Surgery Research Conference

Trauma and Acute Care Surgery
Research Update
July 11, 2018

To receive 1.0 credit for this session, text the SMS code: FEGROK to 414-206-1776. This code will expire in 5 days.

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Research Highlights
Congratulations to our Faculty
On their promotion to
Professor of Surgery

Dave R. Lal, MD, MPH
Division of Pediatric Surgery

Qing R. Miao, PhD
Division of Pediatric Surgery

Tracy S. Wang, MD, MPH
Division of Surgical Oncology
Congratulations on the promotion to Associate Professor of Surgery

Thomas W. Carver, MD
Division of Trauma and Acute Care Surgery
Dr. Carmen Bergom, receives 2018 Michael H. Keelan Jr., MD Scholar Award

“Unique genetic models to identify mediators of radiation-induced heart disease.”

Carmen R. Bergom, MD, PhD
Radiation Oncology, Surgery Research
SAVE THE DATE!

2018 Fall Research Symposium

The Fall Research Symposium will consist of research presentations, done in quick shot format, with special emphasis on projects completed during the summer in preparation for regional or national presentations.

Date: Friday, September 14th
Time: 12:00-4:00pm
Location: Helfaer Auditorium

Abstract submission deadline: August 14th, 5:00pm
Submit to Heidi

- Medical Students
- Residents
- Fellows
MCW Office of Research presents:

SAVE THE DATE!

Research Day

Date: Monday, September 24th
Poster Session: 1:00-3:00pm, HUB Gallery, 1st Floor
Keynote Address: 3:00-4:00pm, Kerrigan Auditorium

Michael Rosbash, PhD
Investigator, Howard Hughes Medical Institute
Peter Gruber Professor of Neuroscience, Brandeis University
**Publications**

June

### Pediatric Surgery

"Is isomerism a risk factor for intestinal volvulus?" *Journal of Pediatric Surgery.*
(Landisch RM, Loomba RS, Salazar JH, Buelow MW, Frommelt M, Anderson RH, Wagner AJ)

“Screening practices and associated anomalies in infants with anorectal malformations: Results from the Midwest Pediatric Surgery Consortium.” *Journal of Pediatric Surgery*

### Vascular/Cardiothoracic Surgery

“Migration of endovascular plug in hybrid repair of dysphagia lusoria.” *Journal of Vascular Surgery Cases & Innovative Techniques*
("Soo Hoo AJ, Rokkas CK, Rossi PJ)

### Surgical Oncology

“Improved surgical outcomes following radical cystectomy at high-volume centers influence overall survival.”

Urologic Oncology
("Scarberry K, Berger NG, Scarberry KB, Agrawal S, Francis JJ, Yih JM, Gonzalez CM, Abouassaly R)

“Studying a Rare Disease Using Multi-Institutional Research Collaborations vs Big Data: Where Lies the Truth?” *Journal of the American College of Surgeons*

### Vascular Surgery

“Endovascular management of an acute type B aortic dissection in a patient with fibromuscular dysplasia.” *Journal of Vascular Surgery Cases & Innovative Techniques*
(Man JH, Rothstein A, Patel PJ, Lee CJ)

### Pediatric Congenital Cardiac Surgery

“Total Artificial Heart Using Bilateral Paracorporeal Pulsatile Ventricular Assist Devices in an 8.2-kg Child.” *Annals of Thoracic Surgery*
(Woods RK, Kindel SJ, Mitchell ME, Hraska V, Niebler RA)
Cardiothoracic Surgery
“Current trends in bilateral internal thoracic artery use for coronary revascularization: Extending benefit to high-risk patients.”
Journal of Thoracic & Cardiovascular Surgery

“Uh-oh, some CO2 has gone missing.”
Journal of Thoracic & Cardiovascular Surgery
(Woods RK & Hoffman GH)

“Rotational Thromboelastometry Rapidly Predicts Thrombocytopenia and Hypofibrinogenemia During Neonatal Cardiopulmonary Bypass.”
World Journal for Pediatric & Congenital Heart Surgery
(Scott JP, Niebler RA, Stuth EA, ENeWman DK, Tweddell JS, Bercovitz RS, Benson DW, Cole R, Simpson PM, Yan K, Woods RK)

“Atrial fibrillation after transhiatal esophagectomy with transcervical endoscopic esophageal mobilization: one institution’s experience.”
Journal of Cardiothoracic Surgery
(Colwell EM, Encarnacion CO, Rein LE, Szabo A, Haasler G, Gasparri M, Tisol W, Johnstone D)

General Surgery
“Robotic skills can be aided by laparoscopic training.”
Surgical Endoscopy
(Davila DG, Helm MC, Frelich MJ, Gould JC, Goldblatt MI)

“The impact of preoperative anemia and malnutrition on outcomes in paraesophageal hernia repair.”
Surgical Endoscopy

“Preoperative immobility significantly impacts the risk of postoperative complications in bariatric surgery patients.”
Surgery for Obesity & Related Diseases
("Higgins RM, Helm M, Gould JC, Kindel TL)

Colorectal Surgery
“Pouch Volvulus in Patients Having Undergone Restorative Proctocolectomy for Ulcerative Colitis: A Case Series.”
Diseases of the Colon & Rectum
(Landisch RM, Knechtges PM, Otterson MF, Ludwig KA, Ridolfi TJ)
“The Word on Medicine: where Knowledge is changing life”

Fetal Surgery

July 28, 2018 3:00pm

Advanced Fetal Care: medical experts and patients discuss advanced fetal care and the Fetal Concerns Center of Wisconsin. Panelists for this show include Dr. Amy Wagner, Dr. Erika Peterson, Dr. John Kryger, Dr. Mohit Maheshwari, Kristi Rapp, Fetal Program Direct, and Kim Mangarelli, Nurse Care Coordinator. The show will also feature the stories of grateful patients who were willing to share their stories.
Next Month:

Education Surgery Research Update

Thomas W. Carver, MD  Michael Malinowski, MD  Andrew Kastenmeier, MD

Wednesday, August 8
5:00-6:00 pm
Location: Cancer Center Conference Room M
Next Month:

Special Surgery Research Conference

Academic Metrics: Understanding H-index and Blue Ridge NIH Award Rankings

Raul Urrutia, MD
Director, Genomics Sciences and Precision Medicine Center
Warren P. Knowles Professor of Genomics and Precision Medicine

Wednesday, August 15
5:00-6:00 pm
Location: HUB A1015/A1035
To receive credit for this session, text the SMS code: **FEGROK**
to **414-206-1776**. This code will expire in 5 days.
Trauma/Acute Care Surgery Research

Marc de Moya, MD
Chief of Division

Terri deRoon-Cassini, PhD
Director of Research
TRAUMA TIME-LINE

- Pre-Hospital
- Acute Phase
- Sub-Acute
- Recovery

- T0
- T3
- T12
- T>1week

Tourniquet Use
**Trauma**

**Pre-Hospital**
- Tourniquet Use

**Acute Phase**
- Thoracic Irrigation
- HDACI
- Pneumothorax Treatment
- B/P as a predictor of mortality in elderly
- FAST ultrasound
- Use of Ctscan in Penetrating Trauma
- Redefining the Cardiac Box
- Use of Pigtail catheters for Hemothorax
- Use of point of care TEG *

**Sub-Acute**
- Vascular Trauma Treatment
- Ketamine and Rib fx/QoL
- Vital Capacities to predict outcomes
- Management of Zone II Hematomas
- Rib Fixation
- Use of Early Intervention for PTSD

**Recovery**
- Prospective Rib Fracture Recovery
- Clavicular and rib fractures
- Tracheostomies
- Traumatic bile leaks
- Wound closure in open abd
- Trauma and Resilience
Acute Care Surgery

**Pre-Hospital**
- HDACI for Sepsis
- Role of CT-Scan in SBO
- Predictors of therapeutic laparotomy for ischemic bowel after cardiac surgery
- Use of AB103 in NSTI

**Acute Phase**
- Treatment of Adhesive SBO
- MIT-Treatment of Cholecystitis with Perc Chole

**Sub-Acute**
- MIT-appendicitis treatment
- Use of indirect calorimetry in enterocutaneous fistula
- Psychological Fx in Emerg Gen Surgery

**Recovery**
Global Surgery

• Burden of Surgical Disease in Southern Haiti
• Trauma outcomes in Havana: A 10 year longitudinal study
• Implementation of Point of Care Trauma Clinical Decision Making Guide in Low to Middle Income Countries (Cuba, Belize, Haiti)
Thoracic Irrigation

Pneumothorax Management Guidance

Predicting Mortality Using the EMR
• Thoracic injuries in trauma
  • Present in nearly 50% of poly-trauma patients
  • Traumatic Hemothorax (HTx) occurs ~300,000 annually
  • Pneumothoraces Occur in 8% of all trauma cases

• Retained HTx in up to 20% of patients
  • Focus on management of retained HTx in the literature
  • Role of early Video Assisted Thoracoscopic Surgery (VATS)

• Lack of focus on prevention of retained HTx
Effect of Direct Suction Evacuation

- 199 Patients
- Retrospective Controls (100 pts)
- Prospective SEPS (99 pts)

Hypothesis → Suction evacuation prior to TT placement would decrease rate of retained complications.

<table>
<thead>
<tr>
<th></th>
<th>Odds Ratio</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrent PTx</td>
<td>0.332</td>
<td>0.0076</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>1.021</td>
<td>NS</td>
</tr>
<tr>
<td>Retained Fluid</td>
<td>0.453</td>
<td>NS</td>
</tr>
<tr>
<td>Surgical Intervention</td>
<td>0.531</td>
<td>NS</td>
</tr>
<tr>
<td>Death</td>
<td>4.313</td>
<td>NS</td>
</tr>
</tbody>
</table>

SEPS vs. Thoracic Irrigation

• **SEPS**
  - Prior to TT Placement
  - Yankaneur Suction advanced into dependent portion of chest
  - 2\textsuperscript{nd} pass of Yankauer
  - Standard TT Placement

• **Thoracic Irrigation**
  - After TT Placement
  - Suction advanced within TT
  - Irrigation of the thoracic cavity
Irrigation Protocol

1. Identification of traumatic HTx, HPTx
2. Aseptic 32 or 36-French TT placement
3. Initial suction evacuation following TT placement
4. 60 mL Toomey syringe is attached to the TT
5. 500 mL warm sterile saline instilled
6. Complete suction evacuation
7. Steps 4-6 repeated → total 1,000mL irrigation
8. TT connected to standard atrium setup
Pilot Study

- Total Recruitment = 20 patients
  - Age (median, IQR) = 35 years (28,54)
  - Blunt Mechanism = 45%
  - ISS (median, IQR) = 13 (9,18)
  - AIS-Chest (median, IQR) = 3 (3,3)
  - TT Duration (median, IQR) = 5 days (4,6)
  - Length of Stay (median, IQR) = 7 days (5,7)

- Secondary Intervention Rate = 5%

Hypothesis

• Thoracic irrigation at the time of initial thoracostomy tube placement will reduce the rate of clinically significant retained hemothorax.
Methods

• Prospective Observational Trial
  ▪ Control Cohort = TT placement
  ▪ Investigational Cohort = TT placement + thoracic irrigation
Methods

• **Inclusion Criteria**
  1. CXR confirmed HPTx or HTx
  2. TT placed within 24-hours

• **Exclusion Criteria**
  1. Hemodynamic Instability
  2. Need for immediate thoracotomy
  3. TT removal within 24-hours
  4. Death within 30-days

Analysis: propensity score matching on age, sex, MOI, AIS-Chest, TT Size
## Results

### Table 1. Patient and Trauma Demographics

<table>
<thead>
<tr>
<th></th>
<th>Irrigated</th>
<th>Non-Irrigated</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total Patients</strong></td>
<td>n = 60</td>
<td>n = 236</td>
</tr>
<tr>
<td><strong>Age (years)</strong></td>
<td>33 (26,51)</td>
<td>42 (27,55)</td>
</tr>
<tr>
<td><strong>Male (n / %)</strong></td>
<td>49 (81.7%)</td>
<td>190 (80.5%)</td>
</tr>
<tr>
<td><strong>ISS</strong></td>
<td>13 (9,18)</td>
<td>14 (9,22)</td>
</tr>
<tr>
<td><strong>AIS Chest</strong></td>
<td>3 (3,3)</td>
<td>3 (3,3)</td>
</tr>
<tr>
<td><strong>Blunt Trauma (n / %)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>29 (48.3%)</td>
<td>121 (51.3%)</td>
</tr>
<tr>
<td>Motor Vehicle Collision</td>
<td>14 (23.3%)</td>
<td>52 (22.0%)</td>
</tr>
<tr>
<td>Fall</td>
<td>7 (11.7%)</td>
<td>31 (13.1%)</td>
</tr>
<tr>
<td>Motor Pedestrian Collision</td>
<td>3 (5.0%)</td>
<td>8 (3.4%)</td>
</tr>
<tr>
<td>Motor Cycle Collision</td>
<td>2 (3.3%)</td>
<td>22 (9.3%)</td>
</tr>
<tr>
<td>Assault</td>
<td>1 (1.7%)</td>
<td>5 (2.2%)</td>
</tr>
<tr>
<td>Other</td>
<td>3 (5.0%)</td>
<td>5 (2.2%)</td>
</tr>
<tr>
<td><strong>Penetrating Trauma (n / %)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>31 (51.7%)</td>
<td>115 (48.7%)</td>
</tr>
<tr>
<td>Gun Shot Wound</td>
<td>23 (38.3%)</td>
<td>70 (29.7%)</td>
</tr>
<tr>
<td>Stab Wound</td>
<td>8 (13.3%)</td>
<td>44 (18.7%)</td>
</tr>
<tr>
<td><strong>TT indication (n / %)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemothorax</td>
<td>35 (58.3%)</td>
<td>121 (51.3%)</td>
</tr>
<tr>
<td>Hemopneumothorax</td>
<td>25 (41.7%)</td>
<td>115 (48.7%)</td>
</tr>
</tbody>
</table>

All numbers Median (Interquartile Range) unless otherwise stated.

ISS = injury severity score, AIS = abbreviated injury score, TT = thoracostomy tube
## Results

<table>
<thead>
<tr>
<th>Table 2. Primary Reason for Data Analysis Exclusion</th>
<th>Irrigated</th>
<th>Non-Irrigated</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total Patients Excluded in Final Analysis</strong></td>
<td>6 (10%)</td>
<td>30 (12.7%)</td>
</tr>
<tr>
<td>TT Removal in 24-hours</td>
<td>3 (5.0%)</td>
<td>12 (5.1%)</td>
</tr>
<tr>
<td>Accidental / Bedside Removal</td>
<td>3 (5.0%)</td>
<td>7 (3.0%)</td>
</tr>
<tr>
<td>OR removal for VATS (non-retained HTx)</td>
<td>0 (0%)</td>
<td>5 (2.1%)</td>
</tr>
<tr>
<td>Immediate Thoracotomy</td>
<td>2 (3.3%)</td>
<td>6 (2.5%)</td>
</tr>
<tr>
<td>Death within 30-days</td>
<td>1 (1.7%)</td>
<td>12 (5.1%)</td>
</tr>
</tbody>
</table>

All values are number (%) unless otherwise stated. OR: Operating Room.
Results

• Compliance with Protocol → 85%

• TT Duration (median, IQR)
  - Control = 6 days (4,7)
  - Investigational = 6 days (4,8)

• Primary Outcome: secondary intervention for retained HTx
  - Control = 21.8%
  - Investigational = 5.6%
Pneumothoraces?
Objective

To validate **The 35 Millimeter Rule** in predicting **successful observation** of PTX detected on chest Computed Tomography (CT) \(^1, \) \(^2\)

**Hypothesis**

PTX measuring \(\leq 35 \text{ mm}\) on chest CT can be **safely** observed in both penetrating and blunt trauma mechanisms

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Methods

- **Site:** Froedtert Hospital ➔ level 1 trauma academic medical center with 550+ beds
- **Design:** single-center, retrospective analysis
- **Time frame:** January 2011 - December 2016
- **Primary Outcome:** successful observation of PTX ≤35 mm:
  - No need for delayed TT
  - No need for secondary intervention (surgery or intrapleural lytic therapy)
Methods

• Inclusion Criteria:
  • 18 years and older
  • Patients with chest CT done at the time of trauma
  • No walk-in diagnosis of PTX

• Exclusion Criteria:
  • Associated hemothorax
  • Diagnosis of PTX based on CXR
Methods

• **Measurement**
Radial distance between the parietal and visceral pleura/mediastinum in a line perpendicular to the chest wall.
Results

Screened
1767 patients

Hemo/hemoPTX
935 (53%)

PTX only
832 (47%)

CXR only
380 (46%)

Chest CT
452 (54%)

@MCWTraumaACS
Results

Chest CT
452 (54%)

> 8hrs

Observed
385 (85%)

Succeeded
345 (90%)

≤35 mm
327 (95%)

>35 mm
18 (5%)

Delayed TT/Intervention
40 (10%)

≤35 mm
31 (78%)

>35 mm
9 (22%)
Conclusion

- **The 35 mm Rule** is safe as a general guide for initial observation, regardless of mechanism, with only 5% of stable patients failing.

- Simple and rapid method → one measurement on axial chest CT
Percent Change From Pre-Injury Blood Pressure Is An Independent Predictor Of Mortality In Elderly Trauma
Hypothesis

Decrease from baseline (preinjury) systolic blood pressure (SBP) is an independent predictor of mortality among elderly trauma patients.
Methods

• **Site:** Froedtert Hospital → level 1 trauma academic medical center with 550+ beds
• **Design:** single-center, retrospective analysis
• **Time frame:** January 2010 - December 2017
• **Primary Outcome:** in-hospital mortality after trauma
• **Patient identification & data collection:** trauma registry and electronic health records
• **Analysis:** univariant and multivariant analysis using SAS V9.4
Methods

• **Inclusion Criteria:**
  • 65 years and older
  • Admitted under trauma service
  • Has baseline vital signs in EPIC from outpatient setting

• **Exclusion Criteria:**
  • Under 65
  • Multiple trauma presentations
  • Dead on arrival
  • Vital signs only from inpatient admission
Methods

- **Baseline SBP (bSBP):** average of the last 3 SBP measurements recorded within 2 years of the trauma date in outpatient setting
- **Trauma SBP (tSBP):** first SBP reading in the Emergency Department after presentation for trauma
- **Delta SBP (dSBP):** percent change of tSBP from bSBP
Results

- 2059 patients → 533 (25.9%) with a decrease in tSBP from their bSBP
- **Age mean:** 79.8 years (65.0 - 102.0, ±8.4)
- **bSBP mean:** 131.3 mmHg (75.3 – 209.0, ±17.5)
- **Mortality:** 5%
Results

- **Multivariate Analysis:**
  - 10% change from bSBP [OR= **1.39**, (95% CI: 1.02, 1.90)]
  - Male sex [OR=**3.45**, (95% CI: 1.49, 8.01)]
  - GCS 13-15 [OR=**0.03**, (95% CI: 0.01, 0.07)]
Results
Conclusion

A decrease from baseline preinjury SBP by 10% or more is an independent predictor of mortality in the elderly trauma patient.
Trauma/ACS Research Program

• Full time-line of Patient Care and Global efforts
• DOD Funding line for Phase II HDACI study of TBI
• Grant proposals for NIH, Fogarty, DOD
• Future: Epigenomics, Proteonomics with GSPMC collaboration; Expand Military Program (Military/Civilian Research Partnership Symposium, June 4/5th 2019)
Quality of Life (QoL) after Trauma

Kiely et al., (2006)

PF = Physical functioning
RP = Role pain
BP = Bodily pain
GH = General health
VT = Vitality
SF = Social functioning
RE = Role emotional
MH = Mental Health
Quality of Life (QoL) after Trauma

MH = Mental Health
PF = Physical functioning
RP = Role pain
BP = Bodily pain
GH = General health
VT = Vitality
SF = Social functioning
RE = Role emotional

Kiely et al., 2006
Quality of Life (QoL) after Trauma

- Pain
- Psychological Health
- Geriatric Population
  - Frailty and outcomes
- Health Disparities
Posttraumatic Stress Disorder (PTSD)

PTSD is a strong contributing factor to lower physical and emotional QoL after a traumatic event

Kiely et al., (2006)
PTSD after Traumatic Injury

(deRoon-Cassini, Mancini, Rusch, & Bonanno, 2010)
PTSD after Traumatic Injury

<table>
<thead>
<tr>
<th>Time since injury</th>
<th>PTSD Symptom</th>
<th>Severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 mo.</td>
<td>Chronic distress</td>
<td>21.8%</td>
</tr>
<tr>
<td>1 mo.</td>
<td>Delayed distress</td>
<td>5.6%</td>
</tr>
<tr>
<td>3 mo.</td>
<td>Acute distress</td>
<td>12.1%</td>
</tr>
<tr>
<td>6 mo.</td>
<td>No distress</td>
<td>60.5%</td>
</tr>
</tbody>
</table>

(deRoon-Cassini, Mancini, Rusch, & Bonanno, 2010)
Secondary prevention
Injured Trauma Survivor Screen (ITSS)

• American College of Surgeons Committee on Trauma (ACS - CoT)
  • Recommends PTSD and depression screening for trauma centers
  • No valid screen was created at the time of the recommendation
Utility of the injured trauma survivor screen to predict PTSD and depression during hospital admission

Joshua C. Hunt, PhD, Marty Sapp, EdD, Cindy Walker, PhD, Ann Marie Warren, PhD, Karen Brasel, MD, MPH, and Terri A. deRoon-Cassini, PhD, Milwaukee, Wisconsin

<table>
<thead>
<tr>
<th>Injured Trauma Survivor Screen (ITSS)</th>
<th>PTSD</th>
<th>DEP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before this injury</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Have you ever taken medication for, or been given a mental health diagnosis?</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>2. Has there ever been a time in your life you have been bothered by feeling down or hopeless or lost all interest in things you usually enjoyed for more than 2 weeks?</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>When you were injured or right afterward</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Did you think you were going to die?</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>4. Do you think this was done to you intentionally?</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Since your injury</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Have you felt emotionally detached from your loved ones?</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>6. Do you find yourself crying and are unsure why?</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>7. Have you felt more restless, tense or jumpy than usual?</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>8. Have you found yourself unable to stop worrying?</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>9. Do you find yourself thinking that the world is unsafe and that people are not to be trusted?</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>≥ 2 is positive for PTSD risk</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 2 is positive for Depression risk</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SUM =</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Funding: MCW RAC (deRoon-Cassini)

Hunt et al., Journal of Trauma and Acute Care Surgery, 2017
Key Concept: PTSD

- PTSD = anxiety-related disorder that develops after trauma
  - Intrusive
  - Hyperarousal
  - Avoidance
  - Mood disturbance

- Not related to injury severity

- Perceived life threat -> Impaired extinction of fear memories -> intrusive recollections and re-experiencing of the original traumatic event (flashbacks or nightmares)

  - Emotion dysregulation - Includes persistent alarm and distress, numbing, avoidance, increased arousal, as well as aberrant memory processes

Sripada et al, 2013
Neumeister et al, 2013
Emotional dysregulation evident early after trauma

deRoon-Cassini & Larson, 2014

Funding: MCW IRC
Emotion dysregulation evident early after trauma

Funding: NIH/NIMH R01 (Larson, deRoon-Cassini)
So what about a system that can respond to and buffer against the heightened stress response?
Endocannabinoid signaling system

**Background:**
- Endocannabinoid signaling system (ECSS)
  - Neuromodulary system in CNS
  - Lipids (arachidonate based)
    - 2AG & Anandamide (AEA)
  - Receptors (CB1)
- Plays a regulatory role in response to stress by:
  - Regulating amygdala activation and medial prefrontal cortical activity
Endocannabinoid → CB1 receptor signaling opposes the effects of stress

- Reduce fear and anxiety
- Oppose sympathetic (fight or flight) response
- Increase drive to sleep
- Promote shut off of HPA axis following stress

Hypothesis: Higher endocannabinoid functioning posttrauma is related to less PTSD symptoms by 6 months
2-AG PTSD Diagnosis

Mechanism of Injury (N = 278)

- Fall: 17%
- GSW: 21%
- MVC: 33%
- Stab: 10%
- Ped struck: 5%
- MCC: 7%
- Other: 7%
- Other: 1%
- Crush/recreational injury: 1%
- Assault: 1%

Funding: NIH/NIMH (deRoon-Cassini & Hillard)
2-AG PTSD Diagnosis

- Levels of 2-AG are high acutely after trauma for all subjects
- For those who are PTSD positive at 6 months, trending significantly lower 2-AG

2-AG at 6-month follow up for PTSD Positive v. PTSD Negative: $t(143.96) = 1.85; p = 0.06$

Funding: NIH/NIMH (deRoon-Cassini & Hillard)
AEA and PTSD Diagnosis

- Higher AEA at baseline for those with PTSD at 6 months

Gender Differences
- For women, significant correlations between baseline and 6 month AEA and higher PTSD symptom severity in total and individual symptom clusters

AEA at baseline for PTSD Positive v. PTSD Negative: \( t(63.40) = 2.00; p = 0.050 \)
Next Steps with our PTSD research

• Reviewed
  • R01 – linking emotion dysregulation neurologically with the endocannabinoid system to identify phenotypes of risk
    • discussed and scored with MESH
    • Goes to NIMH council review in September for funding

• Under Review
  • Risk phenotypes before trauma exposure (DoD & Strong STAR)

  • Acute intervention
    • EEG guided activation of the amygdala to provide biofeedback to reduce hyperactivity of the amygdala acutely after trauma (R61/R33, NIMH)

• Future submission (October?)
  • Clinical effectiveness of our stepped behavioral health model in trauma
Six-month follow-up of the injured trauma survivor screen: Clinical implications and future directions

Joshua C. Hunt, PhD, Samantha A. Chesney, MS, Karen Brasel, MD, and Terri A. deRoon-Cassini, PhD, Milwaukee, Wisconsin

**Tier 1:** The ITSS is administered by a social worker during the inpatient screening process (< 5 minutes).

**Tier 2:** Trauma/Critical Care providers receive a Best Practice alert recommending a trauma psychology consultation.

**Tier 3:** Symptoms are assessed by a psychologist as a part of a full initial consultation and evaluation.

**Tier 4:** Implementation of psychological intervention.

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*Figure 1: Multi-tier Approach to Psychological Intervention after Traumatic injury (MAPIT)*

Note. PCL-5 = Posttraumatic Stress Disorder Checklist for DSM-5; CESD-R = Center for Epidemiologic Studies Depression Scale–Revised; white = evidence provided for use; grey = emerging evidence; black = further evidence needed

Hunt et al., Journal of Trauma and Acute Care Surgery, 2018
Pain after Traumatic Injury

• 80% of Traumatic Injury survivors have chronic pain at 4 months

• Highly correlated with psychological distress

• Discharge pain score >4 = best predictor of who develops chronic pain

Trevino et al., 2010
Pain after Traumatic Injury

• What biological targets lead to the conversion from acute to chronic pain?
  • Preliminary data:
    • Higher acute cortisol and endocannabinoids lead to reduce pain by 6 months and less pain interference in life
  • Submitted R01 NIH/NINR
    • Discussed and scored, will resubmit

Funding: NIH/NIMH R21 (deRoon-Cassini) & MCW CIC (Trevino)
Trauma Quality of Life Clinic

- What clinical changes can be made acutely to prevent chronic pain?
  - Pilot clinic is active
  - Submitting funding proposal to MCW CTSI
Health Disparities

Socio-environmental Stress
- Low SES
- Exposure to community violence
- Perceived discrimination

Allostasic load
- Changes in intestinal microbiome

CTRA gene expression profile
- Poor physical health
- Poor psychological health

Funding: MCW CTSI & Marquette Innovation Award (deRoon-Cassini) & MCW CTSI (Codner)
Health Disparities

Socio-environmental Stress

- Low SES
- Exposure to community violence
- Perceived discrimination

Allostatic load

Changes in intestinal microbiome

CTRA gene expression profile

Traumatic Injury

- Poor physical health
- Poor psychological health

Funding: MCW CTSI & Marquette Innovation Award (deRoon-Cassini) & MCW CTSI (Codner)
Microbial Dysbiosis and Gene Expression May Explain Disparate Health Outcomes in Ethnic Minorities after Injury
P Codner, J Knight, L Torres, T deRoon-Cassini

**Background:**
- Environmental forces including social and biological factors are unequally distributed across populations, creating added risk for minorities
- These forces confronting vulnerable populations may result in changes in intestinal microbial composition.

**Hypothesis:**
1. Pre-trauma socioenvironmental stressors will be associated with changes in intestinal microbial composition
2. Socioenvironmental stressors, the intestinal microbial composition, and increased biological vulnerability (CTRA gene expression and increased AL) will significantly predict reduced QoL among traumatically injured ethnic minority adults at 6 months post-injury.

**Progress to date:**
**Baseline**
- Total N=21 (17 samples collected, 4 missing (80%))

**6 months**
- Total N=4 (4 samples collected 100%)

Panna Codner, MD
Traumatic Injury and Microbial Dysbiosis

• Next Steps
  • Data analysis of ongoing study
  • Long term goal – develop tailored nutritional therapeutics based on intestinal microbial composition in patient at risk for poor outcomes
  • Grant under review – We Care
    • To establish the link between intestinal microbial composition/diversity and frailty and outcomes
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  • Marquette University – Innovation Award
Next Month:

Education Surgery Research Update

Wednesday, August 8
5:00-6:00 pm
Location: Cancer Center Conference Room M

Thomas W. Carver, MD
Michael Malinowski, MD
Andrew Kastenmeier, MD
To receive credit for this session, text the SMS code: **FEGROK** to **414-206-1776**. This code will expire in 5 days.