect size and shape; however, this has been used successfully in combination with other closure techniques. The Narrow Pedicle Transposition Flap is a simple to use reconstructive technique which decreases flap tension and subsequent risk for skin necrosis, while ultimately resulting in a shortened and cosmetically acceptable surgical scar.

Research Topic: Cancer
Funding agencies: N/A
Grant support: N/A

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21. A Novel Modification in Mohs Micrographic Surgical Technique: Improving Surgical Management of Squamous Cell Carcinoma of the Dorsal Hand in Solid Organ Transplant Patients

Demer, Addison [1]; Hurliman, Elisabeth [1]; Lindgren, Bruce [1]; Kaizer, Alexander [1]; Reich, Hilary [1]; Lee, Peter [1]

1. University of Minnesota Dermatology Department

Abstract: Transplant patients are at a significantly increased risk of cutaneous squamous cell carcinoma (SCC), for which, the treatment of choice is Mohs micrographic surgery (MMS). Unfortunately, clinical clearance of these sun-exposed tumors with MMS is difficult, and associations include high rates of local recurrence, multiple stage Mohs, and large surgical defects. In an effort to mitigate these challenges, we propose use of one-cycle electrodessication and curettage (ED&C) immediately prior to first Mohs stage. Rational is two fold; removal of epidermis improves clinical delineation of invasive tumor component, while the destructive technique treats background actinic damage. A retrospective analysis was conducted using our academic institution's MMS database. Sixty transplant patients who underwent Mohs micrographic surgery (MMS) for SCC of the dorsal hand from 2013 to 2016 were identified. Two treatment groups were included: (1) one cycle of light electrodessication and curettage prior to MMS (the modified MMS group) and (2) traditional MMS alone. Primary outcome was local recurrence, while secondary outcomes were defect size and number of Mohs layers. Descriptive statistics were performed, and treatment group comparisons were conducted using Fisher exact tests and nonparametric Wilcoxon rank sum tests. From 2013-2016, 113 tumors were treated; 32 (28.3%) with Modified MMS, and 81 (71.7%) with traditional MMS. 40% of patients had multiple sites. Overall recurrence rate was 8.0%; 5.6% in Modified MMS group, and 9.4% (3/32) with traditional MMS (P = 1.000). Modified MMS with ED&C required fewer Mohs layers for lesion clearance (One stage MMS: 63.3% vs. 29.0%, P = 0.001). Despite no statistical difference in initial lesion size (P = 0.632), surgical defects were smaller in the modified MMS group at the conclusion of treatment (P = 0.044). Modified MMS is associated with similar recurrence rates to traditional MMS, but importantly yields smaller final surgical defects and is associated with decreased number of required Mohs layers. While removal of epidermis prior to MMS goes against classical dogma where presence of epidermis is critical, we advocate that this practice improves clinical delineation of ilinical tumor margins and provides field treatment of background actinic damage. These concepts are highlighted in observed trend towards improved local recurrence, and statistically significantly decreased surgical defect size and required Mohs layers.

Research Topic: Cancer
Funding agencies: N/A
Grant support: N/A

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22. Trauma Exposure Moderates Spontaneous Neural Activity Differences between PTSD Cases and Controls

Disner, Seth [1]; Marquardt, Craig [2]; Sponheim, Scott [1-2]

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

Abstract: Spontaneous neural activity, measured at rest using various imaging techniques (e.g. regional homogeneity, amplitude of low frequency fluctuations), may provide valuable insights about localized abnormalities contributing to posttraumatic stress disorder (PTSD). We used activation likelihood estimation (ALE) meta-analysis on 22 resting-state neuroimaging studies (N = 457 PTSD cases; 292 trauma-exposed controls [TECs]; 326 non-traumatized controls [NTCs]) to identify regions of abnormal spontaneous activity in participants with PTSD. Compared to all controls, PTSD cases showed decreased left limbic activity. However, separately analyzing PTSD vs. TEC and PTSD vs. NTC yielded dramatically divergent results. PTSD vs. NTC replicated the initial decreased left limbic activity, along with decreased activity in the right caudate head. However, relative to TEC, PTSD cases showed increased activity in the left parietal lobule and a trend towards hyperactivity in the same left limbic area that was hypoactive compared to NTCs. The latter results were validated in an independent sample of combat-exposed Veterans (N = 205), in which PTSD symptom severity was positively correlated with regional homogeneity in the left parietal lobule cluster (p0.007), left limbic cluster (p = 0.022). These findings underscore the neural impact of trauma, even in the absence of post-traumatic symptomatology.

Research Topic: Mental Illness
Funding agencies: RR&D; DOD
Grant support: Congressionally Directed Medical Research Program (W81XWH-08–2–0038: Sponheim), Department of Veterans Affairs, Rehabilitation R&D Program (I01RX000622: Sponheim; 1IK1RX002325: Disner)

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23. Prevalence of Thyroid Incidentalomas in Radiology Reports from 1995-2016

Drake, Tyler [1]; Westanmo, Anders [1]; Billington, Charles [1]

1. Minneapolis VA Health Care System

Abstract: Thyroid incidentalomas are nodules detected on non-thyroid directed imaging, such as CT, MRI or carotid ultrasound. Large database studies have found that < 1% of imaging studies report a thyroid incidentaloma, yet when imaging of 734 neck CT's were reevaluated, 123 (16.8%) were found to have a thyroid incidentaloma, with 10% of these incidentalomas being malignant. It is clear that not all thyroid incidentalomas are reported, but with the increasing use of imaging studies for screening purposes, it is important to study the rates of reported incidental thyroid findings to help understand the growing thyroid cancer epidemic. All radiology reports from March 1995 to September 2016 for chest CT with or without contrast and carotid ultrasound and from June 2001 to September 2016 for MRI cervical spine and MRI neck/orbit/face from the Minneapolis VAHCS were included in our study. Reports were screened for the word "thyroid", and excluded if the word "thyroid" did not appear. Reports were then excluded if the word "thyroid" appeared near the word "normal" or "unremarkable" or if the word "thyroid" appeared in the clinical history/reason for exam section. The remaining reports were then manually reviewed to verify the presence of a thyroid nodule, defined as mention of 1) a nodule, mass, or lesion within the thyroid, 2) focal attenuation abnormality within the thyroid, 3) calcifications within the thyroid, or 4) nodularity of the thyroid. 39,262 non-contrast chest CT's, 23,526 contrast chest CT's, 25,763 carotid ultrasounds, 8745 cervical spine MRI's, and 758 neck/orbit/face MRI's were included. 1289 thyroid incidentalomas (3.28% prevalence) were reported on non-contrast chest CT, 1082 (4.60%) on contrast chest CT, 129 (0.50%) on carotid ultrasound, 244 (2.79%) on cervical spine MRI, and 14 (1.85%) on neck/orbit/face MRI. Of these reported thyroid incidentalomas, the average age was 70.6 years old for CT scans, 69.6 for carotid ultrasounds, and 61.5 for MRI scans. 93.9% of patients with a thyroid incidentaloma on CT scan were male, 93.8% of those on carotid ultrasound were male, and 86.4% on MRI were male. In a predominately older male population, thyroid incidentalomas are reported on roughly 4% of chest CT's, 3% of cervical spine MRI's, and < 1% of carotid ultrasounds. This represents a significant number of thyroid incidentalomas that are reported and are likely a significant contributor to the current rise in thyroid cancer incidence.

Research Topic: Health Systems
Funding agencies: N/A
Grant support: N/A

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24. High fat diet increases cognitive decline and neuroinflammation in a model of orexin loss

Duffy, Cayla [1-3]; Kotz, Catherine [1,4-6]; Billington, Charles [1,4,7]; Nixon, Joshua [1-2]; Butterick, Tammy [1-2,4]

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4. Minnesota Nutrition and Obesity Center, University of Minnesota, St. Paul, MN
5. Geriatric Research Education Clinical Center, Minneapolis VA Health Care System, Minneapolis, MN
6. Department of Integrative Biology and Physiology, University of Minnesota, Minneapolis, MN
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Abstract: Midlife obesity is a risk factor for cognitive decline and is associated with the earlier onset of Alzheimer's disease (AD). Diets high in saturated fat can potentiate the onset of obesity, microglial activation, and neuroinflammation. Signaling deficiencies in the hypothalamic peptide orexin A (OXA) and/or orexin fiber loss are linked to neurodegeneration in humans and animal models. Prior studies in orexin/ataxin-3 (O/A3) mice, a transgenic mouse model of orexin neurodegeneration, demonstrate that OXA treatment improves cognitive processes. In

separate studies we have demonstrate that OXA can suppress neuroinflammation and is neuroprotective against the saturated fatty acid palmitate. Our overall hypothesis is that OXA treatment attenuates hippocampal neuroinflammation and prevents cognitive decline in obesity during high fat diet (HFD) feeding. Our short term goal for this project is to determine if OXA loss increases neuroinflammation and impairs cognition during HFD feeding. To examine this, we tested male O/A3 mice (7-8 mo. of age) in a two-way active avoidance (TWAA) hippocampus-dependent memory task. We tested whether 1) OXA loss impaired cognitive function; 2) HFD worsened cognitive impairment; and 3) HFD increased microglial activation and neuroinflammation. We show that O/A3 mice have significant impairments in TWAA task learning vs. wild type (WT) mice (increased escapes $p < 0.05$, reduced avoidances $p < 0.0001$). Mice were then placed on HFD (45% total fat, 31.4% saturated fat) or remained on normal chow (NC; 4% total fat and 1% saturated fat), and TWAA was retested at 2 and 4 weeks. Learning impairment was evident at both 2 and 4 weeks in O/A3 mice fed HFD for following diet exposure vs. WT mice on normal chow or HFD (increased escapes, reduced avoidances $p < 0.05$). Additionally, O/A3 mice had increased gene expression of the microglial activation marker, Iba-1 (measured via qRT-PCR, $p < 0.001$). Characterization of the microglial immune response (M1 neurotoxic vs. M2 protective phenotypes) is ongoing and will include gene and protein markers (such as TNF-a, iNOS, UCP2, and Arg1). Collectively, our results indicate that OXA loss impairs memory, and that HFD accelerates hippocampus-dependent learning deficits and the onset of neuroinflammation. Future studies will focus on restoration of OXA within hippocampal circuits to reduce neuroinflammation and improve cognitive function.

Research Topic: Central Nervous System Injuries & Associated Disorders
Funding agencies: BLR&D; UMN; MVMREF
Grant support: This work is funded by grants University of Minnesota-MnDRIVE-Brain Conditions (CMD), US Department of Veterans Affairs BLR&D IK2 BX001686 (TAB), 1I01BX003004-01A2 (CMK), and a grant from the Minnesota Veterans Medical Research and Education Foundation (TAB).

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25. Identification of a Fatty Acid Binding Protein4-UCP2 Axis Regulating Microglial Mediated Neuroinflammation

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Abstract: Hypothalamic inflammation contributes to metabolic dysregulation and the onset of obesity. Dietary saturated fats activate microglia via a nuclear factor-kappa B (NF.B) mediated pathway to release pro-inflammatory cytokines resulting in dysfunction or death of surrounding neurons. Fatty acid binding proteins (FABPs) are lipid chaperones regulating metabolic and inflammatory pathways in response to fatty acids. Loss of FABP4 in peripheral macrophages via either molecular or pharmacologic mechanisms results in reduced obesity-induced inflammation via a UCP2-redox based mechanism. Despite the widespread appreciation for the role of FABP4 in mediating peripheral inflammation, the expression of FABP4 and a potential FABP4-UCP2 axis regulating microglial inflammatory capacity is largely uncharacterized. To that end, we hypothesized that microglial cells express FABP4 and that inhibition would upregulate UCP2 and attenuate palmitic acid (PA)-induced pro-inflammatory response. Gene expression confirmed expression of FABP4 in brain tissue lysate from C57Bl/6J mice and BV2 microglia. Treatment of microglial cells with an FABP inhibitor (HTS01037) increased expression of Ucp2 and arginase in the presence or absence of PA. Moreover, cells exposed to HTS01037 exhibited attenuated expression of inducible nitric oxide synthase (iNOS) compared to PA alone indicating reduced NF.B signaling. Hypothalamic tissue from mice lacking FABP4 exhibit increased UCP2 expression and reduced iNOS, tumor necrosis factor-alpha (TNF-a), and ionized calcium-binding adapter molecule 1 (Iba1; microglial activation marker) expression compared to wild type mice. Further, this effect is negated in microglia lacking UCP2, indicating the FABP4-UCP2 axis is pivotal in obesity induced neuroinflammation. To our knowledge, this is the first report demonstrating a FABP4-UCP2 axis with the potential to modulate the microglial inflammatory response.

Research Topic: Central Nervous System Injuries & Associated Disorders
Funding agencies: BLR&D; NIH; UMN
Grant support: US Department of Veterans Affairs BLR&D IK2 BX001686 (to TAB), the University of Minnesota Healthy Foods, Healthy Lives Institute (to CMD, JPN and TAB), the National Institutes of Health NIH R01 DK053189 (to DAB), and the Minnesota Nutrition and Obesity Center (NIH P30 DK050456).

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26. Military Couple Communication During Deployment: Development and Psychometric Evaluation of the Deployment Communication Inventory (DCI)

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3. Binghamton University - State University of New York
4. National Center for PTSD, VA Boston Health Care System

Abstract: Intimate partner communication has become a part of the daily routine of military couples during deployment. However, there is a scarcity of research examining the individual and relationship implications of communication during deployment, likely due in part to the lack of existing measures of deployment communication. The current study examined the psychometric characteristics of a newly developed, multidimensional tool for assessing communication during deployment in a sample of 391 recently deployed male Army National Guard Soldiers and their female intimate partners. The Deployment Communication Inventory (DCI) contains six Soldier and six partner scales that assess (a) Frequency of Communication; (b) nature of communication (Assurance/Support, Problem-solving/Disclosure, and Conflict); and (c) perceived consequences of communication (Benefits and Costs). Scales demonstrated good reliability, as well as convergent validity, as evidenced by associations with measures of relationship and family functioning, and individual mental health for military couples. The DCI may serve as a useful assessment tool for both researchers and clinicians interested in examining the impact of deployment communication on military families.

Research Topic: Mental Illness
Funding agencies: HSR&D
Grant support: HSR&D SDR 10-398

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27. Improving Automatic Control of an Ankle-Foot Prosthesis using Machine Learning Algorithms

Fairhurst, Stuart [1]; Koehler-McNicholas, Sara [1]; Slater, Billie [1]; Nickel, Eric [1]; Koester, Karl [1]; Voss, Gregory [1]; Hansen, Andrew [1-2]; Ferguson, John [1-2]

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

Abstract: This poster describes improved automatic mode switching of a bimodal ankle-foot system. In order to compare different machine learning algorithms that could be used in the automatic mode, gyroscope and accelerometer data were recorded during a sequence of actions performed using a pseudo-prosthesis. We also developed an easy-to-use switch to control the automatic mode of the prosthesis. The results of this study can improve the control, stability, and functionality of prosthetic ankle-foot systems.

Research Topic: Special Populations
Funding agencies: RR&D
Grant support: A1531-R

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28. Cardiac Remote Ischemic Preconditioning Prior to Elective Vascular Surgery (CRIPES): A Prospective, Randomized, Sham-Controlled Phase II Clinical Trial

Garcia, Santiago [1-2]; Rector, Thomas [1]; Zakharova, Marina [2]; Herrmann, Rebekah [1]; Adabag, Selcuk [1]; Bertog, Stefan [1]; Sandoval, Yader [3-4]; Santilli, Steven [1]; Brilakis, Emmanouil [5-6]; McFalls, Edward [1-2]

1. Minneapolis VA Health Care System
2. University of Minnesota
3. Hennepin County Medical Center
4. Abbott Northwestern Hospital
5. VA North Texas Health Care System
6. University of Texas Southwestern Medical Center

Abstract: Vascular surgery is considered a high-risk operation with an anticipated perioperative risk of either death or nonfatal myocardial infarction (MI) of 10% to 15%. Myocardial injury during non-cardiac surgery is associated with an increased risk of long-term mortality and can be detected with routine measurement of cardiac biomarkers, preferably cardiac troponins (cTn). We have previously shown that prophylactic coronary revascularization before elective vascular surgery does not result in improved perioperative or long-term clinical outcomes, highlighting the need to test novel strategies for cardioprotection. Remote ischemic preconditioning (RIPC) is characterized by brief, reversible episodes of ischemia and reperfusion in vascular territory that renders protection to remote tissue during a subsequent episode of ischemia. The mechanism by which RIPC affords cardioprotection is not well defined, but may be related to production of a humoral factor. Although RIPC has been well validated in preclinical models, generalizing those findings to clinical situations has yielded conflicting results. Because of the known risks associated with vascular surgery, we conducted a randomized, clinical trial to test the hypothesis that RIPC, applied noninvasively within 24 hours before a vascular operation, would reduce the proportion of patients with detectable increases in cTn, and/or the magnitude of such increases, in the immediate perioperative period.

Research Topic: Health Systems
Funding agencies: MVMREF
Grant support: The CRIPES trial was supported by a Career Development Award from the VA Office of Clinical Research and Development (1IK2CX000699-01)

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29. Identifying predictors of clinical response to deep transcranial magnetic stimulation in medication refractory depression with co-morbid traumatic brain injury

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

Abstract: Objective: Evaluate the safety and efficacy of deep TMS for medication refractory depression (MRD) in mTBI and identify potential clinical predictors of response. Background: Traumatic brain injury (TBI) is a common problem with 1.5 million new injuries in the United States each year. In the military, over 25,000 TBIs were reported in 2014 with 84% classified as mild (mTBI). Depression is present in as many as 50% of mTBI cases. Unfortunately, those with mTBI that develop psychiatric complications have overall poorer outcomes. Patients with mTBI and depression typically get management in line with their non-mTBI depressed counterparts. These interventions have varying degrees of success. In the general population, approximately 80% of people treated for depression respond to medications. In mTBI, success rates are much lower (Ashman et al., 2009) with increased side effects. Ultimately, many mTBI patients require psychostimulants to improve mood and cognitive symptoms and many mTBI depressed patients experience severe MRD. Deep transcranial magnetic stimulation (dTMS) has shown tremendous promise in MRD, but it has yet been evaluated in comorbid mTBI and depression. Design/Methods: This study is an open-label clinical trial. Participants will complete 20 dTMS treatments and three follow-up visits (1, 3, and 6 months). Results: To date, two patients have received treatment. Both patients tolerated the treatments well and experienced a reduction in symptom severity from severe to mild after 20 treatments. Conclusions: Initial results are promising with good clinical response. The study is continuing to recruit with a target of 60.

Research Topic: Mental Illness
Funding agencies: N/A
Grant support: Defense and Veterans Brain Injury Center

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30. Transcranial Direct Current Stimulation (tDCS) Paired with a Cognitive Task Reduces Impulsivity in a Clinical Population of Veterans

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Abstract: Impulsivity, behavior without adequate forethought or consideration of consequences, is often present in many clinical conditions and is difficult to treat and manage. In this study, we sought to determine if combining tDCS with practice of a risk taking task might reduce measures of impulsivity. A randomized controlled design was employed with participants randomized to either active or sham tDCS. Veterans were referred to the study because of observed problems with impulsivity. Participants trained on a Balloon Analogue Risk Task (BART), an interactive computer task in which subjects try to inflate a virtual balloon as large as possible without bursting it. Participants were randomly assigned to receive either active tDCS or sham stimulation with their training during two 25 minute sessions per day over five days. tDCS was applied with two 25 cm2 saline soaked electrode sponges with anode at F4 (right) and cathode at F3 (left) for 25 minutes concurrent with the BART at 2 mA current (Neuroelectrics Starstim). To evaluate generalization, an untrained Risk Task was performed before and after the five days of training. Additionally, participants returned for one and two month follow-up sessions, where they completed the BART and Risk Task without stimulation. Participants were 30 Veterans (15 active tDCS, mean age 60.4 ± 6.6 years, 1 woman; 15 sham tDCS, mean age 58.3 ± 7.6 years, 2 women). For the trained BART task, growth curve analysis (GCA) examining individual variation of the growth rates over time (across all 10 tDCS sessions and the 1- and 2-month follow-ups) showed that there were no significant variations in individual trajectory changes over time ($\beta = 0.02$, $p > 0.05$). For the untrained Risk Task, GCA showed that the active tDCS group showed a significant decrease in risky choice from pre- to post-treatment as compared with the sham group (a Group x Time interaction, $p = 0.01$). Post-treatment through the follow-ups, however, the trajectories were similar for both groups, i.e. the active tDCS group's decreased risky behavior stabilized and remained at that level across follow-up sessions. Results suggest that active tDCS (compared to sham) can effectively reduce risk-taking propensity and impulsivity. This study provides preliminary evidence that tDCS may reduce impulsive and risk-taking behavior in participants who exhibit clinically-relevant impulsivity, extending previous research that has only included healthy participants.

Research Topic: Mental Illness
Funding agencies: DOD
Grant support: This work was supported by the Defense and Veterans Brain Injury Center.

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31. Assessment of Neural Dynamics in Severe Traumatic Brain Injured Patients with Disorders of Consciousness

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Abstract: Severe brain injury can cause a profound disturbance of consciousness (DOC), including minimally conscious state (MCS), vegetative state (VS), or coma. Typical evaluation of the level of consciousness relies on subjective behavioral assessment of patients' responsiveness using clinical scales. The determination of the level of consciousness has important ethical and medical consequences in regard to the selection of care, treatment, and end-of-life decisions. For these reasons, it is important to have an objective method that assists practitioners in determining the presence of willful brain activity even when patients are not able to demonstrate a willful response. The current study aims to develop an objective method of evaluation of willful brain activity in disorders of consciousness using electroencephalography (EEG). Preliminary resting state EEG data (5 minutes, 8 electrodes) were collected from two neurologically healthy controls and two patients (both males; 21 and 31 years-of-age) who each had a severe traumatic brain injury as a consequence of a vehicular accident. The recordings for the two patients were done while in MCS and again several weeks later while in MCS+ (i.e., emerged). Power spectral density (PSD) and phase-locking index (PLI; a measure of the strength of phase synchronization between oscillatory activities from two different locations) were calculated in different frequency bands (delta, theta, alpha, beta). The PSD profiles for both patients in MCS decreased progressively across frequency bands without noticeable characteristics. In contrast, the PSDs in MCS+ state had a strong beta-band peak (~20 Hz), whereas those of Controls had a clearly defined alpha-band peak (~10 Hz). For PLI, we found that both short- and long-range interactions were significantly weaker in MCS than MCS+ and Controls. In addition, the long-range interactions were significantly weaker than short-range in MCS (bootstrap t-test, $p < 0.05$), but not in MCS+ and in Controls. The results indicate that 1) the profile of the resting state PSD can be used to differentiate the level of consciousness of DOC patients, and 2) functional connectivity measures may provide valuable information in the assessment of DOC patients. These preliminary results support the idea that the analysis of neural oscillatory activity with EEG can provide a sound basis for evaluating the level of consciousness of an individual, and monitoring changes in that level over time.

Research Topic: Central Nervous System Injuries & Associated Disorders
Funding agencies: CSR&D
Grant support: CX00437

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32. Contact Dermatitis To Personal Hygiene Soaps And Cleansers: Retrospective Analysis Of North American Contact Dermatitis Group Data 2000-2014

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9. Division of Dermatology, Royal Victoria Hospital, McGill University, Montreal, QC CAN
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11. Division of Dermatology, Sunnybrook Health Sciences Centre, University of Toronto, ON CAN

Abstract: Background: There is limited information regarding the use of teledermatology (TD) in the context of assessing skin patch test reactions. Objective: The focus of this study was to compare the difference in assessments of an in-person (IP) evaluator of skin patch test reactions versus those utilizing store-forward teledermatology. Methods: Patients undergoing skin patch testing to the North American Contact Dermatitis Group (NACDG) series were recruited for this study. Digital images were taken of the test area 48 hours after application of the allergens. These photographs were in turn given to eight members of the NACDG, who were blinded to the IP ratings, to assess for possible reactions. Furthermore, teledermatologists evaluated image quality for each set of patients to potentially account for any discrepancies. TD readings were then compared to the individual IP data to determine extent of agreement. Depending on IP/TD pairings, readings were placed into eight agreement categories and further grouped into three final clinical outcomes: "success", "indeterminate", and "failure". Results: Ninety-nine patients were enlisted in this study for a total of 6930 opportunities of comparison between IP and each TD. Not taking into account negative/negative agreement, the "success" of TD readings ranged from 15.5-36.4% with an average of 29%. The rate of "failure" – that is clinical significance between readings – was 2.8-6.8%. Overall, there was a large degree of "indeterminate" agreement, which

could potentially be of clinical significance. There was no statistical significance between TD's. The years of experience and average number of patients patch tested by the TD monthly in his/her clinical practice did not correlate to "success" or "failure" of readings. Conclusions: Teledermatology may be a useful tool for clinicians to assess skin patch testing results. However, there are still limitations as evidenced by the low average "success" rate and large degree of "indeterminate" agreement.

Research Topic: None indicated
Funding agencies: N/A
Grant support: N/A

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33. Stigma and Diagnostic Decision Making in Mental Health Providers

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2. University of Minnesota

Abstract: Introduction: A growing literature on stigma among health care providers points to professional cultures of nondisclosure as a factor that perpetuates stigma. The resulting lack of access to role models facilitates "disidentification" with the stigmatized group, facilitating negative attitudes and discriminatory behavior. Research on primary care providers has demonstrated that providers' discomfort with seeking mental health services for themselves was related to clinical decisions that provided fewer resources to patients with psychiatric diagnoses. This study assessed the extent to which this phenomenon extends to mental health providers. Methods: One hundred fourteen mental health providers responded to a survey that included a measure of disidentification with other mental health providers who manage mental health challenges. These providers were then asked to review one of three randomly assigned case vignettes, and identify diagnoses they would consider for this case. Case A was a young adult, Caucasian male Veteran seeking assistance with vocational concerns, and also reporting marital stress and a range of somatic symptoms. Case B was the same case, with the addition of current use of an SSRI since exposure to combat trauma. Case C was the same as Case A, with the addition of a history of a brief psychotic episode several years in the past. Hypothesis: Both vignette (i.e., A, B, or C) and disidentification with other providers with mental health challenges will be related respondents' decisions to consider the most stigmatizing diagnostic response options (borderline personality disorder, bipolar disorder, and schizophrenia). Analysis: Three ANCOVA's were run using vignette condition as the independent variable, disidentification with providers managing mental health challenges as a covariate, and each of the three target, stigmatizing diagnoses (borderline personality disorder, bipolar disorder, schizophrenia) were dependent variables. Results: For borderline personality disorder and bipolar disorder, disidentification emerged as statistically significant, while vignette condition did not. For schizophrenia, vignette condition emerged as statistically significant, while disidentification did not. Conclusions: The hypothesis was partially supported. Results indicate that for some stigmatizing diagnoses, providers' stigma explains more variance than the clinical data upon which the diagnosis is based.

Research Topic: Mental Illness
Funding agencies: N/A
Grant support: n/a

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34. Magnetoencephelography in the Eyes of an Engineer

Heffernan, Jacob [1]; Goodwin, Shikha [1]

1. Brain Sciences Center, Minneapolis VA Health Care System

Abstract: The human brain is one of the most complex organized structures known to exist, and for us, it is also the most important. Magnetoencephalography is a non-invasive functional neuroimaging method of mapping brain activity by recording the magnetic fields which are naturally produced by electrical currents in the brain using Super-Conducting Quantum Interference Devices (SQUIDs). The main principles of MEG include a safe, non-invasive, direct measurement of neuronal activity with excellent temporal resolution, reasonable spatial resolution and no impedance offered by intervening structures. These reasons make MEG suitable for studying the human brain as a network of interacting brain areas during the performance of various tasks as well as spontaneous neuronal activity. This paper examines Magnetoencephalography (MEG) as seen through the eyes of an engineer. The forward and inverse problems provide different techniques for analyzing the data, which in turn pose questions that need to be addressed by the varying analysis modalities. The goal of the forward problem is to predict the magnetic field vector or electric potential that is measured externally given an active source inside the brain (unit dipole). The inverse problem is comparable to reconstructing an object based solely on its shadow, some elements, such as the shape, are known, but other features must be found using prior knowledge, inferences, and additional constraints. Inverse modeling using single and multiple dipole methods address the question: where are the strongest sources located and how many are there? Distributed dipole models ask: what is the distribution of activity over the brain? Spatial filtering inverse models pose the question: what is the likelihood for activity at a given brain location? The purpose of these questions is to examine these varying imaging modalities behind the analysis of the acquired data during MEG. MEG is considered as an excellent tool for investigating the dynamic characteristics of brain regions during information processing. Understanding the brain coincides with understanding ourselves and there is a lot about the human brain that is left to be

uncovered. MEG plays an increasingly important role in comprehending what has yet to be discovered about the human brain along with aiding in diagnostics of neuropsychiatric disorders, as well as clinical preoperative planning.

Research Topic: None indicated
Funding agencies: N/A
Grant support: N/A

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35. Systematic hypercorrelation across time in brain networks in schizophrenia

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2. University of Minnesota

Abstract: Schizophrenia (SZ) is a serious psychiatric disorder with diverse manifestations and of unknown etiology. Although several hypotheses have been advanced concerning the biological nature of the disorder, very little is known about the abnormalities in brain function that lead to schizophrenia's complex phenotype. In 2007, we reported on abnormalities of neural communication signals in SZ that enabled us to distinguish and 100% correctly classify SZ patients from healthy particiapants and from patients suffering from other brain diseases, including multiple sclerosis, Alzheimer's disease, chronic alcoholism, Sjogren's syndrome and temporomandibular joint disorder (Georgopoulos et al., Synchronous neural interactions assessed by magnetoencephalography: A functional biomarker for brain disorders. J. Neural Eng. 4: 349-355, 2007). Those communication signals consisted of zero-lag crosscorrelations (CC) between prewhitened magnetoencephalographic (MEG) time series acquired for 45 s at rest, in a task-free state. Here we report on the differences between 21 SZ patients and 23 matched healthy controls with regard to CCs extending up to 50 ms lags.

Research Topic: Mental Illness
Funding agencies: UMN
Grant support: University of Minnesota

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36. Effect of Dietary CoQ10 on Hibernating Myocardium

Hocum Stone, Laura [1]; Wright, Christin [1]; Kelly, Rosemary [1]; McFalls, Edward [2]

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2. Cardiology Division, Minneapolis VA Health Care System

Abstract: Our novel swine model of chronic hibernating myocardium is characterized by tissue with reduced blood flow and reduced function that remains viable. Our previous studies have shown that hibernating myocardium results in decreased expression of electron transport chain proteins and mitochondrial fusion proteins, suggesting that the functional impairment may be due to mitochondrial dysfunction. Clinical studies have suggested a beneficial effect of chronic administration of Coenzyme Q10 (CoQ10) in ischemic heart disease. We tested the effect of administration of dietary CoQ10 in swine with established hibernating myocardium. Twelve pigs underwent placement of a constrictor around the LAD artery and established hibernating myocardium by 12 weeks. Once established, six pigs were given daily dietary CoQ10 for 30 days, while the remaining six swine were given normal chow. Cardiac function was assessed by ECHO, and expression of mitochondrial proteins were analyzed by Western Blot. We found that administration of CoQ10 increased the expression of the electron transport chain proteins, but did not improve the regional functional impairments characteristic of hibernating myocardium.

Research Topic: Heart Disease
Funding agencies: BLR&D
Grant support: VA Merit Review: I01 BX000760

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37. MRI assessment of cardiac function in a swine model of hibernating myocardium three months following bypass surgery

Hocum Stone, Laura [1]; Swingen, Cory [1]; Holley, Christopher [1]; Wright, Christin [1]; Chappuis, Erin [1]; Ward, Herbert [1]; McFalls, Edward [2]; Kelly, Rosemary [1]

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

Abstract: OBJECTIVE: Clinical studies demonstrate delayed recovery of hibernating myocardium (HM) following coronary artery bypass graft (CABG) surgery. Cardiac magnetic resonance (CMR) imaging has proven effective in identifying HM in clinic. Our animal model of HM shows partial but incomplete functional recovery one month following CABG using echocardiography. This study uses CMR imaging to determine

completeness of recovery 3 months post-CABG. METHODS: Swine (N = 12) underwent left anterior descending artery (LAD) 1.5cm constrictor placement creating a territory of HM over 12 weeks. CMR at 12 weeks confirmed hibernation without infarction (N = 12). Off-pump left internal mammary artery (LIMA) to the LAD was performed in 9 animals. 3 animals were sacrificed as HM controls. CMR imaging was repeated in revascularized animals prior to sacrifice at one (N = 4) or three months (N = 5). CMR imaging was performed at baseline and with dobutamine infusion (5 µg/kg/min). Results: 12 weeks post constrictor placement, CMR imaging confirmed viability in LAD region and LAD stenosis in all animals. In HM, wall thickening is reduced at baseline but with contractile reserve present during dobutamine infusion. Following revascularization, CMR imaging confirmed patent LIMA graft (N = 9). Analysis of baseline regional function shows incomplete recovery of HM following CABG, with reduced contractile reserve at both 1 and 3 months post CABG. Conclusion: CMR imaging provides accurate spatial resolution of regional contractile function and confirms the presence of HM at 12 weeks following instrumentation of the LAD. Three months following CABG, partial recovery of HM with contractile reserve is present in the single LAD territory.

Research Topic: Heart Disease
Funding agencies: BLR&D
Grant support: VA Merit Review: I01 BX000760

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38. Plasma Sphingolipids Associated with HIV-associated Chronic Obstructive Pulmonary Disease (COPD)

Hodgson, Shane [1]; Griffin, Tim [2]; Reilly, Cavan [3]; Harvey, Stephen [2]; Witthuhn, Bruce [2]; Sandri, Brian [4]; Kunisaki, Ken [1]; Wendt, Chris [1]

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2. Department of Biochemistry, Molecular Biology and Biophysics, University of Minnesota
3. Division of Biostatistics, School of Public Health, University of Minnesota
4. Department of Medicine, University of Minnesota

Abstract: Introduction: Chronic obstructive pulmonary disease (COPD) is a significant cause of morbidity in persons living with HIV (PLWH) and HIV appears to uniquely cause COPD, independent of smoking. The mechanisms by which HIV leads to COPD are not clear. Our objective was to identify metabolomic biomarkers and potential mechanistic pathways of HIV-associated COPD (HIV-COPD). Methods: We performed case-control metabolite profiling via mass spectrometry in plasma from 38 individuals with HIV-COPD (cases), comparing to matched controls with/without HIV and with/without COPD. Untargeted metabolites of interest were identified liquid chromatography with mass spectrometry (LC-MS/mass spectrometry (MS)), and targeted metabolomics for tryptophan (Trp) and kyurenine (Kyn) were measured by selective reaction monitoring (SRM) with LC-MS/MS. We used mixed effects models to compare metabolite concentrations in cases compared with controls while controlling for relevant biological variables. Results: We identified 1689 analytes associated with HIV-COPD at a false discovery rate (FDR) of 10%. In PLWH, we identified 263 analytes (10% FDR) between those with and without COPD. LC MNS/MS identified Trp and 17 lipids, including sphingolipids and diacylglycerol. After adjusting for relevant covariates, the Kyn/Trp ratio measured by SRM was significantly higher in PLWH ($p = 0.022$), but not associated with COPD status ($p = 0.95$). Conclusions: There is a unique metabolite profile in HIV-COPD that includes sphingolipids. Trp metabolism is increased in HIV, but does not appear to independently contribute to HIV-COPD.

Research Topic: Other Chronic Diseases
Funding agencies: NIH
Grant support: The project was supported by the University of Minnesota Developmental Center for AIDS Research (Research Award). START and its Pulmonary Substudy were funded by the National Heart, Lung and Blood Institute (USA, R01 HL096453), the National Institute of Allergy and Infectious Diseases (USA, UM1AI068641 and UM1AI120197), Agence Nationale de Recherches sur le SIDA et les Hipatites Virales (France), National Health and Medical Research Council (Australia), National Research Foundation (Denmark), Bundes ministerium für Bildung und Forschung (Germany), European AIDS Treatment Network, Medical Research Council (UK), National Institute for Health Research, National Health Service (UK), and the University of Minnesota. Antiretroviral drugs were donated to the START central drug repository by AbbVie, Bristol-Myers Squibb, Gilead Sciences, GlaxoSmithKline/ViiV Healthcare, Janssen Scientific Affairs and Merck. COPDGene was supported by the National Heart, Lung and Blood Institute (USA, R01HL089897 and R01HL089856) and the COPD Foundation through contributions made to an Industry Advisory Board comprised of AstraZeneca, Boehringer Ingelheim, Novartis, Pfizer, Siemens, Sunovion, and GlaxoSmithKline.

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39. Apolipoprotein E: The Resilience Gene

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1. Brain Sciences Center, Minneapolis VA Health Care System

Abstract: The apolipoprotein E (apoE) gene has been implicated in various conditions, most notably Alzheimer's disease and coronary artery disease. A predisposing role of the apoE4 isoform and a protective role of apoE2 isoform in those diseases have been documented. Here we investigated the role of apoE in resilience to trauma. Three-hundred- forty-three U.S. Veterans were genotyped for apoE and were assessed for their lifetime trauma exposure (trauma score, T) and severity of posttraumatic stress disorder symptoms (PCL). The ratio PCL/T indicates sensitivity to trauma, hence its inverse indicates resilience, R, to trauma. R was square-root transformed to normalize its distribution and its

variation with apoE genotype evaluated. We found a significantly higher resilience in participants with apoE genotype containing the E2 allele (E2/2, E2/3) as compared to participants with the E4 allele (E4/4, E4/3). In addition, when the categorical apoE genotype was re-expressed as the number of cysteine residues per apoE mole (CysR/mole), a highly significant positive association was found between resilience and CysR/mole, such that resilience was systematically higher as the number of CysR/mole increased, from zero CysR/mole in E4/4 to 4 CysR/mole in E2/2. These findings demonstrate the protective role of the CysR/mole apoE in resilience to trauma: the more CysR/mole, the higher the resilience. Thus they are in accord with other findings pointing to a generally protective role of increasing number of CysR/mole (from E4/4 to E2/2) in other diseases. However, unlike other conditions (e.g. Alzheimer's disease and coronary artery disease), resilience to trauma is not a disease but an adaptive response to trauma. Therefore, the effects of apoE seem to be more pervasive along the CysR/mole continuum, most probably reflecting underlying effects on brain synchronicity and its variability that we have documented previously (Leuthold et al. 2013).

Research Topic: Mental Illness
Funding agencies: N/A
Grant support: VACO Service Directed Research; American Legion Brain Sciences Center Chair; William L. Anderson Chair in PTSD Research

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40. Anti-oxidant Therapy and Postoperative Cardiac Events: ACE Trial

Johnson, Debra [1]; Herrmann, Rebekah [1]; Nguyen, Jennifer [1]; Mazzula, Franchesca [1-2]; Zakharova, Marina [1-2]; Garcia, Santiago [1-2]; McFalls, Edward [1-2]

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

Abstract: Principal Investigator: Edward McFalls, MD Study Coordinator: Debra Johnson, RN. Purpose: The purpose of the study is to determine whether receiving the antioxidant coenzyme Q10 prior to vascular surgery reduces inflammation levels (measured with biomarkers or blood samples) and troponins (a heart biomarker that indicates heart tissue damage). Background: Patients undergoing vascular surgery have an increased risk of developing cardiac events during or following their surgery. Recent studies have shown that these may be due to an inflammation process that happens following surgery. Additionally, several studies have shown that certain medications may interrupt the inflammation process, thereby decreasing the number of cardiac events. One medication may be an antioxidant called Coenzyme Q10. Hypothesis: Brief pretreatment of coenzyme Q10 before elective vascular surgery reduces peak cardiac biomarker elevations, as estimated by a troponin I level at 24 hours post-vascular surgery. Description of Study: 147 eligible vascular surgical patients. Randomization. Coenzyme Q10 400 mg or placebo x 3 consecutive days prior to surgery. Pre-surgical Labs & ECG. Post surgical 24 & 48 hr Labs: Troponin, BNP, C-Reactive Protein. Post surgical 30 day follow up phone call & medical record review. Eligibility: 1) Advanced vascular disease; 2) Candidate of major elective vascular operation; 3) 18 years of age or older; 4) Willing and able to give informed consent. Exclusion: 1) Known allergic reactions to CoQ10; 2) Enrolled in research study that would confound interpretation of endpoints; 3) Urgent need for vascular operation that would preclude screening.

Research Topic: Heart Disease
Funding agencies: N/A
Grant support: N/A

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41. Drug-Eluting Stents vs. Bare Metal Stents in Saphenous Vein Graft Angioplasty (DIVA)

Johnson, Debra [1]; Herrmann, Rebekah [1]; Joseph, Brown [1]; Bavana, Rangan [1]; Lauren, Uyeda [1]; Beverly, Ventura [1]; Santiago, Garcia [1-2]; Edward, McFalls [1-2]; Emmanouli, Brilakis [1]; Subhash, Banerjee [1]

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

Abstract: Local Principal Investigator: Edward McFalls, MD Study Coordinator: Debra Johnson, RN. Purpose: VA Cooperative Studies Program #571 is designed to prospectively evaluate the efficacy of drug-eluting stents (DES) in reducing aortocoronary saphenous vein bypass graft (SVG) failure when compared to bare metal stents (BMS) in patients undergoing stenting of de novo SVG lesions. Research Question: SVGs often develop luminal stenoses that are most commonly treated with stent implantation. Approximately 60,000-100,000 percutaneous SVG interventions are performed annually in the USA. Two types of coronary stents are currently available: bare metal stents and drug eluting stents. Bare metal stents are the standard of care for the percutaneous treatment of SVG lesions, but are limited by high rates of in-stent restenosis (as high as 51% after 12 months) often leading to repeat percutaneous or surgical SVG treatments. Drug-eluting stents have been shown to significantly reduce in-stent restenosis and the need for repeat target vessel and lesion revascularization in native coronary arteries, yet their efficacy in SVGs is not well studied, with conflicting results from various small studies. The Cooperative Studies Program study will be the first large prospective, randomized, multicenter, blinded clinical trial without routine angiographic follow-up comparing DES and BMS in SVG lesions. It will provide critical knowledge to assist the cardiac interventionalist in selecting the optimum stent type for these challenging lesions. Study Aim of Hypotheses: DES will reduce the 12-month incidence of target vessel failure (TVF, primary study endpoint)

compared to BMS. TVF will be defined as the composite of cardiac death, target vessel myocardial infarction and target vessel revascularization, and is the primary clinical endpoint used in all FDA-approved DES pivotal trials. Design & Methods: At the 26 participating VA hospitals, patients with prior coronary artery bypass graft surgery scheduled to undergo coronary angiography and/or percutaneous intervention to a SVG were screened. Patients who needed SVG stenting and who meet all the inclusion and none of the exclusion criteria were asked to participate in the study. They were randomized to one of two types of stents. Cardiac biomarkers were collected prior to and post stent placement. 12 Months of ADP P2Y12 Inhibitor Treatment. Follow up visits were completed every 6 months through study completion

Research Topic: Heart Disease
Funding agencies: CSR&D
Grant support: N/A

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42. Excellence In Peripheral Artery Disease Thrombin Receptor Antagonist Intervention In Claudication Evaluation (XLPAD-TRACE Trial)

Johnson, Debra [1]; Herrmann, Rebekah [1]; Preeti, Kamath [2]; Suhash, Banerjee [2]; Emmanouli, Brilakis [2]; Santiago, Garcia [1]

1. Minneapolis VA Health Care System
2. VA North Texas Health Care System

Abstract: Objective: Primary trial objective: To evaluate whether addition of Vorapaxar 2.08 mg daily vs. placebo daily on background antiplatelet therapy, prescribed for 6 months to patients with established PAD and IC treated with standard medical therapy (SMT) would lead to an improvement in the peak walking time (PWT). Study endpoints: Primary endpoint: Change from baseline to 6 months in the PWT on a graded treadmill test (GTT per Gardner protocol) between participants enrolled in the test and control arms of the study (Gardner, Parker, Montgomery, Scott, & Blevins, 2011). Secondary endpoints: 1) Change from baseline to 6 months in the claudication onset time (COT) on GTT between participants enrolled in the test and control arms of the study; 2) Change from baseline to 6 months in the walking impairment questionnaire distance scores (WIQ) between participants enrolled in the test and control arms of the study (Mays et al., 2015); 3) Change from baseline to 6 months in self-reported quality of life score using the Medical Outcomes Study 12-Item Short form survey (SF-12) between participants enrolled in the test and control arms of the study (McBurney et al., 2002). Study Design: This is a Phase 4 randomized, double-blind placebo controlled trial. Approximately 200 patients in 20 centers in the US will be enrolled. Following confirmation of eligibility, patients will undergo a baseline graded treadmill test (GTT) before being randomized to receive Vorapaxar 2.08mg or placebo. Patients will monitor activity levels at home for a period of 6 months following which they will return to the clinic to undergo the final GTT test. Patient participation will last 7 months from the time of consent. Each site will be expected to enroll approximately 10 subjects. The Dallas VA will enroll approximately 20 subjects. This is a multi-site project with the Dallas VA as the coordinating center.

Research Topic: Other Chronic Diseases
Funding agencies: MVMREF
Grant support: Merck Sharpe & Dohme, Corp via DVARC (Dallas VA Research Corporation)

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43. Predictive Characteristics of Methicillin-Resistant Staphylococcus Aureus (MRSA) Nasal Swab for MRSA Positive Culture in Hospitalized Veterans

Johnson, James [1-2]; Fox, Teresa [3]

1. Minneapolis VA Health Care System
2. University of Minnesota Medical Center
3. University of Minnesota Medical Center, Internal Medicine Residency

Abstract: When caring for patients with suspected or proven Staphylococcus aureus (SA) infection, providers face the dilemma of whether to treat empirically for methicillin-resistant SA (MRSA) in addition to methicillin-susceptible SA (MSSA). MRSA nares swabs are performed routinely in hospital for infection control purposes. In previous studies a positive nares swab has predicted an increased risk of clinical MRSA infection. Because nares swab results often return prior to clinical culture results, nares swabs might help with clinical decision-making. Our study's goal was to define the predictive characteristics of routine MRSA nares swabs for MRSA-positive clinical cultures. We performed a retrospective medical record review at the Minneapolis VAHCS. Subjects included all hospitalized Veterans with SA isolated from a clinical culture between 2013 and 2016. We determined each isolate's MRSA vs. MSSA status, and noted whether the patient's temporally closest nares swab tested positive or negative for MRSA. The study cohort comprised 559 hospitalized Veterans. The 599 SA clinical isolates (1 per subject) were from: skin and soft tissue (n = 281), blood (n = 99), respiratory (n = 90), urine (n = 62), and bone or joint (n = 27). Overall, for identifying clinical MRSA isolates the MRSA nares swab's sensitivity was 63.2%, specificity 96.0%, PPV 90.5%, and NPV 81.0%. The overall odds ratio (OR) of a positive MRSA nares swab for a positive MRSA culture was 40.9 (95% confidence interval [CI] 22.4-74.7). The overall false-negative rate was 19.0%, representing 79 false-negatives among 411 negative MRSA nares swabs. By site, nares swabs were most predictive for respiratory cultures (OR 64.1 [95% CI 13.3-309.5]) and least predictive for urine cultures (OR, 13.5 [95% CI 3.7-49.5]). Bone and joint cultures

had the highest specificity (100%), but the lowest sensitivity (20%). Understanding the predictive value of the MRSA nares screen for MRSA infection can help to guide empiric antibiotic use among hospitalized Veterans. Overall, our study showed that if a Veteran has positive MRSA nares swab, this greatly increases the odds that a SA isolates is MRSA. However, we also found a lower sensitivity and NPV than some prior studies. Thus, for Veterans with a severe infection that might be due to SA, a negative MRSA nares screen provides insufficient negative predictive power to allow confident omission of MRSA-active antibiotics from the empirical treatment regimen.

Research Topic: Infectious Diseases
Funding agencies: N/A
Grant support: N/A

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44. Brain Function in Gulf War Illness (GWI) and Associated Mental Health Comorbidities

Johnson, Rachel [1]; Engdahl, Brian [1]; James, Lisa [1]; Miller, Ryan [1]; Leuthold, Arthur [1]; Lewis, Scott [1]; Carpenter, Adam [1]; Georgopoulos, Apostolos [1]

1. Brain Sciences Center, Minneapolis VA Health Care System

Abstract: Background: Gulf War Illness (GWI) affects a substantial number of Gulf War Veterans. Neurological, cognitive and mood (NCM) symptoms are frequently at the root of chronic ill-health and disability in Veterans with GWI. In addition, diagnosable mental health disorders frequently co-occur. Here we investigated the possibility that increased GWI severity leads, above a threshold, to a diagnosable mental health disorder using both GWI symptom severity scores and resting-state brain functional connectivity patterns, as determined by magnetoencephalography (MEG). Methods: GWI and mental health status were obtained for 230 participants resulting in 3 groups: healthy controls (N = 41), Veterans with GWI only (GWI group, N = 91), and Veterans with both GWI and mental health disorder (GWI+MH, N = 98). We collected GWI symptom domain severity scores and 9 summary measures of the distribution of Synchronous Neural Interactions (SNI) derived from the MEG recordings. We performed logistic regression on the GWI population to test the hypothesis that, in the presence of GWI, the appearance of a diagnosable mental health disorder may depend on GWI symptom severity. We performed a second logistic regression to test the hypothesis that the presence of a MH disorder can be predicted by the SNI distribution patterns. Findings: GWI symptom severity differed significantly across groups (GWI+MH > GWI > Control). SNI distributions of the GWI group also differed significantly from the other groups in a systematic hemispheric pattern, such that the presence of GWI involved predominantly the left hemisphere, and presence of mental health disorders involved, in addition, the right hemisphere. Both logistic regressions yielded highly significant outcomes, demonstrating that both GWI symptom severity and SNI distribution measures can predict the presence of MH disorder in GWI. Remarkably, the prediction probabilities for MH presence derived from the symptom-based and SNI-based logistic regressions were positively and highly statistically significantly correlated. Interpretation: Both objective (neural) and subjective (symptoms) indices suggest that GWI is distinct from healthy controls and varies in severity in a continuum that, at the higher end, leads to a diagnosable MH disorder. The positive correlation between the GWI symptom-based and brain-based predicted classifications provides a key link between GWI symptom severity and SNI in the context of mental illness.

Research Topic: Gulf War Veterans Illness
Funding agencies: N/A
Grant support: VA Central Office Service Directed Research Grant

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45. Exploring the Efference Copy/Corollary Discharge Mechanism of Predictive Coding in Response to Cued Action and as a Function of Cognitive Control in Schizophrenia

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1. University of Minnesota
2. Minneapolis VA Health Care System
3. University of Missouri–Kansas City

Abstract: The efference copy (EC)/corollary discharge (CD) mechanism of predictive coding has been hypothesized to function as a neural indicator of self generation of action. According to this hypothesis, action performance generates a copy of the motor command (the EC), which results in a CD (representing the sensory consequences expected from performing that action). As a result, activity in the sensory cortex related to the sensory consequences of performing the action is suppressed. This mechanism has been shown to be dysfunctional in individuals with schizophrenia (SZ). There is some evidence that this mechanism is conserved even when the action and sensory consequence are not mechanically coupled (i.e., an EC and CD are generated in response to pushing a button to hear a tone, respectively), indicating that information related to self-initiation in addition to self-generation of action may be carried by the EC. We investigated the CD strength in SZ and controls (CN) in response to cued action across varying degrees of cognitive control (CC). We hypothesized that increased CC would recruit increased intentionality (i.e., greater degree of self-initiation) of motor actions, possibly resulting in a more robust CD compared to a simple reaction time task, wherein intention to move is largely offloaded onto the stimulus cuing action. 67 SZ and 56 CN completed a stop signal (SS) task while undergoing EEG. There were 5 blocks, each consisting of 40 Go Only (GO) and 120 Go/Stop (GS) trials. GO trials consisted of fixation followed by a cue to quickly press a button with the left or right hand. On 20%of GS trials, a SS was presented. Low (GO trials, no

chance of SS) and high initiation (4th, 5th and 6th consecutive Go trials during GS blocks, relatively high probability of SS) conditions were derived; right hand responses were analyzed. CD was quantified by comparing early (0-50 ms) post-response activity over contra- and ipsilateral sensory areas (C3 and C4); decreased amplitude of the contralateral early somatosensory ERP indicated intact CD. A condition x electrode x group repeated measures ANOVA revealed an electrode x group interaction, with significantly greater amplitude at the contra- vs ipsilateral electrode in CN only. Intact CD in SZ but not CN is inconsistent with previous work. It also appears that increased CC does not impact CD. Future studies should directly manipulate movement intentionality to more directly examine the effect on predictive coding.

Research Topic: Mental Illness
Funding agencies: CSR&D; NIH
Grant support: This work was supported by a Merit Review Grant from the Department of Veterans Affairs (VHA CSR&D I01CX000227-01), and ACoRD (R24MH069675) and R03 (R03MH106831) grants from NIMH to Scott Sponheim.

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46. Targeting the Cell Cycle and Mitochondrial Antioxidant Defense in Mesothelioma

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

Abstract: Background: Mesothelioma is a highly fatal cancer with limited therapeutic options. Low expression of the endogenous cyclin-dependent kinase 4 (CDK4) inhibitor p16INK4A has been demonstrated in up to 90% of mesothelioma tumors. CDK4 has also been demonstrated to activate manganese superoxide dismutase, which can decrease superoxide levels in cells and may make them less susceptible to induction of apoptosis. Downregulation of the key mitochondrial antioxidant protein, thioredoxin 2 (Trx2) has been demonstrated to increase reactive oxygen species production in mesothelioma cells resulting in reduced mesothelioma tumor growth. Gentian violet has been demonstrated to result in decreased expression of Trx2, a key mitochondrial antioxidant protein. The goal of this project is to determine whether concomitant targeting of the cell cycle and mitochondrial antioxidant pathways lead to improved efficacy against mesothelioma. Methods: Mesothelioma cells were treated with compound or control and proliferation was evaluated using Cell Counting Kit 8 (Dojindo). For immunoblotting experiments, detection was performed using enhanced chemiluminescence. Apoptosis was detected via Cell Death Detection ELISAPLUS(Sigma-Aldrich). All experiments were done in duplicate or triplicate. Results: Previously, we have demonstrated that palbociclib inhibits mesothelioma cell proliferation, inhibits retinoblastoma protein (Rb) phosphorylation, and results in cell cycle arrest. Mesothelioma cells in culture were treated with palbociclib and gentian violet alone and in combination. After 72h incubation with gentian violet, decreased cell proliferation was observed for 3 separate cell lines (IC50 = 365 nM, 870 nM, and 920 nM, respectively). Incubation with gentian violet for 24h resulted in decreased expression of Trx2 in all cell lines and also induced apoptosis in all cell lines. Gentian violet sensitized mesothelioma cells to palbociclib in a cell proliferation assay. Conclusions: Gentian violet resulted in a significant decrease in mesothelioma cell proliferation. Palbociclib also sensitizes mesothelioma cells to gentian violet. Further investigation of this combination approach may demonstrate these combinations are useful for mesothelioma treatment.

Research Topic: Cancer
Funding agencies: DOD
Grant support: DOD Peer-Reviewed Cancer Research Program, CDA; Development of Novel p16INK4a Mimetics as Anticancer Therapy

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47. Outcomes of a mixed-mode multiple contact survey approach in the Effects of Prescription Opioid Changes for Veterans (EPOCH) study

Krebs, Erin [1-2]; Martinson, Brian [1,3]; Jensen, Agnes [1]; Bangerter, Ann [1]; Clothier, Barbara [1]; Linden, Erin [1]; Rutks, Indy [1]; Vang, Derek [1]; Bassett, Cody [1]; Balk, Ruth [1]

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

Abstract: Background: The project recruited a nationally-representative sample of VA primary care patients receiving long-term opioid therapy (LTOT) to collect longitudinal patient-reported pain outcomes data. Specific aims are to examine: 1. The relationship between changes in opioid daily dose and changes in patient-reported pain and quality of life outcomes; and 2. associations of patient, provider, and facility factors with changes in patient-reported pain and health-related quality of life. Methods: Data to determine eligibility were extracted from national VA databases. The sample was drawn from patients receiving LTOT and associated with primary care panels of = 500 patients at VA facilities. Within each VA facility, patients were selected at random from randomly selected primary care providers. Eligibility criteria: 1) LTOT defined as = 180 days of opioid medications dispensed with no gaps >40 days between prescriptions in the past 6 months; 2) Patients treated for opioid use disorder, cancer, dementia or end-of-life care in the prior 12 months were excluded. Eligible patients were contacted until they responded or opted out. We sent up to 5 mailings: notification letter, survey packet, reminder postcard, second survey packet, and second postcard. Two weeks after the final mailing, patients were called up to 3 times and offered a telephone interview. Voice mails were

left if participant was not reached. Contacts were tracked using a custom study application. Opioid doses were converted to morphine equivalent (ME) mg using standard formulas. Daily dosage category was defined as follows: low (<50 mg), moderate (50-99 mg), high (100-199 mg), very high (=200). Results: Of 14,114 patients contacted, 9,238 (65.5%) participated, 1656 (11.7%) refused, and 3220 (22.8%) did not respond. Study staff called 5,512 patients and spoke with 3172 (57.5%). Of all responders, 772 (8.4%) responded via telephone and an additional 504 (5.5%) returned a mailed survey after phone contact. Responders who completed a telephone survey are 8.3% of male responders, 9.5% of female responders, 8.0% of white responders, and 10.3% of black responders. Telephone mode effort was approximately 1168 person-hours total or 55 minutes per additional completed response. Conclusions: Using a mixed mode approach with telephone calls after multiple mailings increased respondents by 1,276 (absolute response rate increase 9.0%) and improved representation of women and black patients.

Research Topic: Other Chronic Diseases
Funding agencies: HSR&D
Grant support: VA Health Services Research and Development Service (HSR&D) IIR #14-295

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48. Spontaneous Pain In A Monoarticular Osteoarthritis Murine Model: Effect Of Gender And Chronicity On Weight Bearing

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

Abstract: Purpose: To examine gender differences in spontaneous weight bearing pain behaviors in C57Bl6 mice with osteoarthritis (OA) in order to better define pain behaviors in this important model of arthritis pain. Methods: Male and female C57Bl6 mice were examined at twelve weeks of age. Chronic OA was produced by intra-articular (IA) injection of 10 IU Type IV Collagenase into the left knee. The contralateral, non-arthritic knee served as the non-painful control. Pain behavior was measured at four or six weeks post-collagenase injection. Spontaneous pain behaviors were measured by Automated Dynamic Weight Bearing (ADWB) (Bioseb, Vitrolles, France). Evoked pain response (EPR) was measured by calculating fights and vocalizations over a time period of 1 min with repeated firm palpation of the knees (tenderness). Analgesic therapies included 0.02 IU onabotulinum toxin (BTX), 10 µl 0.01% capsaicin (CAP), or 10 µl 0.001% resiniferatoxin (RTX). Results: OA produced significantly increased evoked pain responses ($p < 0.05$) in both male (4.0) and female mice (6.31) after 4 weeks. However, 4 weeks after arthritis induction, neither male nor female mice demonstrated any significant alteration in weight bearing on the arthritic left hind limb. At 4 weeks, female arthritic mice spent a significantly greater percentage of time (61.07, $p < 0.001$) and a greater proportion of weight (21.81, $p < 0.002$) on the forelimbs than nonarthritic mice (36.99, 12.64, respectively). IA BTX in the arthritic joint corrected this offloading in female mice. Arthritic male mice at 4 weeks did not seem to offload the arthritic limb either to the normal contralateral hind limb or to the forelimbs, but after 6 weeks of arthritis, male mice demonstrated increased weight (15.82%) and time (45.22%) on forelimbs ($p < 0.05$) compared to 8.23% and 27.23% weight and time respectively. Both IA CAP and RTX normalized forepaw weight bearing in the arthritic male mice. Interestingly, evoked pain responses were not increased in male mice after 6 weeks of arthritis. Conclusions: These data demonstrate that collagenase induced arthritis pain is detectable in male and female C57Bl6 mice. Joint tenderness is increased in both sexes early in disease and demonstrates an analgesic response. Alterations in weight bearing were seen in both males and females with OA and normalized with IA analgesics, but weight bearing changes in males only appeared after arthritis was more chronic and evoked pain had resolved. Osteoarthritis pain

Research Topic: Degenerative Diseases of Bones and Joints
Funding agencies: RR&D
Grant support: Refining the effect of articular neurotoxin on joint pain and neurochemical signature.

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49. VA Cooperative Studies Program (VA CSP) Network of Dedicated Enrollment Sites (NODES)

Lederle, Frank [1]; Adabag, Selcuk [1]; Condon, Debra [1]; Kantorowicz, Alexandra [1]

1. Minneapolis VA Health Care System

Abstract: The VA Cooperative Studies Program (VA CSP) Network of Dedicated Enrollment Sites (NODES) is a consortium of VA Healthcare Systems that have facility-based teams dedicated to conducting VA CSP Research. The specific aims 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. A Director, Co-Director, Manager, Administrator, and Research Nurse support these efforts at each individual NODES location. NODES shares facility-derived best practices and provides local insights to VA CSP partners for efficient management and conduct of all study activities. The following achievements reflect cumulative data of the NODES sites from October 2012 – Present: Established cross-coverage on all open CSP studies. NODES staffing incorporated as part of local CSP study teams. Created Mentorship Program for new local study coordinators. Created procedures for recruiting at CBOCs. Work stream meetings on improving study design & procedures. Beta testing case report forms. Enhanced recruitment through Mobile Recruiting Equipment. Reduced

logistical and staffing barriers. Development of Partnership between NODES and Non-NODES facilities to assist in study teams with low recruitment. Publication in JAMA. Accepted publication in Contemporary Clinical Trials Communications. Creation of VA CSP-NODES Executive Board.

Research Topic: Health Systems
Funding agencies: CSR&D
Grant support: VA CSP

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50. Pattern of Distant Metastasis in Oropharyngeal Squamous Cell Carcinoma in a Veteran Population

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2. Department of Laboratory Medicine and Pathology, Minneapolis VA Health Care System
3. Department of Hematology and Oncology, Minneapolis VA Health Care System

Abstract: Outcome Objective: To investigate the incidence and pattern of distant metastasis (DM) in oropharyngeal squamous cell carcinoma (OPSCC) in the Veteran population. Methods: Retrospective chart review of all patients diagnosed with OPSCC from 2005-2015 in Minneapolis Veterans Affairs Healthcare System was performed. Patient demographics, tumor staging, p16 status, and the characteristic of DM were reviewed. Patients with other active malignancy simultaneously or lack of follow up were excluded. Results: A total of 169 consecutive patients diagnosed with OPSCC were included. 30 patients (17.8%) were identified to have DM. 7/30 patients presented with DM during initial workup, 23/30 patients developed DM after treatment. P16 status was available in 140/169 patients. The rate of DM was 14.7% (14/95) in P16 positive patients and 22.2% (10/45) in P16 negative patients (P = 0.3). The most common site of DM was lung (26/30), followed by bone (8/30), liver (5/30), brain (3/30) and skin (3/30). 11/30 patients developed DM in multiple sites. There was no significant difference of DM pattern between P16 positive and negative patients, however there is a trend towards higher percentage of multiple DM in p16 positive patients (42.9% vs 30.0%). Conclusion: To our knowledge, this is the first report of the incidence and pattern of DM in OPSCC of the Veteran population. Despite higher rate of tobacco and alcohol exposure, the incidence and pattern of DM in the Veteran population have no significant difference comparing P16 status, although there is a trend towards higher percentage of multiple DM in p16 positive patients.

Research Topic: Cancer
Funding agencies: UMN
Grant support: Lion's Grant

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51. Demographic variation in smokers' attitudes about continued smoking after normal lung cancer screening results: is screening seen as a 'pass'?

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

Abstract: Introduction: Lung cancer screening (LCS) offers the opportunity to address smoking in a high-risk population. There are concerns that a normal scan may be seen as a 'health certificate' or 'pass' to keep smoking. We assessed smokers' attitude towards continued smoking after a normal screen among LCS-eligible Veterans, and evaluated associations between this attitude and demographic characteristics. Methods: Longitudinal survey of participants in the Minneapolis VA Health Care System LCS Clinical Demonstration Project. 926 eligible patients were randomly invited to participate in screening, with mailed surveys at 3 and 9 months. We included smokers who completed the 3 month survey (n = 168) and both surveys (n = 140). Respondents reported how strongly they agreed with the hypothetical statement, 'If I had a normal CT scan result, I could continue to smoke without worry.' On follow-up survey, they reported their smoking behavior. For screened Veterans (n = 48), results were extracted from medical records. Results: 67 of 168 [40%] respondents supported (i.e., did not disagree) that they could continue smoking without worry if they had normal scan results. Support for continued smoking varied with age, with more supporters aged 65 and older compared with younger Veterans (49% vs. 33%; P < 0.05). Among Veterans who underwent screening and received a normal screening result (N = 13), all patients who supported continued smoking (n = 5) smoked daily at follow-up. Conclusions: Our results suggest that the health certificate effect may be relevant in LCS, especially among older smokers. This may limit the effectiveness of tobacco cessation interventions offered at the time of screening. Implications: Smokers' views towards smoking cessation in the setting of lung cancer screening are largely unknown. Previous studies have not demonstrated a clear effect of screening on smoking behavior. Our results show that over a third of smokers eligible for screening endorse the statement that "If I had a normal CT scan result, I could continue to smoke without worry," with this attitude more prevalent among smokers over 65. Smokers, particularly older smokers, may see a normal lung cancer screening result as a 'pass' to continue smoking, potentially limiting the effectiveness of integrated tobacco interventions.

Research Topic: Cancer
Funding agencies: HSR&D
Grant support: VA Lung Cancer Screening Pilot Initiative

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52. International Study of Comparative Health Effectiveness with Medical and Invasive Approaches: ISCHEMIA

Maron, David [1]; Johnson, Debra [2]; Herrmann, Rebekah [2]; Ishani, Areef [2]; Bertog, Stefan [2]; Siddiqui, Rizwan [2]; Garcia, Santiago [2]; Hansen, Ronnell [2]; McFalls, Edward [2]

1. Stanford University
2. Minneapolis VA Health Care System

Abstract: Objective: To compare an initial invasive strategy of catheterization and optimal revascularization (PCI or CABG) + optimal medical therapy (OMT) with a conservative strategy of OMT alone, with catheterization reserved for OMT failure. Significance: Ischemic heart disease is the leading cause of death and disability worldwide and affects 17,600,000 Americans, resulting in about 450,000 deaths in the United States annually. Globally, 7.2 million deaths are caused by ischemic heart disease each year. Medical therapy (medication and lifestyle changes) should always be used to treat ischemic heart disease. Many doctors routinely use an invasive approach in addition to medical therapy to treat ischemic heart disease; however, it is not known if this approach is better than medical therapy alone as the initial treatment of patients with stable ischemic heart disease. Trial Design: The study population will consist of 8,000 patients from over 400 international sites. Minneapolis VAMC enrolling 20 participants. Patients with stable ischemic heart disease and at least moderate ischemia on stress test will be randomized to an invasive strategy of cardiac catheterization followed by revascularization with PCI or CABG in addition to optimal medical therapy, or a conservative strategy of optimal medical therapy alone with cardiac catheterization and revascularization reserved for patients who fail medical therapy. Key Inclusion Criteria: 1) AT LEAST MODERATE ISCHEMIA by stress test modality (ECHO, CMR, NUC, ETT); 2) Willing to comply with all aspects of the protocol, including adherence to medical therapy, follow-up visits, and assigned strategy. Key Exclusion Criteria: 1) LVEF < 35%; 2) History of unprotected left main stenosis >50%; 3) Prior known coronary anatomy unsuitable for either PCI or CABG; 4) History of noncompliance with medical therapy; 5) Acute coronary syndrome < 2 months; 6) PCI < 12 months; 7) Canadian Cardiovascular Society Class III angina of recent onset; 8) Canadian Cardiovascular Society Class IV angina, including unprovoked rest angina; 9) Prior CABG (if preformed >12 months ago with anatomy amenable to PCI or repeat CABG); 10) Stroke < 6 months or intracranial hemorrhage; 11) NYHA class III-IV heart failure or hospitalization for exacerbation of CHF < 6 months.

Research Topic: Heart Disease
Funding agencies: NIH
Grant support: ISCHEMIA is sponsored by a grant from the U.S. National Heart, Lung, and Blood Institute of the National Institutes of Health.

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53. Predicting Posttraumatic Growth in Veterans: The Role of Coping Mechanisms and Personality

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2. Department of Pyschology, University of Minnesota

Abstract: It is already widely established that there are negative psychological effects following a traumatic event, such as posttraumatic stress disorder (PTSD). However, there is some indication that individuals may experience posttraumatic growth (PTG) following such events. This study explores factors including coping mechanisms, PTSD symptom severity, and personality characteristics to better understand the process that facilitates growth following a trauma. The sample included 271 Veterans who completed surveys measuring PTSD symptoms, trauma exposure, personality traits, and posttraumatic growth. Results showed that adaptive coping mechanisms were predictive of posttraumatic growth, and an inverted-U shaped relationship was found to best explain the relationship between PTSD symptoms and PTG. Among Veterans with PTSD, those who experienced growth following trauma exposure scored higher on extraversion, agreeableness, openness, and lower on neuroticism and pessimism. In addition, all five subscales of the posttraumatic growth inventory were significantly correlated with adaptive coping mechanisms. As cognitive coping mechanisms have been suggested to be changeable, these findings have potential implications for clinical intervention.

Research Topic: Mental Illness
Funding agencies: DOD; UMN
Grant support: N/A

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54. Use of chlorhexidine for long-term prevention of ventilator associated pneumonia: A retrospective chart review

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1. St. Cloud VA Health Care System

Abstract: Research Question: Does long-term use of 0.12% chlorhexidine (CHX) for oral care decrease the risk for ventilator associated pneumonia (VAP) in intubated residents? Ventilator associated pneumonia (VAP) is an extremely serious complication of mechanical ventilation. There is significant interest in strategies/treatment that reduce the incidents of VAP. There is clearly documented evidence that the use of (CHX) either alone of in combination with additional oral cares reduces the incidence of VAP in intubated patients in the acute care setting. There is little research on the use of CHX in the long-term care setting. The population understudy in this research are the Veterans residing in a VA Medical Center on long-term mechanical ventilators. The independent variable is administration of 0.12% CHX verses baseline. The dependent variable is the rate of VAP in this population as represented by the number of days that IV antibiotics have been administered on a daily basis. Information was collected regarding incidents of VAP per 1000 days of ventilator care for all Veterans who have received mechanical ventilation since January 2009. Sample/Methods: This study is a retrospective chart review. Given the highly specialized nature of the VA Respiratory Dependent Unit (RDU) program and small sample size, a quasi-experimental design incorporating the use of single-subject multiple baseline procedures was conducted. Although less common in VA settings, single-subject designs have been well demonstrated in rehabilitation, special education, and other setting with small sample sizes. For this study, a maximum number of 12 records of Veterans on the RDU who received mechanical ventilation. All Veterans received CHX as part of their oral health care. Frequency data (i.e., number of days on IV antibiotics administered for VAP) will be collected by review of medical records and recorded on a weekly/monthly basis from approximately 6-12 months before administration of CHX (baseline phase), monthly 6 -12 after the administration of CHX (treatment phase), and at follow-up session 6-12-24 months (follow-up phase). Results: Findings suggest a positive relationship between the use of CHX and a significant reduction in the number of days of IV antibiotic use in Veterans on mechanical ventilation suggesting a reduction in VAP. This is one of the first studies to demonstrate long-term effectiveness of CHX to decrease incidents of VAP.

Research Topic: Central Nervous System Injuries & Associated Disorders
Funding agencies: N/A
Grant support: N/A

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55. Comparison of dictation and electronic templates documentation modalities as the primary means of documenting operative reports in CPRS.

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

Abstract: Background: The limitations of Computerized Patient Record System (CPRS) used at Veterans Health Administration (VHA) hospitals precluded the surgeons from the direct entry of the operative reports. More specifically, operative reports could only be dictated. This problem was solved through the collaboration between our surgeons, software engineers, and health information management services (HIMS), who developed electronic templates as an alternative to dictation. The purpose of this study is to determine whether direct input of the operative reports into the electronic health record (EHR) by the VHA surgeons using templates: i.) results in more complete and accurate documentation of a surgical procedure; ii.) causes faster availability of the full operative reports in CPRS; iii.) has the potential to reduce costs for the VHA; iv) saves time for the surgeon. Methods: A retrospective quality control study of 130 operative reports produced by 5 staff surgeons at the Minneapolis VA Hospital. Half of these randomly selected reports was dictated, while the other half was generated with the aid of electronic templates. Results: A mean of 97% (SD=+/-7%) of the templated and 94% (SD=+/-11%) of the dictated operative reports were complaint with all eight criteria measuring their completeness and accuracy ($P = 0.053$). Signed operative reports produced with the aid the templates were added to the patients' EHR after a median of 53 minutes, while it took 91 hours 39 minutes for those that were dictated ($P < 0.001$). In aggregate, VHA could save $13,477,715 per fiscal year by documenting operative reports with the aid of electronic templates instead of dictation. In addition, with the aid of the electronic templates documentation time per operative report could be reduced by as much as 75.2% for every VHA surgeon. Conclusions: The implementation of the electronic templates instead of dictation will enable a timelier addition of accurate and complete operative reports to the patients' EHR, save a substantial amount of money for the VHA, and reduce the documentation time for its surgeons.

Research Topic: Health Systems
Funding agencies: N/A
Grant support: N/A

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56. Cell growth of Immortalized Arachnoid Cells in the Presence of Fibroblasts and Blood Products

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2. Minneapolis VA Health Care System

Abstract: Background: The pathophysiology of non-obstructive hydrocephalus involves alteration in cerebrospinal fluid (CSF) pathways. The exact mechanism is unknown, but as arachnoid CSF egress is a major route of CSF removal, damage or alteration to the growth of arachnoid cells may influence the rate of CSF absorption. We investigated the effect of soluble factors secreted by fibroblasts and the presence of blood products on arachnoid cell growth. Methods: An immortalized arachnoid cell line was developed and cells were grown on semipermeable membranes in a culture chamber. Arachnoid cells were plated in Transwells®, with fibroblasts separated from the arachnoid cells. Cell phenotype was analyzed and cell growth rates were determined by manual counts. Similar experiments were conducted with biliverdin, bilirubin, as well as fibroblast challenge. DNA content in the cell cultures was then determined as corroborative data. Cell counts for the additional arachnoid cell lines were calculated at each day and represented the controls. Results: Cell counts increased with each time point. Arachnoid cells in the three experimental conditions showed a statistically significant decrease in cell counts for each day when compared to the control group. Post hoc analysis showed differences between the control and experimental conditions but no significant difference between groups. The DNA content for each experimental condition was reduced at all time points when compared to the control arachnoid cells, but only became statistically significant at day 7. Conclusion: Inflammation and hemorrhage are two common conditions associated with the development of hydrocephalus. The arachnoid membrane is exposed to fibroblasts and blood products (bilirubin, biliverdin) in these conditions, and their effect on arachnoid cell growth was studied. We have shown that arachnoid cell growth decreases in the presence of fibroblasts, bilirubin, and biliverdin. Given its intimate relationship with CSF, it is possible that the decreased growth of arachnoid cells may affect absorption and thus contribute to the development of hydrocephalus.

Research Topic: Central Nervous System Injuries & Associated Disorders
Funding agencies: MVMREF
Grant support: VA Merit Review Grant #1I01BX001657-01

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57. Molecular characterization of fecal Escherichia coli isolates from households (HHs) of Veterans, focusing on sequence type 131 (ST131) and other fluoroquinolone (FQ)-resistant E. coli (FQREC).

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

Abstract: Background: Among Veterans, FQREC infections are a significant problem and are caused mainly by E. coli ST131, a recently emerged disseminated clonal group. Infecting FQREC strains emerge from the host's gut reservoir. The molecular characteristics of colonizing ST131 strains and other FQREC among Veterans and their HH contacts may determine which strains persist or cause infection, but as yet are undefined. Methods: Fecal surveillance of 290 randomly selected Veterans and their 300 HH members (including 143 pets) showed that 81 subjects (of 590 total) from 290 households carried ST131 and/or FQREC. Fecal E. coli from households with at least one ST131 and/or FQREC-colonized member were characterized molecularly. Ten E. coli colonies per sample (as available) underwent PCR-based clonal screening. One isolate per clone underwent phylotyping, virulence genotyping, sequence type (ST) determination, and pulsotyping. Results: The 590 total subjects yielded 501 unique (by clone and subject) fecal E. coli isolate. Of these, 61 were FQREC (of which 30 [49%] were ST131) and 49 were ST131 (of which 30 [61%] were FQREC); 210 were from the 86 HHs with at least one ST131 and/or FQREC-colonized member. These 210 E. coli isolates (149 FQ-susceptible [FQ-S], 61 FQREC) included 7 of the 8 E. coli phylogroups (% of 210): B2 (45%), D (17%), B1 (16%), A (12%), F (6%), E (4%), and C (0.5%). Compared with FQ-S isolates, FQREC isolates were more often from group B2 (61% vs. 38%: $P = 0.003$) and had numerically higher virulence gene (VG) scores (median, 10 [range 1-14] vs. 6 [1-19]). The 49 ST131 isolates had significantly higher VG scores than the 161 non-ST131 isolates overall (median, 12 [6-20] vs. 6 [1-19]: $P < 0.001$) or the 31 non-ST131 FQREC (7 [1-12]: $P < 0.001$). The 30 FQREC ST131 isolates had slightly but significantly lower VG scores than the 14 FQS ST131 isolates (median, 12 [6-14] vs. 13 [11-20]: $P < 0.001$). Overall, ST131 was the most prevalent defined ST (23%), followed distantly by ST73 and ST141 (5% each). Pulsotypes varied greatly. Virulence-associated pulsotype 968 accounted for 33% of FQREC ST131 isolates. Conclusion: Among Veterans and their HH contacts ST131 is the single most common cause of FQREC colonization. Colonizing ST131 FQREC strains exhibit extensive VG profiles and represent classic pathogenic pulsotypes. Such colonization likely contributes to the high burden of ST131 disease among Veterans, and may be amenable to preventive interventions.

Research Topic: Infectious Diseases
Funding agencies: NIH; MVMREF
Grant support: T32 AI055433, VA Merit Review grant # 1 I01 CX000920-01A1

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58. Million Veteran Program (MVP): A Partnership with Veterans

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1. Minneapolis VA Health Care System

Abstract: Purpose: The goal is to improve Veterans' health through the collection and testing of blood samples and health information to learn which genes are linked to which health characteristics. MVP is a national, voluntary research program conducted by the Department of Veterans Affairs, Office of Research & Development, that collects genetic and health information to help find new ways of prevention, early detection, and treatment of illnesses. MVP will provide a better understanding of how genes affect health and illness, with the goal of improving health care for Veterans. Genomic analyses, including SNP genotyping, whole genome sequencing, and whole exome sequencing is being conducted on MVP samples. Nationally, 558,693 Veterans have enrolled at 60 VAs with 13,759 at the MVAHCS as of 4-7-17. Methods: Participation involves: 1. Filling out two surveys through the mail 2. Completing a one-time, approximately 20 minute, study visit to provide a blood sample for the genetic testing 3. Permitting authorized MVP staff to access information in your medical record on an ongoing basis 4. Agreeing to future MVP contact. Next Steps - MVP Data Analysis: The first projects approved to utilize the MVP data are focused on issues that are relevant in our Veteran community. These studies will not only provide valuable research results, but are also helping to develop and streamline the data access procedures for future researchers. Current Studies (*Coordinated by VA Boston & VA CT Health Care Systems): The Genetics of Functional Disability in Schizophrenia and Bipolar Illness*, Bronx VAMC; Miami VAMC. Genomic Study of Posttraumatic Stress Disorder*, San Diego VAMC; VA Connecticut Health Care System. Genomics of Gulf War Illness in Veterans*, VA NJ Health Care System; VA Cooperative Studies Epidemiology Center Durham. Genetic Vulnerability of Sustained Multi-substance Use in MVP, VA Connecticut Health Care System; Philadelphia VAMC. Cardiovascular Disease Risk Factors, Prevalent Cardiovascular Disease, and Genetics in the Million Veteran Program, Atlanta VAMC; Boston VA Health Care System. Pharmacogenomics of Risk Factors and Therapies Outcomes for Kidney Disease, VA Tennessee Health Care System. Genetics of Cardio-metabolic Disease in the VA Population, VA Palo Alto Health Care System; Philadelphia VAMC. Genetic Risk for AMD in Diverse Veteran Populations, Cleveland VAMC; VA Western NY Healthcare System

Research Topic: Personalized Medicine & Genomics
Funding agencies: CSR&D
Grant support: VA Cooperative Studies Program (VA CSP)

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59. The Effect of COMT Val158Met Polymorphism and Age on the Glucose Uptake Levels in the Anterior Cingulate

Myers, Olivia [1]; Pardo, Jose [1]; Lee, Joel [1]

1. Minneapolis VA Health Care System

Abstract: The dominant theory of human cognitive aging holds that decline in prefrontal cortical function may have a causal influence on age-associated cognitive decline in otherwise healthy elders. At least in part, this functional decline appears correlated with declining prefrontal dopamine levels that occur with age. The catechol-O-methyltransferease (COMT) enzyme degrades dopamine and is the primary determinant of dopamine levels in the human prefrontal cortex. A functional variant of COMT with a valine at position 158 of the protein shows increased metabolism for dopamine. Consistent with a pivotal role of dopamine in cognition and aging, healthy elders with this Val COMT polymorphism show increased aging-related cognitive decline. Recent work conducted by Dr. Jose Pardo indicates that the principal site of age-associated dysfunction in brain metabolism localizes to the part of the prefrontal cortex known as the anterior cingulate cortex (ACC). It has been shown that the declining ACC metabolism that occurs with aging in otherwise healthy subjects correlates with declining executive function as measured with tests of verbal fluency. These findings therefore motivate the hypothesis that COMT genotype will modulate the changes in ACC metabolism and associated cognitive dysfunction during aging in healthy humans. This study will use data from the Alzheimer's disease Neuroimaging Initiative (ADNI) to test the hypothesized relationship between COMT genotype, ACC metabolism as measured by glucose uptake and positron emission tomography with age.

Research Topic: Aging
Funding agencies: N/A
Grant support: N/A

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60. Buprenorphine/Naloxone Treatment Outcomes - A 12-Year Experience at the Minneapolis VAHCS

Neumeister, Kristen [1]; Swanson, Heather [2]; Westermeyer, Joe [2]; McNairy, Scott [1-2]

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

Abstract: Background: Opioid abuse is epidemic in the United States and the demand for more providers offering medication-assisted treatment (MATx) options for opioid dependence is high. At present, there remains limited data to guide providers on the optimal length of

therapy or adjunctive interventions to help increase outcome success. The Drug Abuse Reporting Program (DARP) Outcome Criteria, an under-recognized rating scale first published in 1975, remains a viable and comprehensive measurement of global outcome of drug treatment. By utilizing the modified DARP criteria, the purpose of this study was to evaluate if the length of buprenorphine/naloxone therapy and patient participation in a peer support group increased the likeliness of treatment success. Methods: A retrospective chart review was completed on patients who had received at least six consecutive months of buprenorphine/naloxone therapy through the Minneapolis Veterans Affairs Health Care System (MVAHCS). Modified DARP criteria was collected on each patient by means of either chart review or patient interview comparing those still on with those off RX. Results: Treatment success, as determined by decreased DARP scores by at least seven points, was seen significantly more often in those patients who were still on buprenorphine/naloxone therapy when compared to those no longer on therapy. While continued buprenorphine/naloxone therapy demonstrated a much higher incidence of outcome success, no clear correlation was identified between the degree of outcome success and length of therapy or participation in peer support group therapy. Discontinuation of treatment however was a significant loss of overall daily function from successful to non successful. There were 28/150 unexpected deaths among those off treatment (all causes). These findings highlight both the morbidity and mortality among chronic relapsing opioid dependent patients. Conclusions: This study provided important insight into the treatment of opioid dependence buprenorphine/naloxone and highlighted the utility of the DARP in measuring broader definitions of treatment success and global function over time. Outcomes support the current guideline recommendations that length of buprenorphine/naloxone therapy should not be rigidly predetermined and should be individualized based on patient progress and tolerability of the treatment.

Research Topic: Substance Abuse
Funding agencies: N/A
Grant support: N/A

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61. Using GoutPro to Make Medical Trainees Gout Pros

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

Abstract: Background/Purpose: Gout is the most common type of inflammatory arthritis in the U.S. Gout also has a large impact on health care costs in the U.S. with $6 billion dollars spent annually. Over 2 million visits to primary care providers (PCP) each year are gout related. Current gout care from PCPs is felt to be suboptimal in the U.S. Barriers to improving care in gout include limited education during medical training, perception of non-importance by providers, and the lack of PCP continuing medical education. In an attempt to address limited education during training, we developed a digital adjunctive teaching tool, GoutPro. Utilizing a clinically integrative model proposed by Khan et al, it takes into consideration different learning styles, current gout guidelines, interactive activities and clinical problem solving. The overall goal of our teaching intervention is to improve medical trainee knowledge and interest in gout. Methods: 15 medical residents and students from the University of Minnesota participated in a 1 hour GoutPro teaching session. The session was a Fellow led didactic using our GoutPro software. GoutPro is structured with lecture content on slides with integrated multiple choice questions. We also incorporated scored mini-games to increase audience participation and satisfaction. At the end of the session, there was a simulation in which participants made clinical decisions based on an evolving scenario. Feedback was provided on choices participants made. Participants utilized their smart devices to operate GoutPro as a means of interacting anonymously during the session. Our primary outcome measure was participant satisfaction assessed by post- session survey. Our secondary outcome measure was level of interest in the topic of gout, educational value of the tool, and usefulness of the tool also assessed by a post-session survey. A descriptive analysis of the data was performed. Results: 1. All subjects were satisfied with the GoutPro session. 2. All subjects agreed that their level of interest increased, and that it was fun, interactive, educational, and likely to effect future patient management. Conclusions: The GoutPro session was effective, fun, interactive and educational. All participants were satisfied with the session. Our study demonstrates that GoutPro can be used as a teaching tool to increase participant satisfaction and interest. Further studies will be needed to assess change in knowledge and quality measures.

Research Topic: Other Chronic Diseases
Funding agencies: N/A
Grant support: N/A

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62. Preventing Perioperative Cardiac Complications

Nguyen, Jennifer [1]; Herrmann, Rebekah [1]; Garcia, Santiago [1]

1. Minneapolis VA Health Care System

Abstract: Major non-cardiac surgery can improve quality of life and longevity of a patient, but it is not without risks. Cardiac complications include myocardial infarction, injury, cardiac arrest, congestive heart failure, or sudden death, and account for at least one-third of perioperative deaths. Recent statistics estimate that of 100 million patients world-wide having a non-cardiac surgical procedure, approximately 1 percent, or 1 million patients, will experience a serious medical complication with major perioperative cardiac complications

as the highest contributor. Multiple studies which have been conducted to prevent perioperative cardiac complications through a safe and effective intervention have thus far been unsuccessful. One promising method was thought to be remote ischemic preconditioning (RIPC). RIPC are brief, nonlethal episodes of ischemia and reperfusion applied to one vascular territory (i.e., the forearm) that confers cardioprotection to remote tissues in the rest of the body, such as the heart. In other words, it is an intervention that is applied elsewhere on the body to potentially prepare the heart against injury from the cardiac stressors that occur during surgery. The mechanism by which RIPC achieves cardioprotection remains unclear, but it may be that preconditioning in the remote vascular territory produces a cardioprotective chemical signal that is conveyed to the heart, where activation of signaling pathways within the heart facilitates this effect. a pilot study of RIPC among 200 patients undergoing vascular surgery. The Cardiac Remote Ischemic Preconditioning Prior to Elective Vascular Surgery trial (CRIPES), was a prospective, randomized, phase 2 trial investigating the effects of RIPC versus a sham control before elective vascular surgery. It was designed to assess the feasibility, efficacy, and safety of using RIPC prior to vascular surgery, and to obtain preliminary estimates of its effects on detectable postsurgical increases in cardiac troponin I (cTnI), a surrogate marker of myocardial injury and perioperative myocardial infarction. Consenting subjects (n = 201) were randomized to RIPC (n = 100) or a sham procedure (n = 101) which was administered 12 to 24 hours before surgery.

Research Topic: Health Systems
Funding agencies: MVMREF
Grant support: VA Office of Research and Development #1IK2CX000699-01

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63. The Aphasia Communication Outcome Measure as an Indicator of Communicative Functioning

Nicholson, Hannele [1]; St. Jacque, Ann [1]; Hula, William [2]; Irwin, William [3]; Doyle, Patrick [2]; Kellough, Stacey [2]; Cox, Lindsey [3]

1. Minneapolis VA Health Care System
2. VA Pittsburgh Healthcare System
3. Tennessee Valley VA Medical Center

Abstract: The ACOM is a 59-item patient-reported measure of communicative functioning developed using item response theory (IRT) methods (Baylor et al., 2011). The purpose of the ACOM is to provide speech-language pathologists and their clients with aphasia with a psychometrically robust instrument for measuring the impact of aphasia on everyday communicative functioning from the client's perspective. The present study reports an "incremental validity" approach (Sechrest, 1963) that tests whether ACOM scores can be validly interpreted as a measure of patient-reported communicative functioning. An incremental validity approach measures whether the target measure contributes unique variance over and above other candidate variables in predicting a relevant criterion variable. We asked whether the ACOM scores of 41 participants with aphasia would predict communication-related well-being when controlling for the contributions of aphasia severity and the frequency of general negative mood states. Participants were recruited in the metropolitan areas of the Minneapolis, Pittsburgh and Nashville/Murfreesburo VA hospitals. All participants completed the ACOM, the Burden of Stroke Scale (BOSS), the Comprehensive Aphasia Test (CAT) and the Geriatric Depression Rating Scale (GDRS). Communication-related well-being was operationalized using the BOSS Communication-Associated Psychological Distress scale (CAPD; Doyle et al., 2003). The BOSS CAPD assesses the extent to which communication difficulties affect the 1) frequency of negative moods, 2) patient satisfaction with life and 3) participation in valued life activities. Aphasia severity was estimated using the CAT modality mean T-score. Scores from the GDRS, which measures depression, were also included. The BOSS CAPD data were regressed on ACOM, CAT and BOSS Negative Mood. In a separate model, BOSS CAPD was regressed on ACOM, CAT, and GDRS scores, with the hypothesis that the GDRS and BOSS Negative Mood scores would produce similar results in this context. The ACOM and BOSS Negative Mood score contributed significant and nearly equal unique variance to the BOSS CAPD Score. CAT scores were not a significant predictor. The second model including the GDRS in place of the BOSS Negative Mood Scale produced similar results. These results support the validity of ACOM scores as a measure of patient-reported communicative functioning, as distinct from aphasia severity, general negative mood, and communicative-related well-being.

Research Topic: Central Nervous System Injuries & Associated Disorders
Funding agencies: RR&D
Grant support: VA RR&D 5I01RX001963-02 Responsivenss, Stability, and Validity of Patient-Reported Outcomes in Aphasia

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64. Validation of Impact Test for Prosthetic Feet

Nickel, Eric [1]; Morin, Steve [1]; Voss, Gregory [1]; Koehler-McNicholas, Sara [1]; Hansen, Andrew [1-2]

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

Abstract: Introduction: In combat, Service Members often find it necessary to jump down from elevated platforms, such as the cargo bed of a vehicle. For Service Members with lower limb amputations, if their prosthesis fails in combat, they become vulnerable to enemy action. At present, there is no accepted standard to simulate impact loading of prosthetic feet. We developed an impact test system to investigate impact resilience of prosthetic feet. Testing has been performed on one specimen to validate the measurement variability, inter-rater

variability, and impact velocity. Methods: The test system drops specimens vertically with the foot plantarflexed 20 degrees and mass equal to half of the user's body weight to simulate shared loading on both limbs. Laser lines project onto rulers indicating specimen height above the base. Ten measurements of the resting (statically loaded) height by one operator were used to calculate measurement variability. Eight measurements of the height at contact with the base (unloaded) were performed by three operators to calculate inter-rater variability. A specimen was dropped 0.1m and was increased by 0.1m until failure. Videos (120fps) were analyzed to determine impact velocity, which was used to calculate impact energy ($E = 0.5*m*v2$). The impact energies were compared to theoretical freefall (potential energy, $E = m*g*h$). Results: The measurement standard deviation was 0.06mm. The standard deviation between raters was 1.4mm. The specimen failed at a drop height of 0.6m. The difference between the calculated and theoretical impact energy was 4.7%. Conclusion: The velocities in the frame prior to impact were on average within 2.3% of theoretical freefall (impact energy within 4.7%). A sensitivity analysis showed that varying the length of the "smear" band by 1mm resulted in a 7.5% change in impact energy. This suggests that the system is achieving freefall within the measurement error of ±1mm. For future analyses, the impact energy can be assumed to be equal to the potential energy of the drop. Measurement variability was below 1mm indicating repeatability within measurement error. Inter-rater variability was greater than 1mm. Future testing should be conducted by one rater for consistency. Significance: This impact test system accurately simulates freefall. It is suitable for testing prosthetic feet to determine impact resilience and may be useful in supporting decisions regarding prostheses for return-to-duty applications.

Research Topic: Other Chronic Diseases
Funding agencies: DOD
Grant support: BADER Consortium, a DoD, Congressionally Directed Medical Research Programs cooperative agreement (W81XWH-11-2-0222)

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65. Plasticity as a predictor of response to cognitive remediation

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

Abstract: Individuals vary considerably in the extent to which they are able to benefit from cognitive remediation (Kurtz et al., 2008). Response to cognitive training is measured in terms of transfer, meaning the magnitude of performance change on untrained conceptually similar (near transfer) and different (far transfer) tasks. This study examined plasticity, defined as training task performance change, as a predictor of transfer to untrained tasks. Sixty-three individuals with schizophrenia who completed 48 1-hour sessions of a working memory focused cognitive remediation training protocol were included in the analysis. Participants completed 2-3 hours of training each week on a variety of working memory, short-term memory, and complex attention tasks. Change in N-back performance during the course of intervention was used to measure plasticity. Post-intervention, change on the N-back training task was a significant predictor of near transfer to an untrained measure of attention, MCCB Attention (IP-CPT), $p < 0.05$. In contrast, baseline cognitive performance on the MCCB Overall composite as well as MCCB Attention and Working Memory indices were not significantly related to near transfer. These finding suggest that plasticity may be an important predictor of an individual's ability to benefit from cognitive training interventions.

Research Topic: Mental Illness
Funding agencies: RR&D
Grant support: Rehabilitation Merit Award D6981R

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66. Category Fluency Task Performance in Healthy Older Adult Population: A comparison of the "vegetable" and "animal" categories

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2. Minneapolis VA Health Care System

Abstract: Measuring cognitive function with age is important in the assessment and treatment of neurodegenerative diseases such as Alzheimer's disease (AD). Category Fluency Task (CFT) was designed to measure executive control and cognitive function (Shao et al., 2014). The CFT measures the production of exemplars within a defined semantic category in a measured interval of time. It is uncertain which semantic category type in the assessment is superior in capturing cognitive decline due to age. Semantic categories such as "vegetables" and "animals" previously were used indiscriminately to measure cognitive decline in older adults. Using data from the Alzheimer's Disease Neuroimaging Initiative (ADNI), a longitudinal study investigating the onset and progression of AD in healthy older adults aged 55-90 years, we calculated correlations between performance on the "animal" and "vegetable" categories of the CFT and age to determine which of these two commonly used semantic categories is most sensitive to age related cognitive decline. We found that the vegetable category is not significantly more sensitive to cognitive decline ($p = 0.221$), and that both categories are not as strongly correlated with age as we predicated (vegetable: $r = -0.165$; animal: $r = -0.074$). These results diverge from previous research which suggested vegetable category to be more sensitive to cognitive decline with age than the animal category (Monsch et al., 1992). However, factors such as education and occupation

could account for the noted disparities and serve as an area for further research. Using an assessment instrument sensitive in capturing age-related cognitive decline is especially crucial in the older adult population as this is when significant cognitive decline occurs, signaling onset of neurodegenerative diseases such as Alzheimer's disease. A sensitive measure can help in early detection of Alzheimer's disease allowing for early treatment that could slow the progression of the disease.

Research Topic: Aging
Funding agencies: CSR&D
Grant support: N/A

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67. Skin Self-Screening Camera for Veterans with Spinal Cord Injury

Olney, Christine [1]; Leetsma, Jennifer [2]; Hansen, Andrew [1,3]; Ferguson, John [1,3]; Murphy Kruse, Mary [1]; Goldish, Gary [1,3]

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

Abstract: Purpose: Our multidisciplinary team has developed a smart phone camera system to aide in SCI Veterans performing skin self-screening inspection. Here we present the development process used by engineers, clinicians and Veterans with SCI to arrive at the current design. Background: Veterans with spinal cord injury are at high risk for developing a pressure injury.1 To prevent development of a pressure injury the Veteran with SCI is encouraged to invoke multiple prevention strategies.2 One recommended prevention strategy is to conduct twice daily skin self-screenings. Skin self-screening is usually conducted in the bed, prior to arising in the morning and prior to sleep in the evening. The Veteran with SCI examines at-risk areas for changes in their skin integrity such as discoloration, swelling, or changes in skin texture using a long handled mirror. In the event there is a change to skin integrity, the pressure injury prevention protocol advises the Veteran with SCI to off-load that area for at least 24 hours. Further, he/she is advised to consult with their skin specialist if the area does not resolve to normal color or texture within that next 24-hour period. Significance: The consequences of ignoring an early stage pressure injury can be serious e.g. weeks to months of hospitalization to heal the injury, tens to hundreds of thousands of dollars in healthcare costs, possible surgery to close the wound and possibly death.3 Finding a pressure injury in the early stages of development and intervening immediately, such as repositioning, can improve the trajectory of the injury. Conclusion: We anticipate this skin self-screening device will offer to persons with SCI other options besides the standard mirror or personal camera for skin self-screening. We have applied for funding to test the efficacy of this skin self-screening camera system within the VA Health Care System. 1. Chen, Y., DeVivio, M.J., Jackson, A. B. Pressure ulcer prevalence in people with spinal cord injury: Age-period-duration effects. Arch Phys Med Rehabil; June 2005; Vol 86. 2. Consortium for Spinal Cord Medicine Pressure Ulcer Prevention and Treatment Following Injury: A Clinical Practice Guideline for Health-Care Providers (2nd Ed.). Washington, D.C.: Paralyzed Veterans of America, 2014. 3. Krause, J.S., Carer, R., Pickelsimer, E.E., & Wilson, D. A prospective study of health and risk of mortality after spinal cord injury. Arch Phys Med Rehabil, August 2008; 89(8); 1482-1491

Research Topic: Sensory Loss
Funding agencies: MVMREF
Grant support: N/A

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68. Human brain metabolism, amyloid, vascular disease: Anterior cingulate cortex (ACC) & cognitive aging

Pardo, José [1]; Lee, Joel [1]

1. Minneapolis VA Health Care System

Abstract: Introduction: Otherwise healthy aging in seniors is associated with declining executive function, while neurodegenerative disorders (Alzheimer's Diseases AD) hit many brain functions especially memory. By far, the anterior cingulate cortex (ACC) is the principal locus of declining metabolism during normal aging—this decline in activity correlates with behavioral declines in executive function.[1] In contrast, the principal locus of brain metabolism in early AD is the posterior cingulate cortex (PCC) that has most to do with memory and the hippocampus.[2] The ACC mediates high level attentional functions.[3] Deficits detected in healthy elders predict subsequent evolution of AD 12 years later.[4] The ACC is the only brain region that thickens with aging[5]; level of education, a protective factor for AD, also correlates with ACC thickness.[6] Goals: To examine the large ADNI dataset for several aims: 1). Confirm the ACC result from our own dataset of healthy elders converges with those from ADNI; 2). Evaluate whether the degree of amyloid deposition and presence of vascular risk factors impacts upon ACC metabolism Methods: Healthy subjects (ages 56+) underwent longitudinal cognitive assessments; FDG & amyloid PET. Recruitment and protocols were designed and implemented by ADNI. Whole brain normalization used the cerebellum. Voxel-wise correlations between age and parameter were used for display. Thresholds were grossly estimate by resels (FHWM). Conclusions: Profound ACC hypometabolism with healthy aging converges with our findings from a previous independent dataset. There was no significant correlation between amyloid deposition and age. In the absence of vascular risk factors, ACC metabolism with age remained significant. In the absence of vascular risk, the correlation between amyloid and age remained insignificant. These findings suggest that neither amyloid nor vascular risk factors are driving

the aging-related ACC hypometabolism. Defining the pathophysiological mechanisms behind aging related ACC metabolic decline that correlates with declining executive function is a priority for translation to preserve quality of life and delay or prevent dementia in elders.

Research Topic: Aging
Funding agencies: CSR&D
Grant support: Merit ("The Anterior Cingulate Cortex and Cognitive Aging"; 5I01CX000501) PI Jose Pardo

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69. Prevalence of Past Year Complementary Integrative Health and Other Nonpharmacological Pain Management Approaches among OEF/OIF National Guard Veterans

Polusny, Melissa [1-2]; Donaldson, Melvin [2]; Erbes, Christopher [1-2]; Kehle-Forbes, Shannon [1-2]; Hagel Campbell, Emily [1]; Leverty, David [2]; Krebs, Erin [1-2]

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

Abstract: Combat deployment is associated with increased risk of chronic post-deployment pain problems with many individuals turning to complementary integrative health (CIH) approaches to manage chronic pain. Despite the evidence that CIH use is widespread, little is known about its use among combat Veterans for chronic pain management. The current study examines the prevalence of past-year use of nonpharmacological approaches to chronic pain management among a longitudinal cohort of combat-deployed National Guard Veterans. Data were obtained from the Readiness and Resilience in National Guard Soldiers (RINGS) Study, a longitudinal investigation of post-deployment health among a cohort of National Guard Veterans deployed to Iraq and Afghanistan. Participants enrolled in the study were invited to complete a follow-up survey in 2015-2016 that assessed participants' experiences with chronic pain, pain-related beliefs and coping, health-related beliefs, mental health symptoms, substance abuse, quality of life, and nonpharmacological pain management strategies. Pain-related disability was assessed using the Graded Chronic Pain Scale. Past-year use of nonpharmacological pain management strategies was assessed using self-report survey items adapted from the National Health Interview Survey and refined with cognitive interviews. Three pain management categories were examined: 1) active CIH approaches (e.g., yoga, meditation/mindfulness, tai chi), 2) practitioner-delivered CIH therapies (e.g., chiropractic, massage, acupuncture), 3) active conventional approaches (e.g., stretching-strengthening exercise, aerobic exercise, psychotherapy). Response rate was 48.3% (N = 1850). Nearly half (n = 747; 48.4%) reported chronic pain, with 40.7% (n = 304, 19.9% of sample) reporting disability as a result of it. Veterans with any chronic pain had higher rates of use of practitioner-delivered CIH therapies (42.8%-48.5%) compared to those with non-chronic pain (29.2%). Among Veterans with chronic pain with interference, chiropractic treatment (37.8%) was the most prevalent CIH modality used for pain management followed by massage (25.1%), while stretching-strengthening exercise (29.1%) was the most prevalent conventional modality used. CIH pain management approaches, especially practitioner-deliver therapies, are being widely utilized by National Guard Veterans. Findings may inform the development of patient-centered integrative, self-management approaches to pain management for Veterans.

Research Topic: Military Occupations & Environmental Exposures
Funding agencies: NIH
Grant support: R01AT008387-01 National Center for Complementary and Integrative Health (NCCIH)

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70. The Effect of Chlorhexidine on the Oral and Lung Microbiota in Chronic Obstructive Pulmonary Disease

Pragman, Alexa [1]; Haupert, Richard [2]; Reilly, Cavan [2]; Wendt, Chris [1]

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

Abstract: Bacteria are important in COPD, with approximately 50% of COPD exacerbations attributed to respiratory pathogens. Patients with COPD are often colonized with bacteria in their lower respiratory tracts even during periods of stable disease. This community of bacteria, or microbiota, may be a key factor in the pathogenesis of COPD by causing exacerbations and promoting inflammation. Using culture-independent methods we were among the first to show that the lung microbiome in COPD is reflective of oral flora. Studies have demonstrated that individuals with COPD have decreased mucociliary clearance and are more prone to aspiration due to reduced laryngotracheal mechanosensitivity. Therefore, we theorize that individuals with COPD have an altered lung microbiota due to increased aspiration of the oral microbiota; this altered lung microbiota contributes to disease manifestations. Chlorhexidine has broad-spectrum bactericidal activity and is used in oral rinses to reduce oral bacteria. Our hypothesis is that twice daily oral rinses with the topical antiseptic chlorhexidine will result in a decrease in the lung microbiota biomass. Furthermore, we postulate that a decrease in lung microbiota will improve symptoms associated with COPD. Our study showed that the COPD lung microbiota consists of bacteria also found in the upper airway. This finding is not due to contamination of the lung sample. The bronchial and lung tissue microbiota are very similar to each other. The upper airway microbiota directly accounts for ~50% of the taxa found in the lung microbiota. The remaining ~50% of taxa reflect either ecologic drift of upper airway taxa (shifts in relative abundance of aspirated bacteria upon reaching the lung) vs. environmental

contamination. In a blinded analysis of subjects receiving twice-daily oral rinses with either chlorhexidine or placebo, oral wash and induced sputum 16S rRNA copy numbers declined over the 8-week study period.

Research Topic: Lung Disorders
Funding agencies: NIH; MVMREF
Grant support: NIH: 1UL1RR033183-01; 8UL1TR000114-02. ALA: RG-348261

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71. Palliative Care In A U.S. Veterans Hospital ALS Program

Ratner, Edward [1-2]; Ratner, Nathan [2]; Lei, Zhang [2]; Stern, Erin [1]; Bradshaw, Katherine [1]; Bateman, Anne [1]

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

Abstract: Background: ALS is a progressive and inevitably fatal motor neuron disease. The AAN Care Guidelines recommend palliative care as a mainstay for ALS treatment. Since prognosis at end stages of ALS is predictable, referral to hospice is considered optimal. Research Question: Does the addition of longitudinal palliative care including home visits to an ALS program improve utilization of hospice care? Research site: MVAMC ALS Clinic, that has a census of ~60. Methods: Retrospective Chart Review, death between 2010-2015. Measures were utilization of hospice and survival after referral to hospice. Statistics: Student t, Wilcoxon, Kaplan Meier. Intervention: Home-based palliative care consultations, starting in 2012. Outcomes: From 2010-2012, 32/70 (46%) of patients were referred to hospice. From 2013-2015, this rate increased to 59 /69 (86%) ($P < 0.001$). Survival after referral to hospice also increased from a median of 17 days to 60 days. ($P < 0.001$). Conclusions: It is possible to embed palliative care professionals in an ALS team to provide consultative home visits and eventually assume primary care. This model is associated with significantly more frequent use of hospice compared to standard models. This model is associated with significantly earlier referrals to hospice. Enrollment in hospice is NOT associated with a reduction in length of survival. A very high percentage of patients with ALS are appropriate for referral to hospice, typically 2 to 6 months prior to death. Summary: Integrating longitudinal palliative care that includes home visits into an ALS program improves patterns of use of hospice, without shortening of life.

Research Topic: Central Nervous System Injuries & Associated Disorders
Funding agencies: N/A
Grant support: N/A

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72. Classification of Movement and Inhibition Using a Hybrid BCI

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Abstract: Following a stroke, patients may be unable to properly execute movements. The motor pathways of these patients run the risk of developing aberrant plasticity that could lead to diminished or slower recovery of motor capabilities. Brain-computer interfaces (BCIs) interpret brain electrical activity into actions, often using motor imagery (MI) as the controlling signal, and could complement stroke patient rehabilitation. MI involves imagining movements without physically performing them, and as such can be produced by individuals who are unable to execute motor commands due to a disability. Virtual reality (VR) is a useful tool for providing feedback on MI performance that the patient needs to promote healthy plasticity and improve motor recovery. One aspect that has been neglected in current BCIs is incorporating the interplay between motion and inhibition, or the ability to precisely start and stop movements, as well as canceling unwanted movements before they occur. To improve BCI action classification, we propose using a hybrid BCI (hBCI) that employs both event-related potentials (ERPs) and MI to classify motion and inhibition. ERPs are generated by go and stop cues in inhibitory tasks: the go/no-go (GNG) and stop-signal tasks (SST). These tasks are done in a gamified VR environment to improve user cooperability and feedback. The hBCI classifies the MI signal, discriminating between reaching and grasping, as well as between left and right hand. Meanwhile, the ERP dictates whether that action should start, be inhibited, or stop. To improve training of the BCI to the individual, both MI and ERP signals help dictate the feedback shown in the VR environment. Furthermore, we propose a machine learning algorithm that will change the extraction and weight of features, as well as frequency bands, based on the success and failure of the algorithm's prediction of the user's intent to move or inhibit. The hBCI proposed is a promising tool for improving the usability of BCIs in stroke rehabilitation. By employing a gamified VR environment using inhibition tasks, the patient is engaged and feedback is improved. Furthermore, by employing both MI and ERP to classify movements, as well as a machine learning algorithm, the hBCI's interpretation of the EEG signal is improved. The hBCI would provide a better experience for users by reducing training time, improving signal identification, and allowing users to more easily stop their movements.

Research Topic: Central Nervous System Injuries & Associated Disorders

Funding agencies: N/A
Grant support: Steven Collazos is supported by: National Science Foundation Graduate Research Fellowship #00039202

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73. Deep Brain Stimulation (DBS) might not be treatment for all Parkinson's Disease (PD) patients: Modeling Study

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Abstract: One of the main treatments for a neural disorder such as Parkinson's Disease (PD) is Deep Brain Stimulation (DBS) in the Subthalamic Nucleus (STN). The outcome of DBS surgery has its benefits and its drawbacks. The surgery leads to a decline in the symptoms for PD subjects but can have various negative effects like speech impairment, cognitive decline, and thus, it is very important to be cognizant of when side effects of the surgery and procedure outweigh the benefits. The modeling study findings show the degradation of the effectiveness of STN-DBS as a function of time, the progression of the side effects of PD with STN-DBS, and the quantification of the quality of life of PD patients with and without STN-DBS over time. This approach shows the time at which the side effects of PD outweigh the benefits of having STN-DBS surgery for patients with PD by using the model of the regression of STN-DBS effectiveness as a function of time. This was done by looking at 270 patients from various studies and modeling the data collected. The data includes the Unified Parkinson's Disease Rating Scale (UPDRS), gait freezing, a number of falls, postural instability, hallucinations, mood/depression, and quality of life rating (PDQ-39 Score). The research conducted indicates a simple model defining the effectiveness of STN-DBS as a function of time.

Research Topic: None indicated
Funding agencies: N/A
Grant support: N/A

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74. Multi-institutional Outcomes of Endoscopic Management of Stricture Recurrence after Urethroplasty

Sukumar, Shyam [1]; Elliott, Sean [2]; Erickson, Bradley [3]

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2. University of Minnesota
3. University of Iowa

Abstract: Introduction and Objective: Approximately 10-20% of patients will have a recurrence after urethroplasty. Initial management of these recurrences is often with urethral dilation (UD) and direct vision internal urethrotomy (DVIU) but the success rates of these procedures are not well known. Methods: We retrospectively reviewed bulbar urethroplasty data from 5 surgeons from the Trauma and Urologic Reconstruction Network of Surgeons (TURNS). Men who underwent UD or DVIU for a <17F lumen plus symptoms of recurrence were identified. Analyses compared success rates of recurrence management (UD vs. DVIU) and initial urethroplasty type (substitution vs. excisional repair, EPA) using time to event statistics: Kaplan Meier curves and Cox regression models. Failure of UD or DVIU was defined as the inability to pass a 17Fr cystoscope through the urethra into the bladder. Results: There were 53 men with recurrence that were initially managed endoscopically, 10 with UD and 43 with DVIU. Mean time to recurrence after urethroplasty was 7.6 months. At a mean follow-up of 16.3 months after UD or DVIU, success was 41.5% in the overall cohort: 48.8% for DVIU vs. 10% for UD. Kaplan Meier curves are shown in Figure 1. On Cox modeling, UD had a higher rate of subsequent failure compared to DVIU (hazard ratio, HR: 3.15, $p = 0.03$). Patients undergoing EPA had a trend towards higher rates of recurrence after secondary endoscopic procedures vs. those undergoing substitution urethroplasty (HR: 2.41, $p = 0.05$) Conclusion: DVIU is more successful than UD in the management of stricture recurrence after bulbar urethroplasty. DVIU appears to be more successful for patients with a recurrence after a substitution urethroplasty compared to after an EPA, perhaps indicating a different mechanism of recurrence for EPA (ischemic) versus substitution urethroplasty (technical)

Research Topic: Acute & Traumatic Injury
Funding agencies: N/A
Grant support: N/A

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75. VA CSP 2005 Veterans Affairs Lung Cancer Surgery or Stereotactic Radiotherapy (VALOR)

Thompson, Katie [1]; Wetherbee, Erin [1-2]; Silva, Joaquin [1]

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

Abstract: Non-small cell lung cancer (NSCLC) kills 5,500 Veterans each year. Recently the National Lung Screening Trial demonstrated a 20% decrease in lung cancer mortality through earlier screening. In response, the VHA plans to implement a system-wide program to screen up

to 1,000,000 Veterans each year. This program is expected to increase the number of Veterans diagnosed with stage I NSCLC by 60-100%. For lung cancer patients diagnosed with stage I disease, a surgical resection has been the standard of care. The average 5-year overall survival rate is 58-77%, and lung cancer surgery carries a 90-day perioperative mortality risk of up to 5%. Emerging data suggests that stereotactic body radiation therapy (SBRT) can provide superior patient outcomes with 3-5 outpatient treatments. While the global experience with SBRT represents thousands of patients, its use has primarily been limited to frail and elderly patients who are medically inoperable and often die of co-morbidities. Over the past decade, various reports have suggested that long-term survival with SBRT is comparable to surgery. Although evidence- based guidelines have yet to endorse SBRT as an acceptable alternative to surgery, radiation oncologists around the world have begun to treat increasing numbers of operable patients. Several single-institution reports of SBRT in medically operable patients with stage I NSCLC now suggests that long-term survival rates may in fact be higher when compared to surgery, particularly since the 90-day mortality rate is approximately 0%. A sample size of 670 randomized study participants is required to obtain at least 85% power to detect a 10% absolute difference in 5-year overall survival rate between surgery and SBRT at the 0.05 significance level. A total of 16 VHA facilities with dedicated multi-disciplinary teams of lung cancer specialists, active programs in thoracic surgery and and radiation oncology, and facility commitments to recruit patients into this study have been identified. With accrual of 9-10 patients each year/per site, it is estimated that accrual can be completed within 4 years after six ramp-up sites recruit 60 subjects in one year. Patients will be treated with either surgical resection or SBRT. Patients will be followed for at least 5 years to compare the primary outcome overall survival. Secondary endpoints include comparisons of cause of death, patterns of relapse, quality of life, changes in respiratory function, and health state utilities.

Research Topic: Cancer
Funding agencies: HSR&D
Grant support: VA CSP

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

Thompson, Katie [1]; Johnson, Debra [1]; Garcia, Santiago [1-2]; McFalls, Edward [1-2]

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2. University of Minnesota

Abstract: The Randomized Endo-vein Graft Prospective (REGROUP) trial (ClinicalTrials.gov NCT01850082) is a randomized, intent-to-treat, 2-arm, parallel-design, multicenter study funded by the Cooperative Studies Program (CSP No. 588) of the US Department of Veterans Affairs. Cardiac surgeons at 16 Veterans Affairs (VA) medical centers with technical expertise in performing both endoscopic vein harvesting (EVH) and open vein harvesting (OVH) were recruited as the REGROUP surgeon participants. Subjects requiring elective or urgent coronary artery bypass grafting using cardiopulmonary bypass with use of =1 saphenous vein graft will be screened for enrollment using pre-established inclusion/exclusion criteria. Enrolled subjects (planned N = 1150) will be randomized to 1 of the 2 arms (EVH or OVH) after an experienced vein harvester has been assigned. The primary outcomes measure is the rate of major adverse cardiac events (MACE), including death, myocardial infarction, or revascularization. Subject assessments will be performed at multiple times, including at baseline, intraoperatively, postoperatively, and at discharge (or 30 days after surgery, if still hospitalized). Assessment of leg-wound complications will be completed at 6 weeks after surgery. Telephone follow-ups will occur at 3-month intervals after surgery until the participating sites are decommissioned after the trial's completion (approximately 4.5 years after the full study startup). To assess long-term outcomes, centralized follow-up of MACE for 2 additional years will be centrally performed using VA and non-VA clinical and administrative databases. The primary MACE outcome will be compared between the 2 arms, EVH and OVH, at the end of the trial duration.

Research Topic: Heart Disease
Funding agencies: HSR&D
Grant support: VA CSP

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77. Impact of Apathy Status on Verbal Fluency

Tianxiang, Fang [1]; Pardo, Jose [1-2]; Lee, Joel [2]; Vorobyov, Yelena [2]

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

Abstract: As people age, their cognitive abilities decline. In this study, the verbal fluency score was used as a measure of cognitive function. The verbal fluency test measures how many category examplars (e.g., BIRDS: robbin, bluejay, etc.) a participant can produce in a given time. Our previous study suggests that verbal fluency score is not correlated with age in a healthy older adult population. However, the degree of apathy (i.e., the loss of interest and activity of a person with their environment) can influence verbal fluency. Furthermore, apathy can be seen in aging-related neurodegeneration such as in Parkinson's disease and Alzheimer's disease. In this study, the apathy status and apathy severity are measured through the Neuropsychiatric Inventory Questionnaire. We analyzed the differences in the verbal fluency score between apathetic and non-apathetic subjects. The test results showed that both animal and vegetable fluency scores differ based on apathy status. The mean vegetable fluency score in the apathetic group was significantly less than the mean vegetable fluency score in the non-apathetic

group (p = 0.0003); the mean animal fluency score in the apathetic group was significantly less than the mean animal fluency score in the non-apathetic group (p = 0.00005). Results indicate that the verbal fluency score can be influenced by apathy status. According to Lezak (1995), verbal fluency tests are commonly used as clinical batteries for the cognitive psychology and neuropsychological investigations. The tradition to use the verbal fluency test aims to find the semantic memory impairment, but one's score on the verbal fluency task may be a reflection of their apathy status but not a reflection of their general cognitive abilities. Further study is suggested to determine if the verbal fluency score is also affected by other aspects in the Neuropsychiatric Inventory Questionnaire such as low mood or depression.

Research Topic: Aging
Funding agencies: CSR&D
Grant support: Alzheimer's Disease Neuroimaging Initiative (ADNI); Merit (5I01CX000501)

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78. Nanomedicine targeting of protein kinase CK2 for cancer therapy

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2. University of Minnesota
3. GeneSegues Therapeutics

Abstract: BACKGROUND. Protein kinase CK2 (former name Casein Kinase II or 2) is recognized as a major cellular signal that plays a critical role in cell growth, proliferation and suppression of cell death. CK2 is expressed ubiquitously, but its involvement in cancer is indicated by its universal dysregulation in all cancers examined. We originally proposed CK2 as a target for cancer therapy. To that end, we have shown in cell culture and xenograft tumor models that molecular downregulation of CK2 results in cell death. To achieve cancer specific delivery, the therapy agent (RNAi-CK2, targeting both catalytic subunits) is administered in an encapsulated form (called TBG nanocapsule). To move the therapy forward, it is important to undertake evaluation of the therapy in "large animal" models of disease. To that end, we decided to expand our therapy studies to include feline oral squamous cell carcinoma (OSCC) which bears strong resemblance to human head and neck squamous cell carcinoma (HNSCC). Methods: TBG-CK2-RNAi was examined for its activity in xenograft models of prostate and breast cancer and HNSCC. CK2 targeting in feline oral cancer cell cultures was examined. 9 feline patients diagnosed with OSCC were enrolled in a trial. The cats received 2 dose levels in a 3+3 escalation, totaling 6 treatments. Pre- and post-treatment biopsy specimens of tumor and normal mucosa were examined for CK2 signal, toxicity, and tumor response. Results: CK2 targeting in feline oral cancer cells resulted in induction of apoptosis in vitro. In cats treated with TBG-RNAi-CK2, the most common adverse effect of the drug was grade 1 or 2 weight loss and anorexia. Tumors from 2 cats showed reduction in CK2 signal. Overall, no serious toxicity was apparent. Studies of treatment of prostate and breast cancer and HNSCC in xenograft models showed a decline in tumor volumes in vivo without any apparent toxicity, and loss of CK2 signal and markers of cell death were detected. Conclusions: The present findings provide support that TBG-RNAi-CK2 warrants further evaluation for its use as a cancer therapy modality. Relevance to Veteran's Health: Cancer is a major concern area for Veteran's health. The need for better therapy that will eradicate the disease is paramount. Our work represents a step in that direction.

Research Topic: Cancer
Funding agencies: BLR&D; NIH
Grant support: 1IO1B001731, 1IO1BX003282, CA-150182, 1UL1 RR033183 (KA)

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79. Neural and Behavioral Abnormalities in Bipolar Disorder and Schizophrenia: An Event-related Potential (ERP) Study using a Stop Signal Task

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Abstract: Both schizophrenia and bipolar disorder are characterized by poor inhibition of behavior (Fortgang, Hultman, van Erp, & Cannon, 2016). To date, no studies have been published comparing electroencephalogram (EEG) data from both groups while they complete a stop signal task that is thought to measure motor inhibition (Logan & Cowan, 1984). In our study, we examined the behavioral and electrophysiological indices in patients with schizophrenia, patients with bipolar disorder, and healthy controls using a stop signal task. The purpose of this comparison was to determine if shared or distinct neural abnormalities were present in these groups while they engaged in a motor inhibition task. Preliminary analyses suggested that the schizophrenia group, but not bipolar disorder group, had significantly longer reaction times than the healthy controls while responding to speeded reaction time stimuli. It was found that the ERPs of the healthy controls were altered depending on the probability of needing to inhibit a behavioral response while patient groups failed to show similar ERP modulations, suggesting limited ability of patient groups to incorporate contextual probabilistic information to shape behavior. In schizophrenia group such an abnormality is accompanied by a generalized slowing in behavioral responding.

Research Topic: Mental Illness
Funding agencies: NIH
Grant support: CSMRF I01CX000227 (from the Veterans Health Administration) and R24MH069675 (from the NIMH)

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80. Association of sleep-disordered breathing and risk of future all-cause hospitalization and rate of facility care days in older men: the Osteoporotic Fractures in Men (MrOS) Study

Vo, Tien [1]; Kats, Allyson [1]; Langsetmo, Lisa [1]; Taylor, Brent [1-2]; Schousboe, John [1,3]; Kwon, Younghoon [4]; Stone, Katie [5]; Redline, Susan [6]; Barrett-Connor, Elizabeth [7]; Ensrud, Kris [1-2]

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Abstract: Study objectives: To determine whether sleep-disordered breathing (SDB) is independently associated with increased risk of all-cause hospitalization and number of inpatient and post-acute facility care days among older men. Methods: Study setting: the Osteoporotic Fractures in Men Study. Study sample: 1316 men (mean age 76.1 yrs) who participated in the Sleep Visit (SV) and had Medicare claims data. SDB measures were collected using polysomnography. Primary predictor: apnea-hypopnea index (AHI) = number of apneas and hypopneas/hr of sleep. Severity of sleep apnea: defined by clinical criteria: AHI <5 (normal), AHI 5 to < 15 (mild), AHI = 15 (moderate/severe). Secondary predictor: % of time during overnight sleep in which arterial oxygen saturation was below 90% (%TST < 0.90). Severity of nocturnal hypoxemia: (%TST < 0.90) < 1% (none), (%TST < 0.90) 1.0% to < 3.5% (mild), (%TST < 0.90) = 3.5% (moderate/severe). Incident hospitalizations and post-acute facility days: calculated from claims data in the 3-year interval after the sleep test. Results: 523 (39.7%) men had at least 1 hospitalization in the 3-year period. Compared to those without sleep apnea, men with moderate to severe sleep apnea had a higher age and site-adjusted odds of hospitalization (OR = 1.43, 95% confidence interval[CI] 1.07-1.90); associations were attenuated after multivariable adjustment for traditional prognostic factors, however the associations remained statistically significant (OR = 1.36; 95% CI 1.01-1.83). Among men who were hospitalized, those with mild sleep apnea had the lowest total length of stay, with age/site-adjusted rate ratio [RR] (RR = 0.62, 95% CI 0.43-0.90) compared to those without sleep apnea, with similar association in the fully adjusted models. The adjusted mean total facility days/year was 1.85(95% CI 1.31-2.27) among men without sleep apnea, decreasing to 1.28 (95% CI 0.91-1.51) among men with mild sleep apnea and increasing to 1.53 (95% CI 1.09-1.91) among men with moderate to severe sleep apnea. There was no statistically significant association between nocturnal hypoxemia and hospitalization or subsequent stay. Conclusions: Older men with SDB have an increased risk of hospitalization partially explained by higher body mass index, demographics, poorer health status, and higher comorbidities. However, the increased risk of hospitalization did not translate into greater inpatient and post-acute care facility days among older men in this study.

Research Topic: Aging
Funding agencies: NIH
Grant support: R01 AG005407, R01 AR35582, R01 AR35583, R01 AR35584, R01 AG005394, R01 AG027574, and R01 AG027576.

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81. Role of Non-Pharmacological Interventions in the Treatment of Multiple Sclerosis: BDNF Theory

Wanberg, Lindsey [1]; Goodwin, Shikha [2]

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2. Brain Sciences Center, Minneapolis VA Health Care System

Abstract: Multiple Sclerosis is a debilitating disorder that affects 2.3 million people worldwide. Currently, there is no cure for multiple sclerosis. Thus, non-pharmacological interventions offer a compelling treatment option. They also allow patients with multiple sclerosis to take treatment in their own hands, with little or no side effects. In this paper, we will review the effects of major non-pharmacological interventions (exercise, yoga, meditation, cognitive training) on the structure and function of the brain in multiple sclerosis. This poster will illustrate that non-pharmacological interventions have widespread effects across the brain, and since brain-derived neurotrophic factor (BDNF) is found throughout the brain, could be the underlying factor. To date, research has not proposed a cohesive mechanism that define how non-pharmacological interventions strengthen the brain in patients with multiple sclerosis. We attempt to do this by developing an argument that non-pharmacological interventions increase BDNF levels in the brain and, therefore, strengthen the brain's ability to counteract the effects of multiple sclerosis.

Research Topic: None indicated
Funding agencies: N/A
Grant support: N/A

82. Exercise influences feeding behavior- A review of our previous experiments

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2. University of Minnesota

Abstract: Exercise influences energy balance, and we study whether exercise negatively affects energy intake in male rats. Here, we review our previous eight experiments, focusing on exercise vs. sedentary status in energy balance. Among the eight experiments, the age starting exercise intervention was from 2.5 months to more than 1 year old, the exercise term was from 7 days to 8 weeks, and the type of exercise included running wheel (8 exp.) and treadmill (3 exp.). It is clear that exercise reduced body weight gain (vs. sedentary animals) in all recruited rats with different ages. However for food intake during exercise, age seems to be an important factor. It appears that in young animals (about 3 months old, < 400 g of body weight), exercise in short-term (7-10 days) reduced daily and cumulated food intake; while with long-term (> 30 days) exercise their daily food intake was increased compared to sedentary rats, eventually leading to no difference in total food intake during entire exercise phase (vs. sedentary), despite their body weight gain was still reduced. This might be because young animals need to have extra energy to meet requirement for both exercise and body growing (indicated by having positive weight gain during exercise). Quite different from young animals, in middle aged rats (6-month or above, >600 g of body weight), exercise reduced food intake in both short- and long-term vs. sedentary rats; and interestingly, the weight gain during exercise became negative, suggesting the rats with middle age might need no extra energy for physiological body growth. Regarding exercise approaches, running wheel exercise appears to be more effective than treadmill exercise in reducing food intake and body weight gain. There are variations among experiments (and individuals) in relationship of feeding and body mass change with exercise intensity. Some experiments (or individual animals) show feeding and body mass was negatively correlated with running distance; while no such association in other experiments, and even some individual animals exhibited a positive association between the two. As suggested by reviewing the data, age as the important factor needs to be considered for studying mechanisms of exercise-influenced food intake.

Research Topic: Other Chronic Diseases
Funding agencies: BLR&D; NIH
Grant support: Merit Review CP252, 1R01DK080782

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83. Contact Dermatitis To Personal Hygiene Soaps And Cleansers: Retrospective Analysis Of North American Contact Dermatitis Group Data 2000-2014

Warshaw, Erin [1-2]; Goodier, Molly [3-4]; Zug, Kathryn [5]; Belsito, Donald [6]; Zirwas, Matthew [7]; Fowler, Joseph [8]; Taylor, James [9]; Sasseville, Denis [10]; Fransway, Anthony [11]; DeLeo, Vincent [12]

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12. Department of Dermatology, Keck School of Medicine, Los Angeles, CA USA

Abstract: Background: There is limited information regarding contact dermatitis associated with personal hygiene products. Objective: (1) Evaluate the prevalence and (2) Identify allergens associated with contact dermatitis from personal soaps and cleansers. Methods: Retrospective cross-sectional analysis of NACDG data from 2000-2014. Results: Of the 32,945 tested patients, 1,069 (3.24%) had either an allergic (ACD) or irritant contact dermatitis (ICD) associated with a personal soap/cleanser. The majority were female (65.1%) and Caucasian (87.9%). Of those, 692 (64.7%) had allergy only, 350 (32.7%) had irritant only, while 27 (2.5%) had a combination of the two. ACD and ICD were significantly more often occupationally related (40.3%) as compared to the overall tested population (10.8%). The most common sites of dermatitis included hands (39.7%), generalized (12.7%), and arms (12.1%). Overall, over 50 allergens were associated with a personal hygiene source; the most common allergens included quaternium-15 (11.2%), cocamidopropyl betaine (9.5%), methylchloroisothiazolone (MCI) /methyl-isothiazolone (MI) (8.4%), coconut diethanolamide (7.9%), fragrance mix I (7.7%), Myroxylon pereirae (5.9%), 4-chloro-3,5-xylenol (5.8%), amidoamine (5.5%), and formaldehyde (4.4%). Conclusions: Many allergens, especially preservatives and surfactants, were associated with personal hygiene sources. As expected, most cases involved the hands, and many were occupationally related.

Research Topic: None indicated
Funding agencies: N/A
Grant support: N/A

84. Lithium For Suicidal Behavior In Mood Disorders (The Li+ Study: CSP 590)

Westermeyer, Joseph [1]; Dickmann, Patricia [1]; Donaire, Marti [1]; Perzynski, Joseph [1]

1. Minneapolis VA Health Care System

Abstract: Purpose: Randomized clinical trial specifically conducted to test lithium's efficacy in preventing suicides. Of primary interest is whether lithium leads to increases in the time to the first repeated episode of suicidal behavior, including suicide attempts, interrupted attempts, hospitalizations specifically to prevent suicide, and deaths from suicide. Additionally, this study will allow us to explore whether Lithium decreases the total number of suicidal behaviors, and whether it has comparable effects on impulsive and non-impulsive behaviors. Experimental treatment in this study supplements usual care for major depression or bipolar disorder, as well as VA's standard, enhanced management for patients at high risk. Methods: Participation involves: 1. Meeting with study staff regularly with follow-up lasting 12 months 2. Adherence to medication regimen according to study protocol 3. Willingness to have blood draws/vital signs taken regularly to maximize safety of medication 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: VA Funded; Office of Research and Development

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

Wilt, Timothy [1-2]; Greer, Nancy [1]; MacDonald, Roderick [1]; McKenzie, Lauren [1]; Rosebush, Christina [1]

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2. University of Minnesota

Abstract: Objective: Provide timely and accurate synthesis of targeted healthcare topics of particular importance to Veterans Affairs (VA) managers and policymakers as they work to improve the health and healthcare of Veterans. Methods: Each of the four ESP sites prepares three or more systematic reviews each year. Topic nominations come from VA Central Office, VISNs, or individuals in the field (e.g. National Program Directors, Chief Consultants, leaders of VA Task Forces). The reviews are developed using standard methods for development of key questions and scope, identification of included evidence, data extraction, data synthesis, and evaluation of risk of bias and strength of evidence. A Technical Expert Panel (TEP) is identified for each topic to guide topic development and assist in refining the key questions and scope of the review. Draft reports undergo peer review by content experts and policy partners. Final reports are posted on VA HSR&D website and disseminated widely throughout the VA. Management Briefs and Cyberseminars are key dissemination strategies. Results: For 2016, the Minneapolis VA ESP developed systematic reviews on The Effectiveness, Harms, and Cost of Alternative Care Models for the Treatment of Obstructive Sleep Apnea, Life Expectancy Calculators, and Women Veterans' Health Research Literature. Topics for 2017 are: Existing Measures for Patients with Chronic Pain, Social Determinants of Health for Veterans, and Enhanced Recovery after Colorectal Surgery. Conclusions: The Minneapolis VA ESP prepares evidence syntheses on important clinical practice topics relevant to Veterans. These reports help develop clinical policies informed by evidence, lead to the implementation of effective services to improve patient outcomes and to, and guide the direction for future research to address gaps in clinical knowledge. Funding Source: Department of Veterans Affairs, Veterans Health Administration, Office of Research and Development, Quality Enhancement Research Initiative (QUERI)Key Words: Systematic reviews, evidence-based, Veterans

Research Topic: None indicated
Funding agencies: HSR&D
Grant support: Department of Veterans Affairs, Veterans Health Administration, Office of Research and Development, Quality Enhancement Research Initiative

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86. The Prostate cancer Intervention Versus Observation Trial (PIVOT): Mortality follow up through nearly 20 years

Wilt, Timothy [1-2]

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Abstract: Background: We previously found no mortality differences between surgery and observation in men with localized prostate cancer. Uncertainty persists regarding nonfatal health outcomes and long-term mortality. Methods: Between 1994 and 2002, we randomly assigned 731 men with localized prostate cancer to radical prostatectomy or observation. We extended follow-up through August 2014 for our primary outcome, all-cause mortality, and main secondary outcome, prostate cancer mortality. We describe disease progression, treatments received and patient reported outcomes through January 2010. Results: During 19.5 years of follow-up (Median = 12.7 years), 223 of 364 men (61.3%)

assigned to surgery died compared to 245 of 367 (66.8%) assigned to observation (Absolute risk reduction (ARR) = 5.5 percentage points, 95% confidence interval [CI], -1.5, 12.4); Hazard ratio(HR)=0.84, 95% CI, 0.70, 1.01, P = 0.06). Prostate cancer mortality occurred in 27 men (7.4%) randomized to surgery vs. 42 men (11.4%) randomized to observation (ARR = 4.0, 95% CI, -0.2, 8.3; HR = 0.63, 95% CI: 0.39 to 1.02; p = 0.06). Radical prostatectomy may have reduced all-cause mortality among men with intermediate (ARR = 14.5 percentage points, 95% CI, 2.8, 25.6) but not low (ARR = 0.6 percentage points, 95% CI, -10.5, 11.8) or high risk disease (ARR = 2.3 percentage points, 95% CI, -11.5, 16.1)(P for interaction = 0.08). Surgery reduced disease progression treatment, primarily androgen deprivation therapy for asymptomatic, local or PSA progression, by 26.2 percentage points (95% CI, 19.0, 32.9). Urinary incontinence, erectile and sexual dysfunction were each greater with surgery through 10 years. Disease or treatment-related limitations in activities of day-to-day living were greater with surgery though 2 years. Conclusions: After nearly 20 years, surgery did not significantly reduce all-cause mortality or prostate cancer mortality compared with observation. Surgery had more adverse effects, but reduced disease progression and subsequent treatments; most asymptomatic, local or biochemical.

Research Topic: Cancer

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