UNIVERSITY of VIRGINIA

SCHOOL of MEDICINE
Department of Anesthesiology

2024 CELEBRATION of RESEARCH

MAY 14 - 15, 2024

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Department of Anesthesiology

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SCHEDULE OF EVENTS

TUESDAY MAY 14, 2024

Oral Presentations
2:30 PM - 4:10 PM
Pinn Hall Conference Center

Poster Presentations
4:10 PM - 5:20 PM
Pinn Hall Ground Floor: G1 & G2

"My Accidental Research Career"
David O. Warner, MD
Emeritus Professor of Anesthesiology
Mayo Clinic College of Medicine and Science
5:30 PM
Pinn Hall Conference Center

WEDNESDAY MAY 15, 2024

"Deadliest Catch: Substance Use Disorder in Anesthesiologists"
David O. Warner, MD
Emeritus Professor of Anesthesiology
Mayo Clinic College of Medicine and Science
7:00 AM
Pinn Hall Conference Center

Publication Awards Announcements
7:55 AM
Pinn Hall Conference Center

“Professionalism Writ Large: Amplifying Your Influence”
David O. Warner, MD
Emeritus Professor of Anesthesiology
Mayo Clinic College of Medicine and Science
8:05 AM
Pinn Hall Conference Center

KEYNOTE SPEAKER

"My Accidental Research Career"
“Deadliest Catch: Substance Use Disorder in Anesthesiologists” &
“Professionalism Writ Large: Amplifying Your Influence”

David O. Warner, MD

Emeritus Professor of Anesthesiology and Perioperative Medicine at the Mayo Clinic College of Medicine and Science

David O. Warner, M.D., is Professor Emeritus of Anesthesiology in the Mayo Clinic College of Medicine and Science in Rochester, MN. He received his medical degree from The Ohio State University and completed anesthesia residency and fellowship training at Mayo Clinic.

He served in a variety of institutional administrative roles, including Director of Educational programs for the Mayo Clinic Center for Clinical and Translational Sciences (CTSA), Associate Dean for Clinical and Translational Research, and Associate Dean for Faculty Affairs for the Mayo Clinic Alix School of Medicine. He also served as President of the American Board of Anesthesiology.

Dr. Warner’s research interests include neurodevelopmental outcomes after pediatric anesthesia and tobacco control in surgical patients. He has received several awards for this work, including the Excellence in Research Award from the American Society of Anesthesiologists and the Alumni Achievement Award from the Ohio State University College of Medicine. He has been funded by the NIH since 1990, mentored over 40 research fellows, and published over 300 peer-reviewed manuscripts. Clinically, he practiced pediatric anesthesiology.

He married his high-school sweetheart and has three grown-up kids who have produced five cute grandkids (so far).

ORAL PRESENTATIONS

MAY 14, 2024 | 2:30 PM - 4:10 PM

2:30 PM

(BV Light and SSI) Ultraviolet Light to Prevent Central Line Associated Bloodstream Infection
Robert H. Thiele, MD; Chelsea Marie, PhD (Immunology); Sayo McCowin, MD, PhD

2:42 PM

Surgery, Anesthesia and Intensive Care Conditions Induce Perineuronal Net loss in aged mice
Jinny Park, BA; Jeffrey Wooters, Undergraduate Student; Navya Atluri, PhD; Meghana Illendula, MPH; Michal Jedrusiak, MD; Hari Prasad Osuru, PhD; Nadia Lunardi, MD, PhD

2:54 PM

ABO-Identical vs. Incompatible Platelet Transfusion in Patients with Intracranial Hemorrhage
Emily Venner, BS; Matthew Nguyen, BS; Jose Perdomo Trejo, BS; Zachary Holley, BS; Bhiken Naik, MBBCh, MSCRBS; Lauren Dunn, MD; Jenna Khan, MD; Michael Mazzeffi, MD MPH FASA

3:06 PM

The Role of the Pglyrp1/TREM-1/SYK Pathway in the Blood-Brain Barrier (BBB) Integrity and Cognitive Dysfunction After Surgery
Klaudia Augustyn, Medical Student; Zhiyi Zuo, M.D, PhD

3:18 PM

Brainstem Neurons Activated During Seizure-Induced Apnea
Selena Garcia DuBar, PhD; Sebastian Moeller Rivera, Undergraduate Student; Miranda Sculimbrene, Undergraduate Student; Dev Kakadiya, Undergraduate Student; Ian Wenker, PhD

3:30 PM

An Integrative Review of Mindfulness and Surgical Patients
Michael A Miller, MSN, CRNA; Lichuan Ye, PhD, RN, FAAN; Maria Van Pelt, PhD, CRNA, FAAN, FAANA; Kara J. Pavone, PhD, RN

3:42 PM

Utilizing Base Editing to Target SCN8A Epileptic Encephalopathy
Caeley Reever, Graduate Student; Manoj K. Patel, PhD

3:54 PM

Effect of a Self-CARE Education Intervention on Anesthesiology Resident Well-being: An Interim Analysis
Lauren K. Dunn MD, PhD; David Watson, MD; Katherine T. Forkin, MD; Amanda M. Kleiman, MD; Stephen Collins, MD; Siny Tsang, PhD; Bhiken I. Naik, MBBCh, MSCR; Edward C. Nemergut, MD

ORAL PRESENTATION | 2:30 PM

(BV Light and SSI) Ultraviolet Light to Prevent Central Line Associated Bloodstream Infection

Robert H. Thiele, MD; Chelsea Marie, PhD (Immunology); Sayo McCowin, MD, PhD

Background

In addition to loss of life and function, hospital-acquired infections (HAI) impose great economic costs to society (estimated at almost $10 BB annually in 2013, with CLABSI being the second most costly at $1.9 BB/year in the United States [1]). New strategies are needed to combat HAI because antibiotic resistance is a growing problem and is worsened by a dry drug pipeline due to lack of economic incentives for novel antibiotic development [2]. One source of infection is healthcare providers. In the operating room environment, bacterial contamination of intravenous stopcock sets occurred in 32% of cases [3]. While the relationship between hand washing and hospital-acquired infections (HAI) is well established, hand hygiene compliance rarely exceeds 60% [4]. A safety mechanism to address this infection source (providers) is needed.

Methods

We utilized a commercially available LED-based ultraviolet lamp (285 nm, AquaSense PearlLab Beam) to test the ability of UV-C radiation to kill two common strains of bacteria – S. aureus and E.coli, using exposures ranging from 0 to 10 seconds. We subsequently tested the ability of commonly used, “light sensitive” medications (epinephrine and insulin) to withstand UV-C radiation by exposing these agents to 0-1000 seconds and measuring concentrations before and after using high performance liquid chromatography or mass spectrometry, as appropriate. We tested the ability of 285 nm UV-C radiation to penetrate a commercially available UV-translucent polymer (TOPAS 8007). Lastly, we worked with the 3D printing lab at UVA to construct a prototype of a “cartridge” that would form the basis of a small, inexpensive, re-usable UV-C filter.

Results

UV-C is highly effective at killing bacteria, requiring approximately 2 seconds of contact time to kill > 95% of bacteria. In contrast, minimal degradation of both epinephrine and insulin was noted after 1000s of exposure.

Conclusions

Development of a UV filter capable of safely sterilizing fluids and medications injected into a patient is technically possible. UV-C radiation has a large therapeutic window (500X), and can be used to sterilize injected fluids and medications with very low likelihood of degrading light sensitive drugs. Relatively minor (solvable) engineering hurdles remain.

References

1. Zimlichman E, Henderson D, Tamir O, et al. Health care-associated infections: a meta-analysis of costs and financial impact on the US health care system. JAMA Intern Med. Dec 9-23 2013;173(22):2039-46. doi:10.1001/jamainternmed.2013.9763
2. Rogers Van Katwyk S, Grimshaw JM, Mendelson M, Taljaard M, Hoffman SJ. Government policy interventions to reduce human antimicrobial use: protocol for a systematic review and meta-analysis. Syst Rev. Dec 13 2017;6(1):256. doi:10.1186/s13643-017-0640-2
3. Loftus RW, Koff MD, Burchman CC, et al. Transmission of pathogenic bacterial organisms in the anesthesia work area. Anesthesiology. Sep 2008;109(3):399-407. doi:10.1097/ALN.0b013e318182c855
4. Mouajou V, Adams K, DeLisle G, Quach C. Hand hygiene compliance in the prevention of hospital-acquired infections: a systematic review. J Hosp Infect. Jan 2022;119:33-48. doi:10.1016/j.jhin.2021.09.016

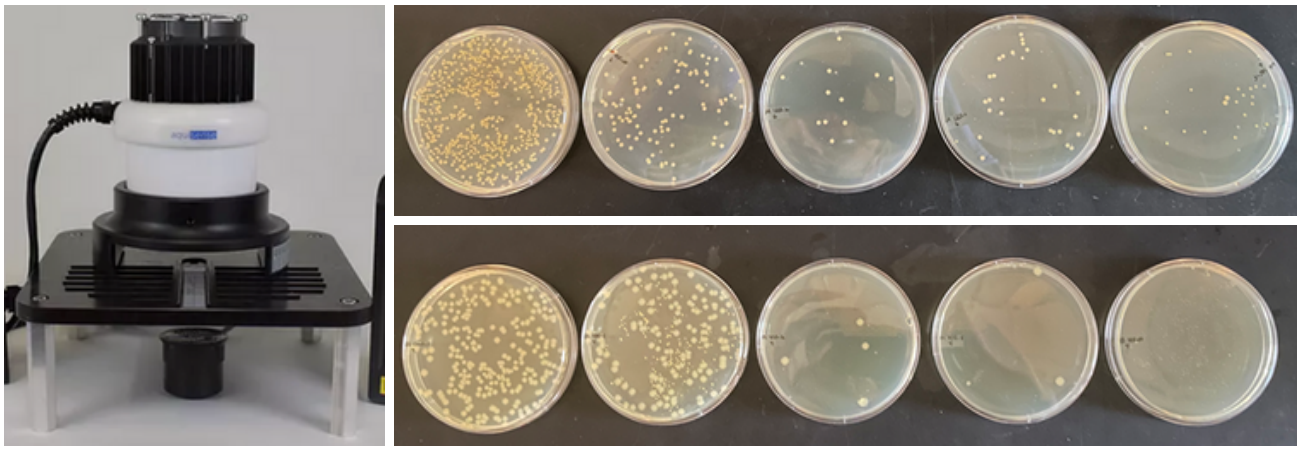

Figure 1. Left: experimental setup; the AquiSense PearlLab Beam applies three different wavelengths of UV light to Petri dishes. Right, upper: MSSA after 0, 1, 2, 5, and 10 seconds of exposure to 285 nm light; Right, lower: E. coli after 0, 1, 2, 5, and 10 seconds of exposure to 285 nm light.

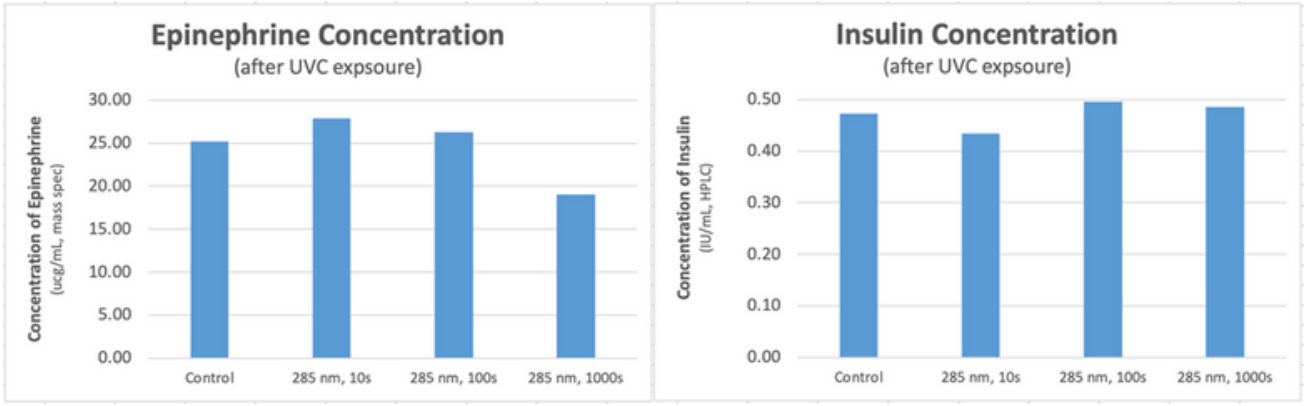

Figure 2. Epinephrine and insulin are two commonly used "UV sensitive" drugs, for whom the manufacturer recommends storing in an opaque container, away from light. We therefore tested the ability of bactericidal doses of UV light (285 nm) to degrade these two important agents with mass spectrometry and high performance liquid chromatography

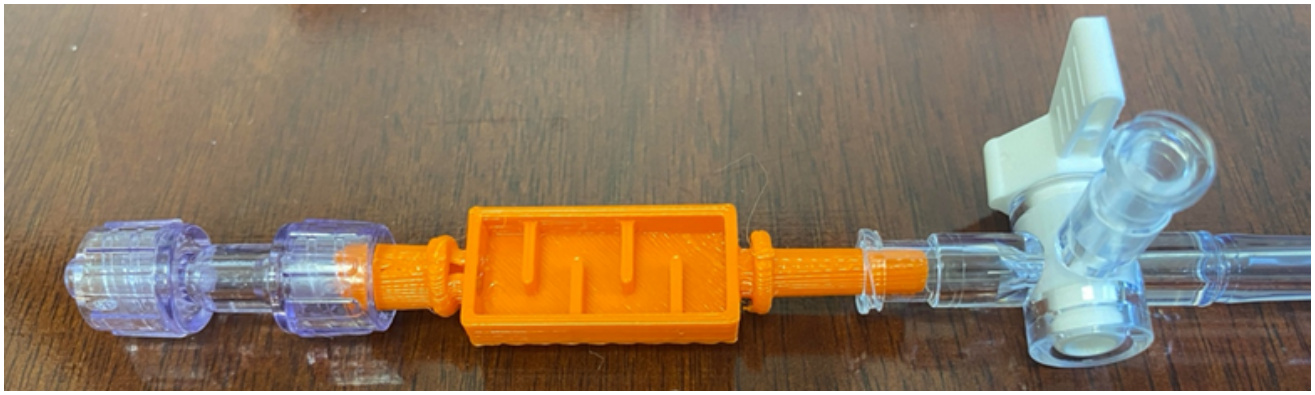

Figure 3. 3D printed UV filter prototype

ORAL PRESENTATION | 2:42 PM

Surgery, Anesthesia and Intensive Care Conditions Induce Perineuronal Net loss in Aged Mice

Jinny Park, BA; Jeffrey Wooters, Undergraduate Student; Navya Atluri, PhD; Meghana Illendula, MPH; Michal Jedrusiak, MD; Hari Prasad Osuru, PhD; Nadia Lunardi, MD, PhD

Background

Postoperative delirium, marked by inattention and confused thinking following surgery and anesthesia, affects a significant portion —up to 80%— of older adults in the Intensive Care Unit (ICU). Delirium leads to prolonged hospitalizations and higher rates of nursing home placement, with a considerable 35% to 40% mortality within a year post-discharge. While previous research has focused on factors like neuronal inflammation, microglia activation, and a compromised blood-brain barrier, attempts to target these have not yielded successful clinical treatments. Overlooked in prior studies, perineuronal nets (PNNs) — protective structures around key parvalbumin-expressing (PV+) interneurons — may play a critical role. Our study examines whether aged mice exhibiting delirium-like behaviors also display hippocampal PNN loss compared to controls, shedding light on a potential new target for intervention.

Methods

Male C57BL/6J mice aged 18-20 months (equivalent to 60-70 years in human age) were randomly allocated to either the Anesthesia, Surgery and ICU group (ASI) or the control group. ASI mice underwent sevoflurane anesthesia, propofol sedation, and 12 hours of ICU-like conditions, while control mice received no ASI treatment (Figure 1). Following ICU conditions, mice were assessed for attention and thought organization using the attention set-shifting task (AST). Next, their brains were collected, and hippocampal sections were used to quantify PV+ neurons surrounded by PNNs through biotinylated lectin Wisteria floribunda agglutinin (WFA) staining. Statistical analysis was conducted using GraphPad Prism 8.0.1 software.

Results

ASI mice demonstrated a significant increase in the number of trials needed to locate the reward cereal in both the reverse compound discrimination (CD-R) and extra-dimensional shift (EDS) tasks of the AST test compared to controls, indicating impaired attention and disorganized thinking (Figure 2). Additionally, the hippocampal sections of ASI mice showed a significant reduction in the number of WFA-labeled PNNs surrounding PV+ neurons, in comparison to age- matched controls (Figure 3).

Conclusions

Our results indicate a notable decrease in the count of PNNs surrounding PV+ neurons in the hippocampus of aged mice exhibiting delirium-like deficits following ASI. These findings suggest that the loss of PNN protection encasing PV+ hippocampal interneurons, triggered by the combination of anesthesia, surgery, and ICU conditions, could contribute significantly to the cognitive impairment observed in postoperative delirium.

*This work was supported by a Local Initiative for Excellence (L.I.F.E) Foundation grant to NL.

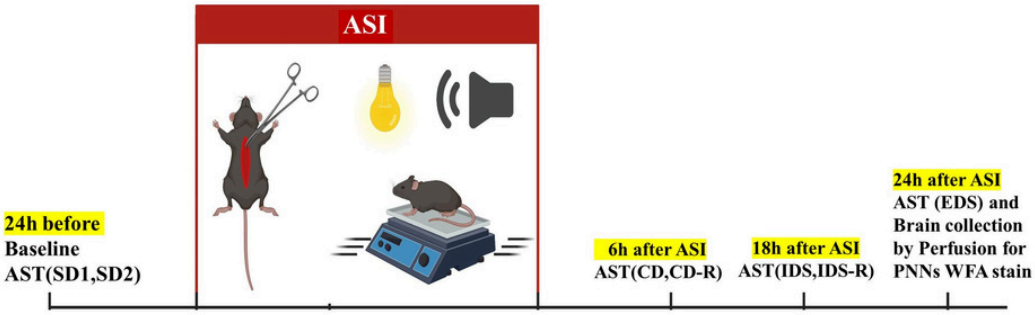

Figure 1: Schematic of the experimental design. SD, simple discrimination; CD, compound discrimination; CD-R, reverse compound discrimination; IDS, intra-dimensional shift; IDS-R, reverse intra-dimensional shift; EDS, extra-dimensional shift.

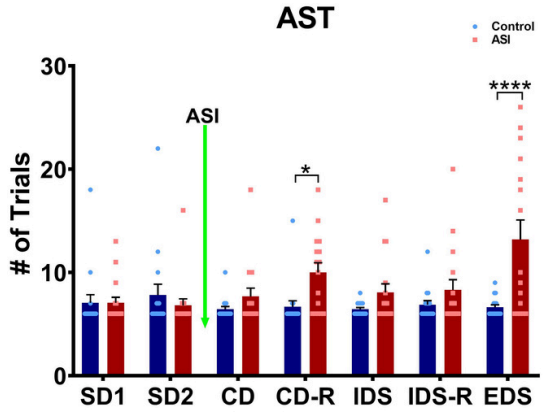

Figure 2: Effects of ASI on mice performance in the AST test. ASI mice required a higher numberof trials to locate the reward cereal in the CD-R (*P=0.0365) and EDS (****P<0.0001) tasks, relative to controls. Two-way ANOVA. N=16 mice/ group.

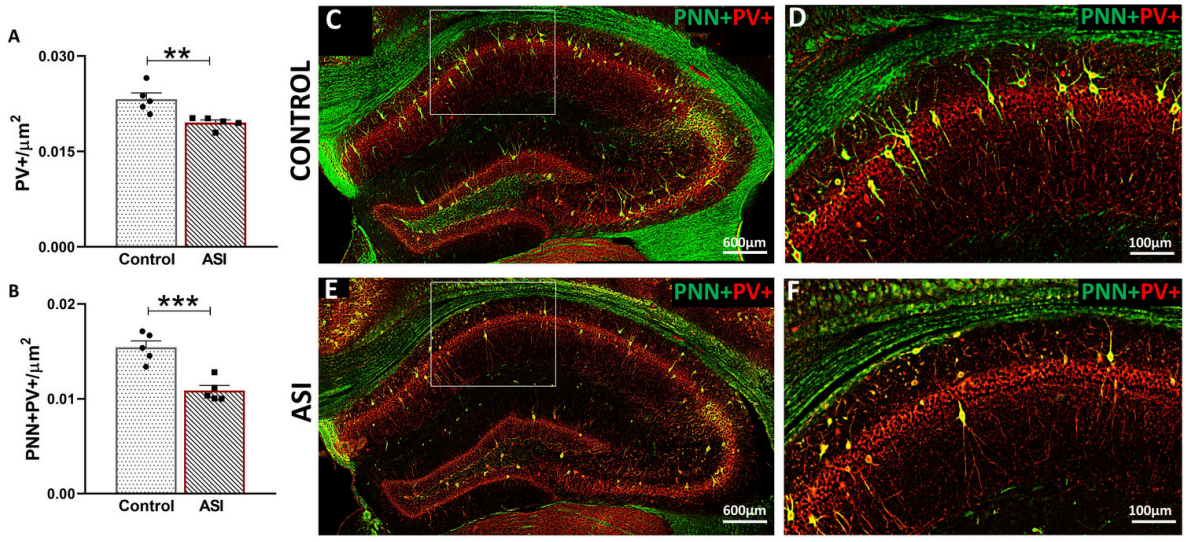

Figure 3: Loss of hippocampal PNNs following ASI. The count of WFA-labeled PNNs surrounding PV+ neurons was significantly decreased in the hippocampus of ASI mice, in comparison to age-matched controls. Panel A: Number of PV+ neurons normalized per hippocampal area (**P=0.0078). Panel B: Number of PV+ neurons enmeshedby PNNs normalized per hippocampal area (***P=0.0008). T- student test. N=5 mice/group. Representative images (20X, 40X magnification). Panels C and D are taken from control mice. Panels E and F are taken from ASI mice.

ORAL PRESENTATION | 2:54 PM

ABO-Identical vs. Incompatible Platelet Transfusion in Patients with Intracranial Hemorrhage

Emily Venner, BS; Matthew Nguyen, BS; Jose Perdomo Trejo, BS; Zachary Holley, BS; Bhiken Naik, MBBCh,MSCR; Lauren Dunn, MD; Jenna Khan, MD; Michael Mazzeffi, MD MPH FASA

Background

Patients with spontaneous and traumatic intracranial hemorrhage (ICH) are frequently transfused platelets to treat thrombocytopenia, platelet function defects, and reverse antiplatelet drugs.1-3 ABO-identical platelet transfusion has been associated with higher post transfusion platelet increments compared to ABO-major incompatible transfusion. We hypothesized that patients who received ABO-identical transfusion would have higher post-transfusion platelet increments. Secondarily, we hypothesized that patients who received ABO-identical transfusion would have superior clinical outcomes.

Methods

Adults who experienced traumatic and non-traumatic ICH from January 1st 2018 to December 31st 2022 were identified using electronic medical records, and international classification of disease (ICD)-10 codes. Patients were excluded if they did not have a platelet count checked within 24 hours of platelet transfusion and also within 24 hours after transfusion. They were also excluded if they received multiple platelet transfusions before their platelet count was rechecked. After stratification by ABO-identical, ABO-major incompatible, and ABO minor-incompatible transfusion post transfusion increments were compared, as were clinical outcomes.

Results

Among 167 patients who received platelet transfusion, there were 76 (45.5%) who received ABO-identical transfusion, 54 (32.3%) who received ABO-major incompatible transfusion, and 37 (22.2%) who received ABO-minor incompatible transfusion. There were no significant differences in platelet increment between the groups, median increment=7 x 109/L for ABO-identical platelets, 10 x 109/L for ABO-major incompatible platelets, and 11x109/L for ABO-minor incompatible platelets, P=0.87. There was also no significant difference in the percentage of patients discharged alive with modified Rankin score of 1 or 2 or cerebral performance category 1 or 2 between groups (P=0.56 and 0.39 respectively).

Conclusions

Our data support similar efficacy for ABO-identical and ABO-incompatible platelet transfusion in patients with ICH who require platelet transfusion.

References

1. Wolff C, Muakkassa F, Marley R, et al.: Routine platelet transfusion in patients with traumatic intracranial hemorrhage taking antiplatelet medication: Is it warranted? Can J Surg. 65:E206-E211, 2022.
2. Mrochen A, Sprugel MI, Gerner ST, et al.: Thrombocytopenia and Clinical Outcomes in Intracerebral Hemorrhage: A Retrospective Multicenter Cohort Study. Stroke. 52:611-619, 2021.
3. Post R, Tjerkstra MA, Middeldorp S, et al.: Platelet transfusion in patients with aneurysmal subarachnoid hemorrhage is associated with poor clinical outcome. Sci Rep. 10:856, 2020.

Table 1. Patient characteristics

Variable	ABO-identical N=76	ABO-major incompatible N=54	ABO-minor incompatible N=37	P value
Age	66 [56, 75]	64 [53, 77]	63 [53, 72]	0.89
Male sex	49 (64.5)	35 (64.8)	14 (37.8)	0.01
Race				
Black	7 (9.2)	3 (5.4)	5 (13.5)	
Am Indian	1 (1.3)	0 (0.0)	0 (0.0)	
Other	3 (4.0)	1 (1.9)	1 (2.7)	0.71
No data	0 (0.0)	1 (1.9)	0 (0.0)	
White	65 (85.5)	49 (90.7)	31 (83.8)	
Body mass index	25 [23, 29]	24 [20, 27]	25 [21, 28]	0.03
Diabetes mellitus	18 (23.7)	12 (22.2)	8 (21.6)	0.96
Hypertension	52 (68.4)	33 (61.1)	20 (54.1)	0.32
Prior CVA	15 (19.7)	6 (11.1)	3 (8.1)	0.18
Prior ICH	7 (9.2)	2 (3.7)	1 (2.7)	0.27
CAD	25 (32.9)	14 (25.9)	9 (24.3)	0.54
CKD	15 (19.7)	5 (9.3)	3 (8.1)	0.12
PVD	3 (4.0)	2 (3.7)	3 (8.1)	0.56
COPD	5 (6.6)	4 (7.4)	1 (2.7)	0.62
Hemoglobin (g/dL)	11.8 [9.7, 13.7]	12.0 [9.9, 14.0]	11.8 [9.0, 13.1]	0.61
Pre-transfusion platelet count (x 109/L)	149 [75, 218]	112 [45, 218]	151 [74, 232]	0.73
INR	1.2 [1.0, 1.4]	1.2 [1.0, 1.4]	1.1 [1.0, 1.4]	0.94
aPTT	27 [24, 32]	27 [25, 30]	28 [27, 32]	0.71
Aspirin within 7 days	42 (55.3)	33 (61.1)	20 (54.1)	0.74
P2Y12 within 5 days	11 (14.5)	7 (13.0)	11 (13.5)	0.97
Statin use	35 (46.1)	22 (40.7)	15 (40.5)	0.78

aPTT=activated partial thromboplastin time, CAD=coronary artery disease, CVA=cerebral vascular accident, CKD=chronic kidney disease, COPD=chronic obstructive pulmonary disease, ICH=intracranial hemorrhage, INR=international normalized ratio, PVD=peripheral vascular disease

Table 2. ICH and platelet transfusion details

Variable	ABO-identical N=76	ABO-major incompatible N=54	ABO-minor incompatible N=37	P value
Type of ICH **SAH only** **IPH only** **SDH only** **Multiple sites**	 18 (23.7) 13 (17.1) 4 (5.2) 41 (54.0)	 21 (38.9) 6 (11.1) 3 (5.6) 24 (44.4)	 14 (37.8) 5 (13.5) 2 (5.4) 16 (43.3)	0.60
Traumatic injury	25 (32.9)	18 (33.3)	8 (21.6)	0.41
Intraventricular hemorrhage	27 (35.5)	16 (29.6)	17 (46.0)	0.28
Suprantentorial ICH	68 (89.5)	50 (92.6)	35 (94.6)	0.62
Craniotomy for bleeding	22 (29.0)	12 (22.2)	13 (35.1)	0.40
EVD placed	14 (18.4)	11 (20.4)	9 (24.3)	0.77
Platelet transfusion during craniotomy	10 (13.2)	8 (14.8)	6 (16.2)	0.90
Hours after transfusion post count checked	4.0 [1.8, 7.3]	4.5 [0.75, 10.3]	4.5 [1.0, 10.0]	0.82

ICH=intracranial hemorrhage, EVD=external ventricular drain, IPH=intraparenchymal hemorrhage, SAH=subarachnoid hemorrhage, SDH=subdural hemorrhage

ORAL PRESENTATION | 3:06 PM

The Role of the Pglyrp1/TREM-1/SYK Pathway in the Blood-Brain Barrier (BBB) Integrity and Cognitive Dysfunction After Surgery

Klaudia Augustyn, Medical Student; Zhiyi Zuo, M.D, PhD

Background

Postoperative cognitive dysfunction (POCD) worsens the outcomes of millions of patients each year. The disruption of the blood-brain barrier (BBB) integrity may play a pivotal role in POCD. However, little is known about the mechanism contributing to BBB disruption, leading to POCD. Peptidoglycan recognition protein 1 (Pglyrp1) is a pro-inflammatory pattern-recognition protein that regulates acquired immunity. It is also a ligand for the Triggering receptor expressed on myeloid cells 1 (TREM-1). TREM-1 interacts with SYK. We hypothesize that the Pglyrp1/TREM-1 pathway via spleen tyrosine kinase (SYK) signaling plays a role in the BBB disruption and cognitive dysfunction after surgery.

Methods

To test this hypothesis, we performed right carotid artery exposure on 6-8-week old CD-1 male mice under isoflurane anesthesia and evaluated cognitive functions 4 days after surgery. The hippocampus was harvested 24 hours after surgery for the qPCR and Western blotting to measure mRNA and protein expression levels, BBB permeability assay, and immunofluorescent staining. Blood was collected 2 hours (TNF-α) or 24 hours after surgery for cytokine concentration measurement (IL-1beta, IL-6). We induced the knockdown of Pglyrp1 by injecting a lentivirus that carried code for short hairpin RNA (shRNA) of Pglyrp1 into the hippocampus.

Results

Surgery increased the expression of Pglyrp1, TREM-1, and SYK in the hippocampus (Fig.1) and induced the permeability of the BBB. Compared to control animals, the surgery group exhibited a higher concentration of TNF-α measured 2 hours after surgery and IL-6 and IL-1 beta measured after 24 hours. Intravenous injection of infliximab (anti- TNF-α) attenuated Pglyrp1 overexpression. Pglyrp1, TREM-1, and SYK were co-localized with CD31 (a marker for endothelial cells) (Fig.2) and CD13 (a marker for pericytes), which are components of the blood-brain barrier. Surgical animals performed worse in the Barnes maze and fear conditioning tests than control mice. The Pglyrp1 knockdown attenuated the harmful impact on the mouse's cognition and BBB disruption.

Conclusions

Our data suggest that Pglyrp1/TREM-1/SYK may play an important role in BBB disruption and cognitive dysfunction after surgery. Thus, targeting this pathway may reduce POCD.

Fig.1

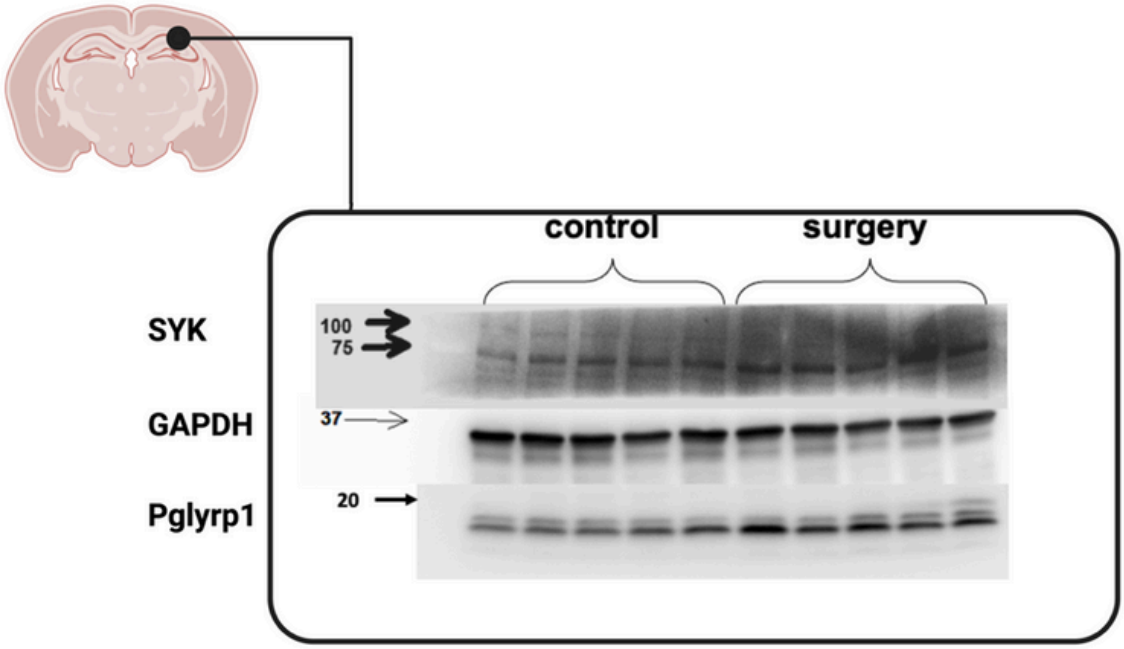

Fig.1
Surgery increases expression of Pglyrp1 and SYK in the hippocampus. Hippocampus was harvested 24 hours after surgery.

Fig.2

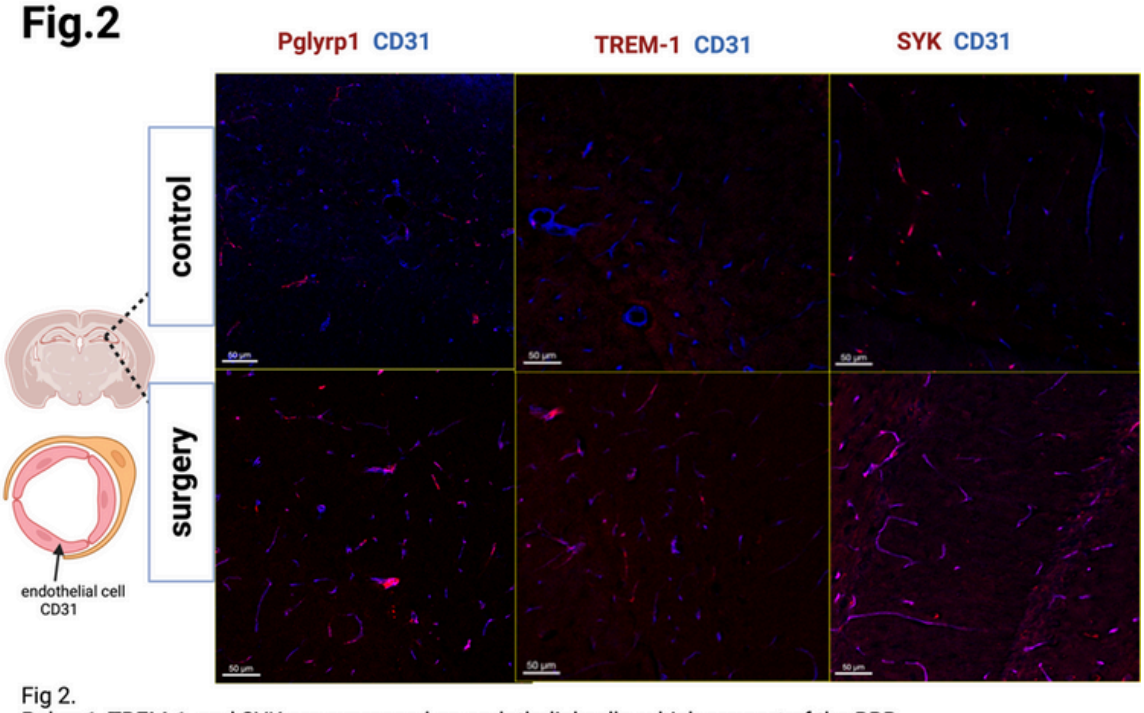

Fig 2.
Pglyrp1, TREM-1, and SYK are expressed on endothelial cells, which are part of the BBB.

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ORAL PRESENTATION | 3:18 PM

Brainstem Neurons Activated During Seizure-Induced Apnea

Selena Garcia DuBar, PhD; Sebastian Moeller Rivera, Undergraduate Student; Miranda Sculimbrene, Undergraduate Student; Dev Kakadiya, Undergraduate Student; Ian Wenker, PhD

Background

Sudden Unexpected Death in Epilepsy (SUDEP) is defined as the sudden, unexpected and unexplained death of a person with epilepsy and accounts for up to 17% of all epilepsy-related deaths and 50% for those patients refractory to treatment. While the mechanisms underlying SUDEP are not fully understood, there is increasing evidence that apnea is the primary cause. Our work using preclinical models of epilepsy shows that seizure-induced apnea (SIA) occurs during the tonic phase, and minutes before terminal asystole. We have also previously observed that SIA is not impacted by inhibition; thus, we hypothesize that overactive brainstem neural circuitry is what produces SIA.

Methods

We used a rapid kindling model in mice, which produces seizures (Fig. 1) that include, wild running/jumping (stage 6), tonic extension and SIA (stage 7), and death from SIA (stage 8). Apnea duration, seizure threshold and duration, EEG power amplitude, heart rate, and breathing rate were assessed for each condition. TRAP 2 mice (Fig. 2A) were kindled until reaching their first stage 6 or 7 and then 30 minutes later injected with 4-hydroxytamoxifen (4OHT) to observe the activated neuronal populations in mice experiencing seizures. In a subset of these experiments, we performed in situ hybridization to assess the subtypes of activated neurons.

Result

The most notable brainstem structure where activated neurons were observed was the periaqueductal gray (PAG). While the PAG has many functions, evidence demonstrates an important role in breathing integration. We found more activated neurons in the PAG of mice that had seizures with apnea versus seizures without (Fig. 2B). We examined the cellular phenotype of these activated neurons and observed them to be glutamatergic (Fig 2C). We also, unexpectedly, observed apnea in a small subset of stage 6 seizures that did not correspond with a tonic phase.

Conclusions

These results suggest that excitatory neurons in the PAG are activated during seizures to produce apnea and SUDEP. The PAG represents a potential target for intervention to prevent apnea and SUDEP that can be examined in future studies.

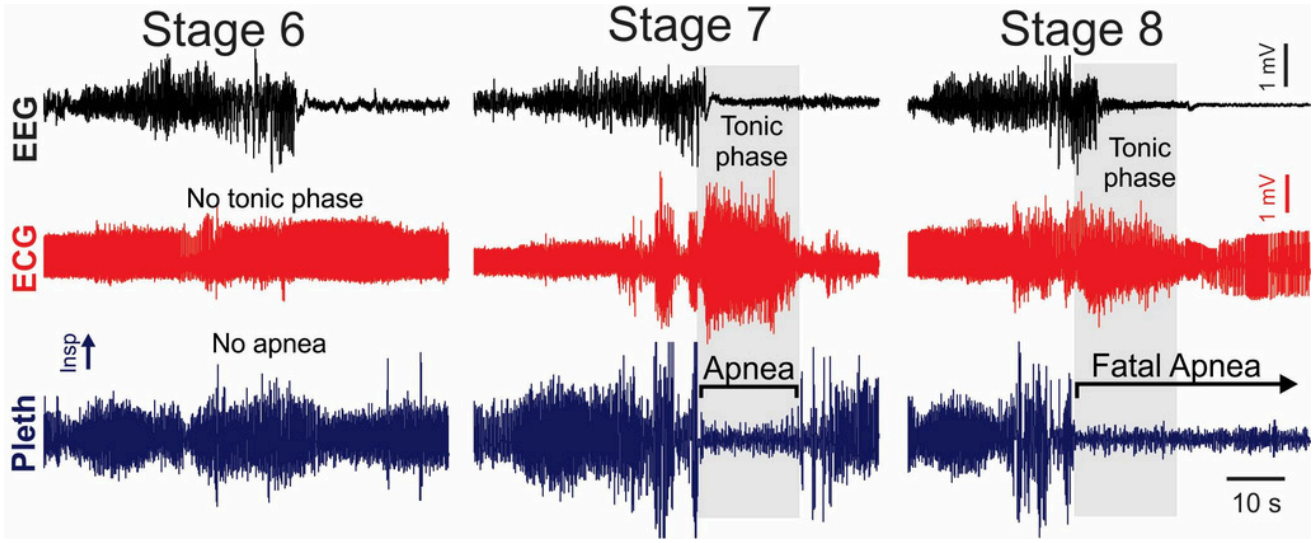


Figure 1. Electroencephalogram (EEG), electrocardiogram (ECG), and plethysmography (Pleth) waveform recordings during three distinct seizure stages produced using a rapid kindling model.

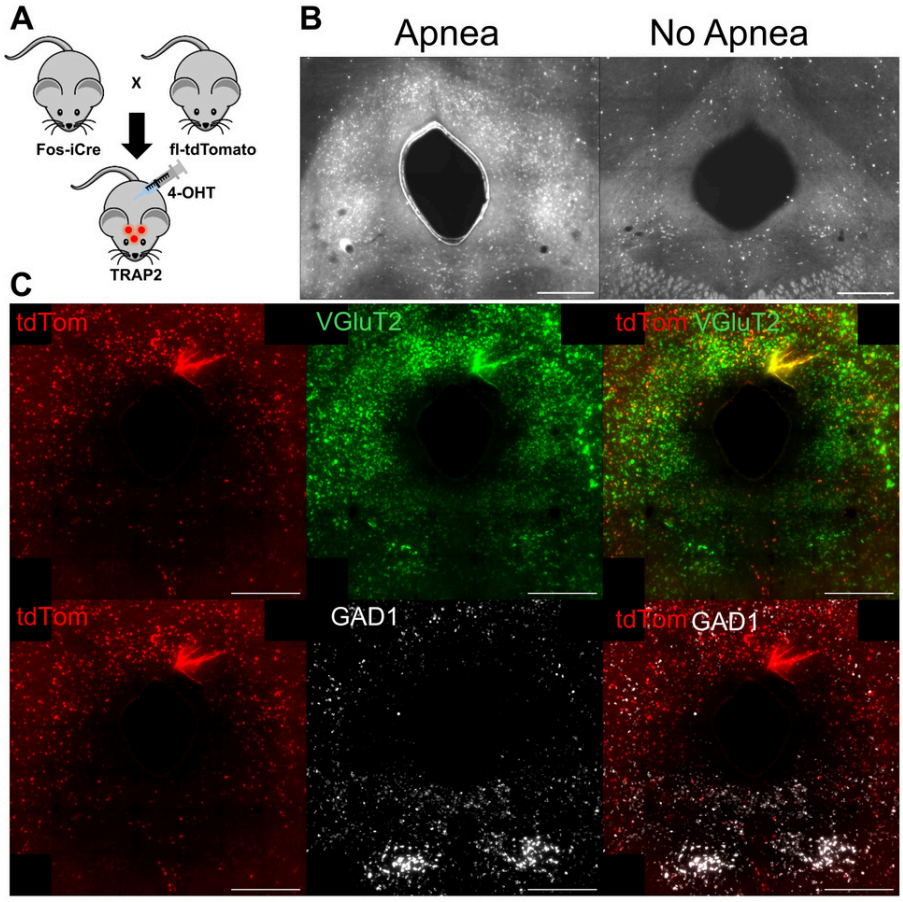


Figure 2. (A) Breeding scheme of TRAP 2 mice. (B) TdTomato expression of Fos-iCre activated cells in the PAG after a seizure with (left) and without (right) apnea. (C) TdTomato and VGluT2 positive cells (top) or tdTomato and GAD1 positive cells (bottom) detected using in situ hybridization. Scale bar = 500 μm.

ORAL PRESENTATION | 3:30 PM

An Integrative Review of Mindfulness and Surgical Patients

Michael A Miller, MSN, CRNA; Lichuan Ye, PhD, RN, FAAN; Maria Van Pelt, PhD, CRNA, FAAN, FAANA; Kara J. Pavone, PhD, RN

Background

This integrative review describes the non-pharmacological use of mindfulness, as a way to reduce pain and anxiety during the surgical period. As an exploratory aim, the relationship between mindfulness and opioids use after surgery was also explored.

Methods

CINAHL, PubMed and EMBASE databases were queried to identify articles examining the relationship between mindfulness and, postoperative pain and opioid consumption, and preoperative anxiety. Seventeen studies were included in the review, encompassing 1500 patients.

Results

Thirteen of the 17 articles reviewed focused on postoperative pain as the primary outcome and 12 reported that mindfulness decreased pain scores after postoperative day 7. Of these, 2 of out of 7 studies reported an association between mindfulness and the use of opioid pain medications. Four of the 17 articles reviewed focused on preoperative anxiety as the primary outcome, and two demonstrated that mindfulness was associated with a statistically significant reduction in anxiety.

Conclusions

Evidence suggests that mindfulness has a significant impact on postoperative pain, particularly pain more than one week after surgery. There was limited evidence supporting the use of mindfulness to reduce opioid consumption postoperatively. Similarly, mixed effects were reported describing the use of mindfulness to reduce anxiety before surgery. More research is needed to investigate the impact of mindfulness on immediate pain after surgery, opioid use and its impact on anxiety before surgery.

ORAL PRESENTATION | 3:42 PM

Utilizing Base Editing to Target SCN8A Epileptic Encephalopathy

Caeley Reever, Graduate Student; Manoj K. Patel, PhD

Background

Overactivity in sodium channels can result in seizures and the onset of epilepsy. In the case of SCN8A early infantile epileptic encephalopathy (EIEE13), this genetic form of epilepsy stems from de novo gain-of-function mutations in the SCN8A gene, which encodes the Nav1.6 sodium channel. Nav1.6 is the primary voltage-gated sodium channel essential for initiating and propagating action potentials in excitable cells. Infants carrying one of these SCN8A mutations experience extensive seizures, risk of SUDEP, and suffer from cognitive and motor impairments.

Methods

We seek to leverage the potential of a groundbreaking gene therapy technique called base editing to target the reoccurring SCN8A patient mutation R1872W (CGG->TGG). Base editing enables the precise incorporation of single-base changes, or substitutions, of a single DNA base pair, into the genome of living cells to target the root cause of the disorder; correcting the genetic mutation itself.

Results

We have proven that our novel base editors targeting this SCN8A mutation can 1) effectively correct the R1872W mutation in cell lines and neurons from mice expressing the R1872W mutation, 2) can prevent the early onset of seizure induced death (SUDEP) of mice carrying the R1872W human mutation (Figure 1).

Conclusions

In conclusion, we show that we can correct the SCN8A genetic mutation which leads to increased survival of mice carrying the mutation, likely due to the suppression of seizures. Presently, the treatment options for SCN8A epileptic encephalopathy are limited and do not address the underlying genetic defects driving the disease. By targeting the root cause - the genetic mutations - we aim to create personalized gene therapy solutions for this form of pediatric epilepsy. Our results represent a major breakthrough for SCN8A epileptic encephalopathy treatment.

A

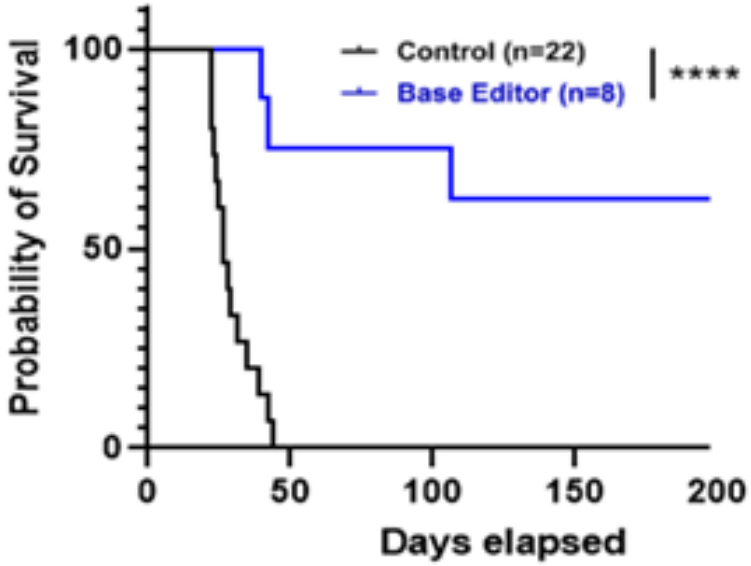
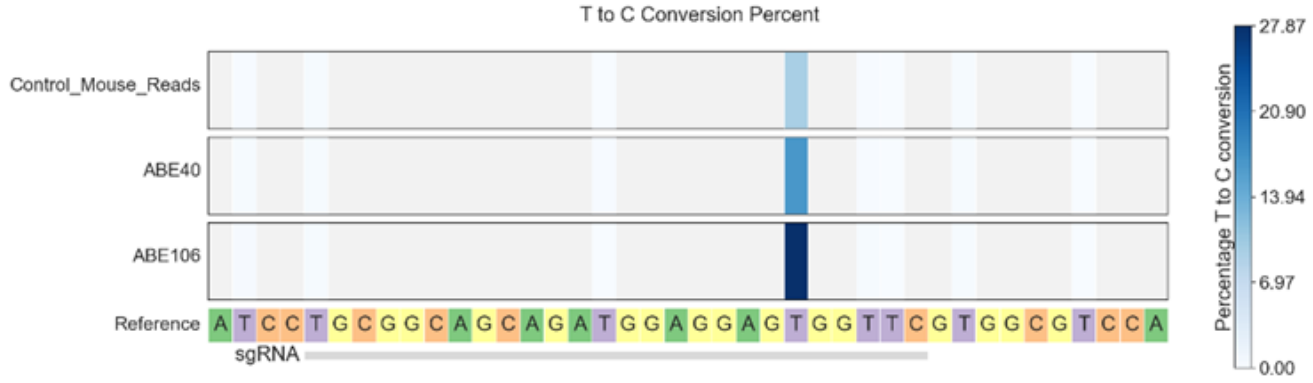


Figure 1. Treatment of mice expressing the SCN8A mutation with a base editor increases survival.

(A) Kaplan-Meier curve depicting increased survival of mice treated with a base editor compared to control mice injected with control virus (p=0.0001)

(B) Editing of SCN8A mutation (C to T) was confirmed by Next Generation Illumina MySeq deep-read amplicon sequencing.

B



ORAL PRESENTATION | 3:54 PM

Effect of a Self-CARE Education Intervention on Anesthesiology Resident Well-Being: An Interim Analysis

Lauren K. Dunn MD, PhD; David Watson, MD; Katherine T. Forkin, MD; Amanda M. Kleiman, MD; Stephen Collins, MD; Siny Tsang, PhD; Bhiken I. Naik, MBBCh, MSCR; Edward C. Nemergut, MD

Background

Anesthesiologists report high rates of burnout with younger, early-career anesthesiologists at especially high risk. Education during residency training on how to cope with and reduce stress is essential to improve physician well-being. We conducted a prospective multi-institutional trial to investigate the effect of a self-CARE (Compassion, Appreciation, Rest and Exercise) education intervention on anesthesiology resident well-being. Here we report the results of an interim analysis for participants from the University of Virginia (UVA).

Methods

The study was approved by the UVA Institutional Review Board for Social & Behavioral Sciences and the Graduate Medical Education Committee and was conducted between January 4, 2022 and June 6, 2022. Anesthesiology residents in Post-Graduate Years 1-5 were eligible to participate, and written informed consent was obtained.

Baseline demographic data and responses to a battery of surveys including the Self-Compassion Scale (SCS)-Trait Short Form and Physician Health Questionnaire (PHQ)-4 were collected using the LifeData RealLife Exp application (LifeData Corp) on the participant's personal smartphone. Responses to ecological momentary assessment (EMA) text message prompts containing the SCS- State Short Form and PHQ-4 were collected weekly. A full battery of follow up questionnaires was administered at 3, 6, 9 and 12 months.

One month after enrollment, participants were exposed to a self-CARE education intervention bundle consisting of 6 mindful self-compassion podcast videos, an online discussion forum, and daily ecological momentary intervention (EMI) reminders of wellness practices. Linear mixed effects regression models (LMERs) were used to examine the effect of the intervention (i.e., mindful self-CARE education bundle) on SCS and PHQ-4 survey responses over time.

Results

This interim analysis included 44 residents (63.6% men); most (59.1%) were 25 – 29 years old. Level of training was relatively evenly distributed across PGY-1 to PGY-4, with a small proportion at PGY-5 or greater. Results demonstrated no substantial difference in SCS state scores between pre and during ($b = -.19$, 95% CI = -.46, .09) or pre and post intervention ($b = .10$, 95% CI = -.10, .31), though the average showed a small increase over time (Figure 1). PHQ-4 depression and anxiety scores were log-transformed to correct for skewness. Although there was no difference in anxiety score between pre and during intervention (OR = .94, 95% CI = .16, 5.63), the average anxiety score was lower during post-intervention than pre-intervention (OR = .23, 95% CI = .06, .88) (Figure 2). No substantial difference in depression score was observed across the three periods (Figure 3).

Conclusions

After the self-CARE educational intervention, interim results showed ~77.4% decrease in anxiety among anesthesiology residents. Although no substantial difference in self-compassion was observed between periods, residents on average reported improvement in self-compassion over time. Our preliminary results showed potential positive effect of the self-CARE intervention on residents' anxiety and self-compassion, which may be beneficial for residents' well-being as they continue onto careers in the field of medicine. Financial support for this study provided by a Foundation for Anesthesia Education and Research in Education Grant to LKD.

Figure 1

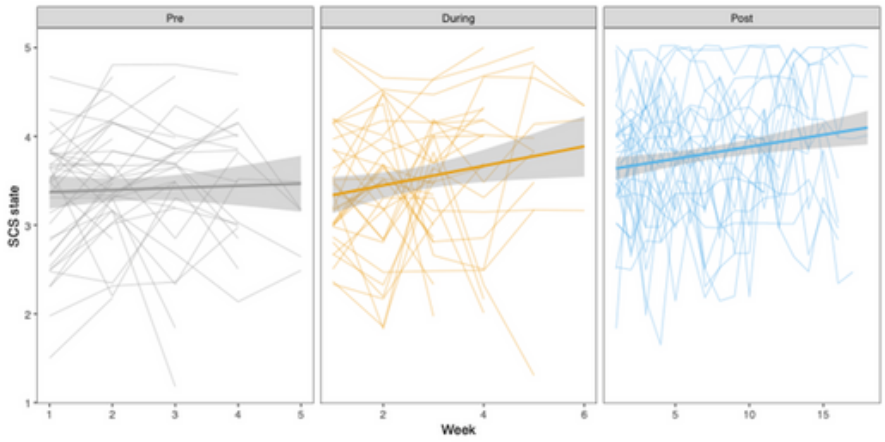


Figure 2

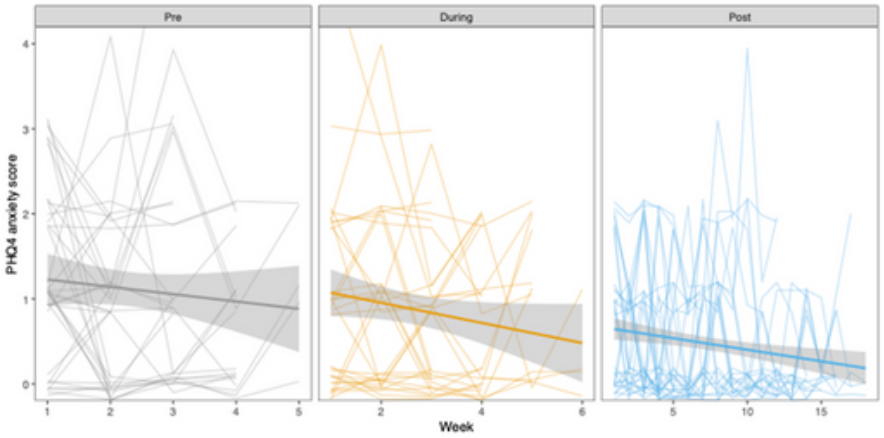
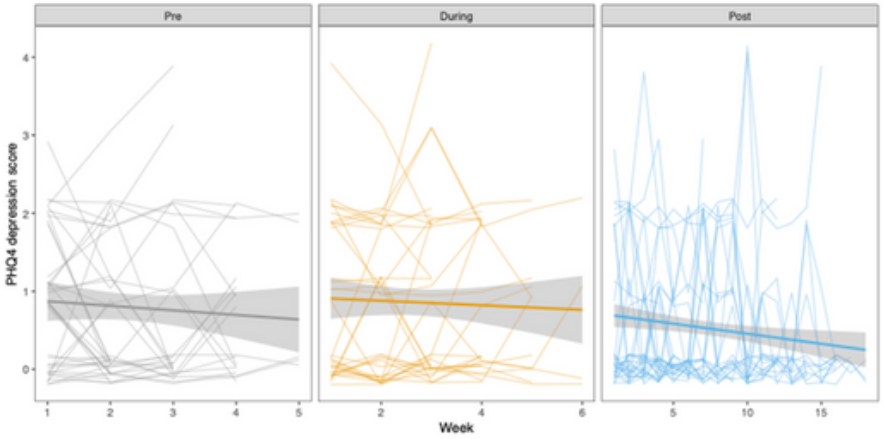


Figure 3



POSTER PRESENTATIONS

MAY 14, 2024 | 4:10 PM - 5:20 PM

POSTER PRESENTATION

One Lung Ventilation During Resection of Congenital Pulmonary Airway Malformation Complicated by a Tracheal Bronchus

Brian Brenner, MD; Abby Lawson, MD; Bridgette Love, MD; Martine Alison, MD; Joseph O'Brien, MD

Introduction

One-lung ventilation (OLV) technique during lobectomy procedures allows the collapse of the pathological lung and promotes a stable surgical field during resection. Typically, dual-lumen tubes or bronchial blockers (BB) are used to obtain lung isolation. However, when a patient's anatomy is abnormal, such as with a tracheal bronchus, there is no formal guidance for obtaining lung isolation. We present the case of right lower lobe (RLL) resection complicated by failed OLV due to a previously undiagnosed tracheal bronchus.

Case Report

Our patient is a 6-year-old female with a history of congenital pulmonary airway malformation (CPAM) with recurrent infections who underwent RLL resection. The patient had previously undergone general anesthesia without complications. Preoperative imaging studies included chest x-ray and chest computed tomography (CT) [Figure 1]. The radiologists did not comment on any abnormal tracheobronchial anatomy other than the known RLL CPAM.

Initially, the BB was placed in the patient's right mainstem bronchus without recognition of the tracheal bronchus. This resulted in continued ventilation of the surgical lung's upper lobe. It was only when the BB needed to be repositioned due to failed lung isolation that the tracheal bronchus was discovered. During airway repositioning, significant purulence, most likely disturbed due to surgical manipulation of the CPAM abnormality, flowed out of the right main stem into the healthy left lung. This resulted in collateral contamination and subsequent trauma to the ventilated lung. Deep suction was performed, and lung recruitment maneuvers were done with 100% FIO2. We then attempted to pass the endotracheal tube (ETT) into the left main stem, but this was unsuccessful due to the size of the ETT, so the BB was repositioned into its original position in the right mainstem after multiple attempts.

As ventilation resumed, there was significant shunting and subsequent hypoxemia with oxygen saturations of 60-70% on 100% FiO2. Airway pressures were also high with peak plateau pressures of 40-50 cmH20. All other vitals remained stable through utilizing a dopamine infusion, calcium gluconate, ephedrine, epinephrine, and phenylephrine boluses. Discussions were had with the surgical team about extracorporeal membrane oxygenation (ECMO), but it was decided that swift removal of the right lower lobe was preferred. The RLL was removed, airway suction was reapplied, and two lung ventilation resumed. The hypoxemia resolved within 20 minutes of surgical resection of the RLL with down-trending peak plateau pressures.

Results

The patient remained intubated and was transported to the PICU in stable condition. They were successfully extubated the following day and postoperative chest x-ray indicated a small right apical pneumothorax, no pleural effusion, and left upper lobe with atelectatic changes. The patient recovered rapidly and was discharged without complications.

Discussion

Our case highlights unsuccessful lung isolation in the setting of failure to identify important abnormal airway anatomy preoperatively. Despite preoperative CT imaging, there was no mention of central airway abnormality on the radiology report. While our case resulted in a positive outcome for our patient, a preoperative diagnosis would have allowed the anesthesia team to better prepare for optimal OLV, including placement and device planning. Routine preoperative review of available CT imaging by the anesthesiologist may improve preparation for airway management and anticipation of complications.

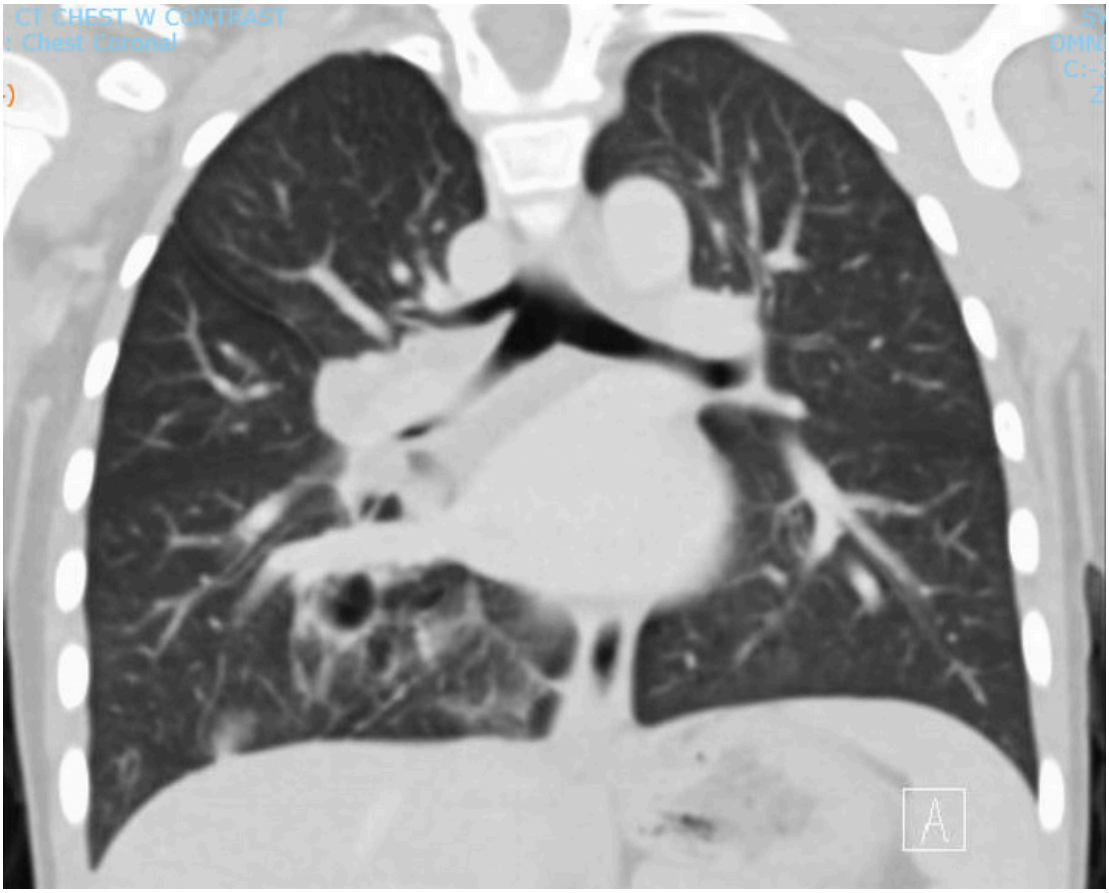


Figure 1. Preoperative CT Chest with previously undiagnosed tracheal bronchus. The official radiology read had no comment regarding any central airway abnormality.

POSTER PRESENTATION

Acute Tibial Shaft Fractures and Peripheral Nerve Blocks: Opioid Usage versus Masking of Acute Compartment Syndrome

Andrew C. Kim; Umar M. Khan; Caitlin Quigley, BA; Max Schulman; Jordan Holland, BS; Mohamed Ray-Zack, MBBS; Jeff Schulman, MD; Greg E. Gaski, MD; Robert Hymes, MD

Background

Peripheral nerve blocks (PNB's) are a well-studied technique that has been used as a method of anesthesia in the perioperative setting as an alternative and in conjunction with general anesthesia. The use of PNB's have been shown to provide effective pain management without the associated adverse effects of opioid analgesia. Furthermore, when used in conjunction with general anesthesia, PNB's have been shown to reduce postoperative opioid use and hospital stays. Due to these benefits, the usage of PNB's in elective orthopaedic procedures has become commonplace. However, in the setting of acute tibia shaft fractures, PNB usage remains controversial. With a high risk of acute compartment syndrome (ACS) with tibial fractures, there is concern whether PNB's will mask developing signs and symptoms and delay treatment. This study hypothesized that PNB's would reduce postoperative opioid requirements. Secondly, cases of postoperative ACS were evaluated for differences in detection and outcomes.

Methods

This study retrospectively evaluated patients aged 18-79 with acute tibial shaft fractures treated with intramedullary fixation at a Level 1 Trauma Center between 2018-2022. Patients with ACS prior to fixation, previous tibia fracture, and other operative long bone, pelvic or spine injuries were excluded from the study. The primary outcome was postoperative opioid requirement measured by Morphine Milligram Equivalents (MME). The secondary outcomes were LOS and incidence of ACS with associated data including time of diagnosis, time from block to diagnosis, time of fasciotomy, presence of necrotic tissue, and number of procedures after fasciotomy.

Results

317 patients were screened and 256 were eligible. 95 patients (37%) received PNB's and 161 (63%) did not. There were no significant differences in demographics between the two groups but patients who did not receive PNB's were more likely to have other nonoperative orthopaedic injuries and surgery within 72 hours of injury. MME were significantly lower in the PNB=yes group compared to the PNB=no group at 24 hours (206 vs. 521, p=0.001), 48 hours (266 vs. 796, p=0.001), and 72 hours (324 vs. 1135, p=0.003). PNB=yes averaged 3.0 postoperative inpatient days compared to 4.4 days for PNB=no (p=0.046). There were 3 cases of ACS in PNB=no and 1 in PNB=yes (p=0.20). All 3 patients without a PNB were diagnosed within 2 days of surgery and underwent fasciotomies without evidence of muscle necrosis. The patient with a PNB was discharged on postoperative day 1, re-presented to the hospital 5 days postoperatively, underwent fasciotomies, and was found to have anterior and lateral compartment necrosis.

Conclusion

PNB's following acute tibial shaft fractures were associated with decreased opioid requirements up to 72 hours. The one ACS case in the PNB=yes group presented with ACS and muscle necrosis 5 days postoperatively and experienced increased adverse outcomes. These results suggest usage of PNB's in tibial shaft fracture patients require careful monitoring postoperatively.

POSTER PRESENTATION

Optimizing Pain Self-Management in Total Knee Arthroplasty

Patrick H. Finan, PhD; Ayshah Asmat, MS; Sadana Padmanabhan, MS

Background

The purpose of this study is to investigate the efficacy of a positive affect enhancing intervention designed to reduce pain and augment reward system function in knee osteoarthritis (KOA) patients undergoing total knee arthroplasty (TKA). The scientific premise is that patient use of a positive emotion generative practice – savoring meditation, which has been demonstrated to reduce pain in experimental laboratory settings, enhanced with a pain neuroscience education component about reward system dysfunction as a chronic pain mechanism – is optimally suited to reduce postsurgical pain and augment reward system functioning relative to a Pain Self-Management and Education (PSME) condition.

Methods

We will randomize 150 patients with KOA undergoing unilateral TKA to a brief, 4-session (20-30 minutes each) course of Savoring Meditation (SM; n = 75) or PSME (n = 75) delivered remotely by trained interventionists in a one-on-one format. We will assess pain and as well as pain-related risk and protective factors both via questionnaire and via weeklong ecological momentary assessment (EMA) data bursts on the following schedule: baseline, post-surgery, and 3-month follow-up. In addition, participants will attend laboratory testing sessions at baseline and 6-weeks post-surgery, during which affective pain modulation and electroencephalographic (EEG) brain biomarkers associated with pain and affect will be recorded. Participants in SM be encouraged to practice their savoring for 5 minutes/day during the week following surgery, as well as to use it to manage pain flares in a self-directed manner. Participants in SM will be given the option to complete a qualitative interview after the follow-up laboratory testing session as well, where they will be asked questions about their thoughts and feelings about the psychological intervention and its impacts on pain and functioning.

Results

Not available yet.

Discussion

Our first aim is to determine if SM is superior to PSME in reducing clinical pain and opioid consumption following TKA. We hypothesize that SM participants will report lower clinical pain and reduced opioid consumption at major assessment time points relative to PSME participants. The study will also aim to determine if SM is superior to PSME in enhancing reward system functioning assessed via self-report and affective pain modulation task performance. It is hypothesized that SM participants will exhibit augmented reward system functioning relative to PSME participants at major assessment time points.

POSTER PRESENTATION

Multi-level Epidural Optical Monitoring for Spinal Cord Ischemia During Simulated Thoracic Aortic Surgery

David R. Busch, PhD; Chia Chieh Goh, PhD. Feng Gao; Nicholas Larson; Joseph Wahl; Thomas V. Bilfinger; Arjun G. Yodh; Thomas F. Floyd, MD

Background

Spinal cord ischemia frequently complicates aortic surgery and can result in paralysis and paraparesis. Unfortunately, current intraoperative monitoring employs evoked potentials that do not directly measure spinal cord blood flow. Additionally, alerts based on evoked potentials can be delayed by 10-20 minutes from ischemia onset, do not axially discriminate the origin of ischemia, are impacted by anesthetics and patient temperature, and suffer from high rates of false positives. Thus, current management of spinal cord ischemia is compromised. To ameliorate these issues, we developed an epidural fiber optic device (FLOXsp) that employs diffuse correlation spectroscopy (DCS) to concurrently monitor spinal cord ischemia at multiple axial levels. Herein we test the ability of this device to identify the axial origin of spinal cord ischemia in a porcine model of simulated thoracic aortic surgery and we validate the method versus Laser Doppler Flow (LDF).

Methods

The FLOXsp device, with sensors at three locations separated by 10 cm, was deployed in 5 pigs across the lumbar to mid-thoracic spinal cord. Flow validation with LDF was carried out during periods of hypercarbia/hypoxia and hypocarbia. Additionally, with fluoroscopic guidance, an intra-aortic balloon was sequentially positioned relative to the probe sensors and inflated to occlude the aorta, creating ischemia at varying levels. (Figure 1a)

Results

FLOXsp and LDF measurements of changes in spinal cord blood flow during periods of acute hypercarbia/hypoxia and hypocarbia were highly correlated ($r=0.83$, 95% confidence interval (CI) (0.79, 0.86)). Spinal cord blood flow measured by DCS caudal to aortic balloon occlusion fell by a median of -62% (95% CI, (-71, -58)). The FLOXsp device had a sensitivity of 0.87 and specificity of 0.91 for detection of a 25% decrement in spinal cord blood flow at any sensor located below the level of aortic occlusion. (Figure 1b)

Conclusion

The FLOXsp device rapidly and accurately discriminates the regional origin of ischemia during aortic occlusion and changes in flow correlated well with LDF. This technology may offer enhanced immediacy, accuracy, and anatomic guidance for management of spinal cord ischemia during aortic surgery.

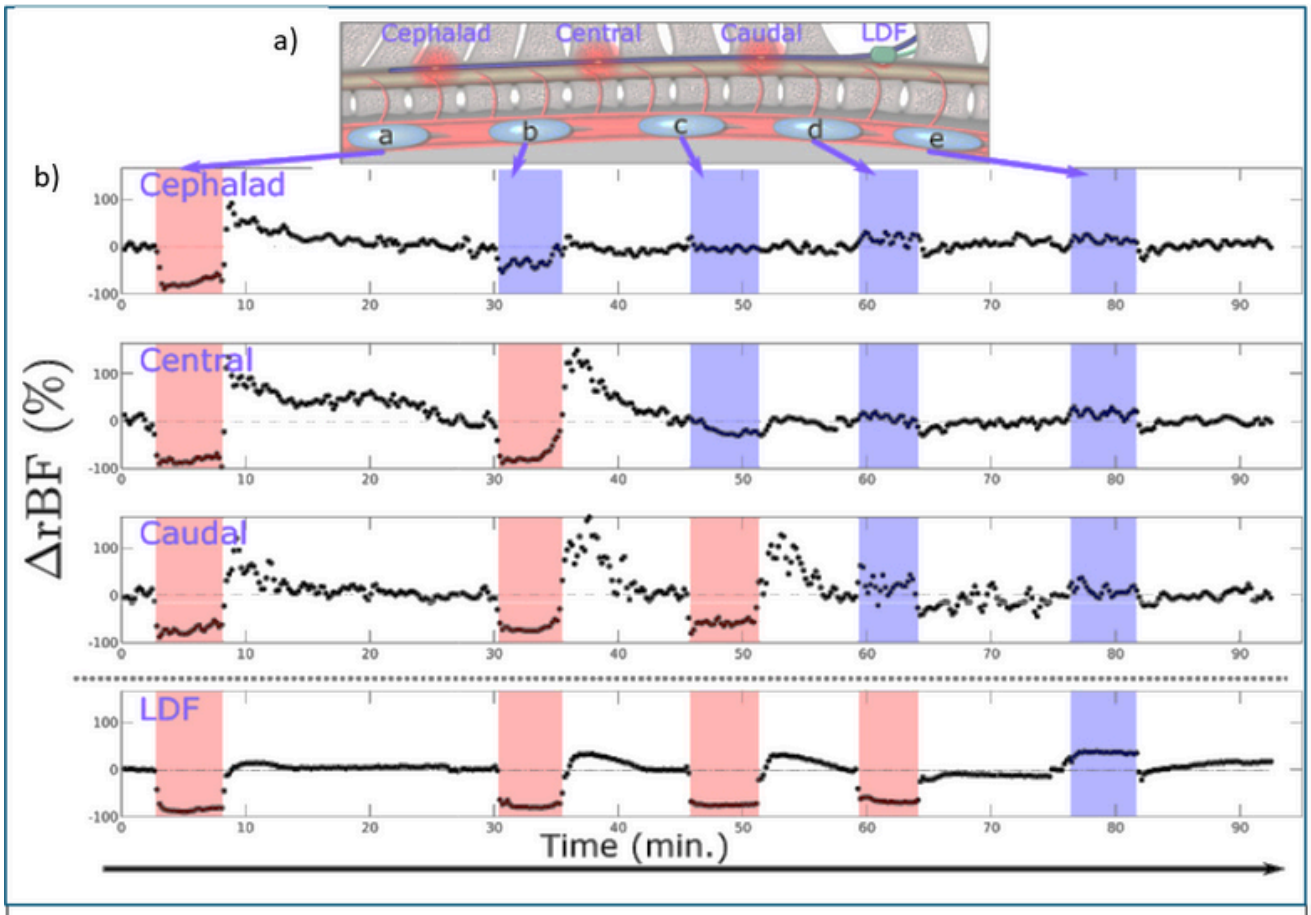


Figure 1. Axially resolved changes in spinal cord blood flow measured with **FLOXsp** and LDF. a) Positioning of epidural **FLOXsp** probe relative to intra-aortic balloon. b) Change in spinal cord blood flow in response to sequential intra-aortic balloon inflations.

POSTER PRESENTATION

Assessment of Intraoperative Opioid Administration and Waste Practices with a Change in Perioperative Controlled-Medication Waste System: A Retrospective Analysis

Jonathan Curley, MD; Benjamin Agnor, BS; Kim McRobbie, MD; Siny Tsang, PhD; Katherine Forkin, MD

Background

Intraoperative opioid medication dosing should be determined primarily by clinical factors. However, external factors such as package size and vial availability affect intraoperative opioid dosing and waste practices of anesthesia providers. On 11/21/2022, our department transitioned from a wasting system that did not require the anesthesia provider in the operating room to obtain a witness for wasted opioids (documented waste syringe was placed in a secure bin) to a system that required a waste witness for every waste event. We hypothesized that this change in wasting requirements altered opioid administration practices resulting in a decrease in opioid waste through increased opioid administration to avoid the need for waste and/or through fewer controlled substances removed from the Pyxis intraoperatively.

Methods

For this quality improvement project, we performed a retrospective analysis of opioid administration and opioid waste 4 months prior to the change in waste practice (pre-intervention: 7/21/2022 to 11/20/2022) and 4 months following the change (post-intervention: 11/21/2022 to 3/21/2023) for fentanyl and hydromorphone in adult patients. Intraoperative opioid administration values and outcome measures were obtained from intraoperative and postoperative EMR documentation. Wasting event data was obtained from the pharmacy and Pyxis records. We used segmented regression models to examine whether opioid administration practices and waste events differed after the change in waste practice.

Results

9,553 cases met inclusion criteria (n=4730 pre-intervention; 4823 post-intervention).
Figure 1 demonstrates the amount of intraoperative opioid (top panel: fentanyl, bottom panel: hydromorphone) administered over time while Figure 2 demonstrates the proportion of cases with opioid waste events over time (top panel: fentanyl; bottom panel: hydromorphone). Red dashed line represents the date the waste system was changed. Shaded areas represent 95% confidence intervals. *p < 0.05, **p < 0.01, ***p < 0.001. There was an immediate decrease in the amount of intraoperative fentanyl administered (Est = -8.59, 95% CI= -14.43, -2.75) and an immediate increase in the amount of intraoperative hydromorphone administered at the time of implementation (Est = 0.13, 95% CI = 0.07, 0.20). For both fentanyl and hydromorphone, there was a decrease in waste events after implementation of the new waste system. At implementation, there was a decrease in the incidence of waste events for fentanyl (OR = 0.30, 95% CI = 0.20, 0.45) and hydromorphone (OR = 0.60, 95% CI = 0.46, 0.78).

Conclusion

Implementation of a new intraoperative system for wasting controlled medications was associated with an immediate change in opioid administration doses and with a decrease in total waste events for both fentanyl and hydromorphone. Further analysis of these data and analysis of secondary clinical outcomes are needed to fully understand the impact of implementing a new opioid wasting system.

Figure 1. Dose of intraoperative opioid administered over time.

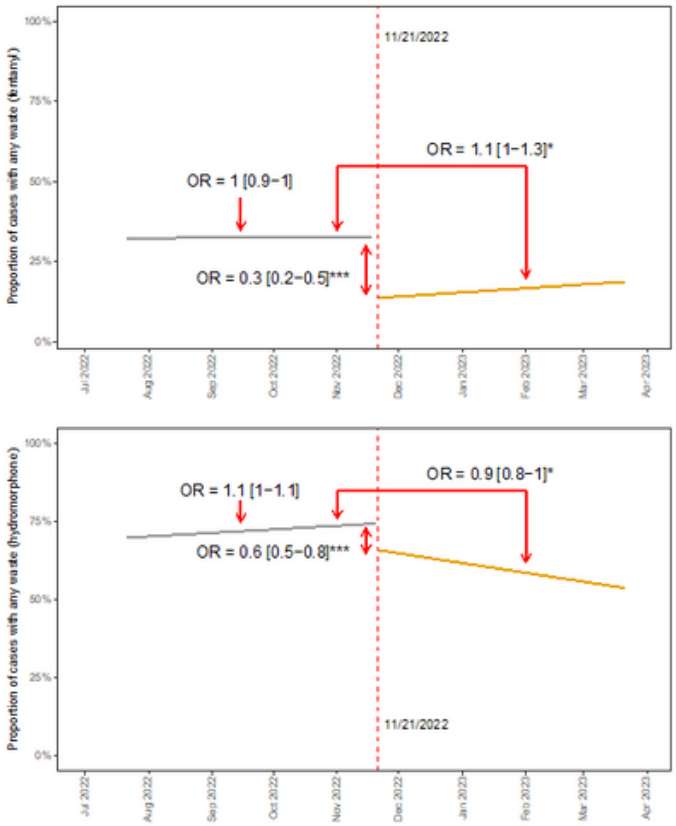
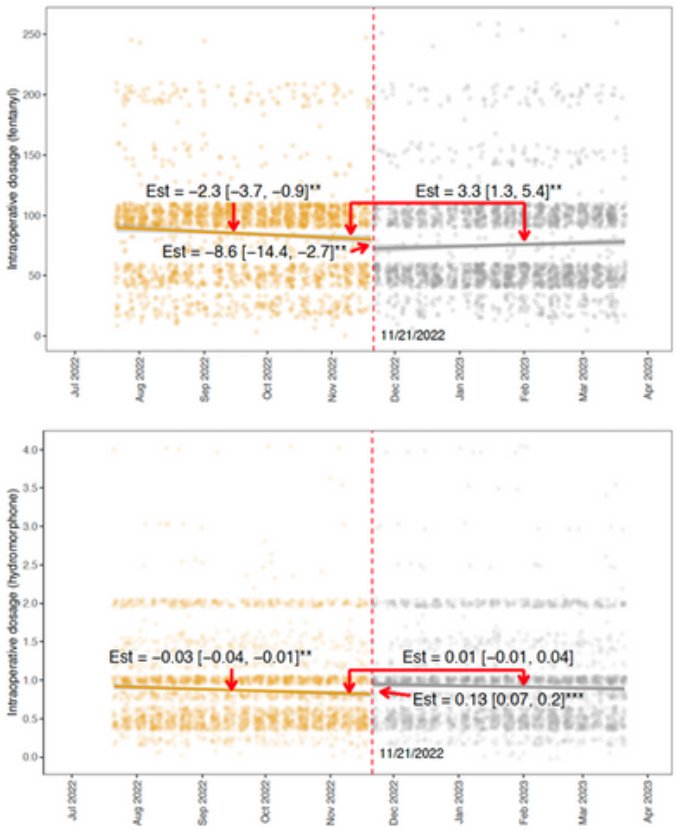


Figure 2. Proportion of cases with intraoperative opioid waste events over time.



POSTER PRESENTATION

Perioperative CVL Management

Scott Jossart, MD; Matthew Saunders, MD; Karen Singh, MD

Background

Central lines (CVLs) are a crucial part of many anesthetic plans, especially for patients who are critically ill. While CVLs are useful tools, they are associated with several risks, including central line associated bloodstream infections (CLABSIs). CLABSIs can have devastating complications resulting in increased mortality, morbidity, and longer hospital stays (1). CVLs placed intraoperatively are predominantly non-tunneled catheters, which can accrue CLABSIs via bacteria migration along the catheter or from contamination of the hub and breach in aseptic technique (1). Multiple studies and retrospective reviews have been performed to evaluate different ways to limit hub contamination. Disinfectant caps are continuously shown to decrease CLABSI rates (2), decrease bacterial burden more than alcohol disinfection (3), and be associated with cost savings for hospital systems (4). While there have been previous efforts to improve sterility of CVL placement and ensure proper sterile management of CVLs in the intensive care unit (ICU) setting at UVA, the intraoperative period following placement lacked a formal set of guidelines for maintaining proper CVL care. Our intervention focused on improving intraoperative CVL maintenance via education and visual reminders.

Methods

Parameters for proper intraoperative CVL maintenance were established utilizing the CDC guidelines regarding CVL maintenance (1). A pre-intervention audit of proper intraoperative maintenance was then conducted among the cardiac cases of a randomly chosen week. Following this audit, education of proper CVL management was conducted in a four ways: posters with proper management tips (including pictures) were placed in the five operating rooms with the highest CVL use and in the resident work area, a copy of the poster and the audit results were published in the weekly department newsletter, slides pertaining to proper CVL intraoperative use were added to the required online yearly CVL training module, and residents were educated by word of mouth about proper management. Several months after intervention, another audit was done of the intraoperative CVL management across another week's worth of cardiac cases.

Results

The pre-intervention audit encompassed 12 cases using CVLs with 8 different residents as primary providers for the cases. In the pre-intervention audit, only 4/12 (33%) CVLs had proper maintenance. Of the 8 cases that had improper management, 7 (58%) had uncapped proximal ports on the central line catheter itself or a Buddy Catheter placed through the central port, and 2 (17%) had open ports running to the CVL touching the floor. The post-intervention audit similarly had 12 cases with 8 different residents as primary providers. Of these cases, 9/12 (75%) CVLs were properly maintained. Only 2 cases (17%) had uncovered proximal ports, and 1 (8%) had an uncapped port on a line running to the CVL touching the floor. Of note, no residents were included in both the pre- and post-intervention audits.

Conclusion

CLABSIs represent a very serious potential complication of CVL use, and unlike many other major complications involved with central lines, they can be limited and/or prevented with proper management. Much effort and emphasis had previously been introduced to ensure proper sterile placement of CVLs both in the ICU and intraoperative settings. In addition, proper CVL aseptic technique and management is included in ICU education as well as daily checklists. Our project sought to fill in the gap by providing education for proper management in the intraoperative period between placement and arrival to the ICU. Multiple different educational intervention steps were undertaken to account for the variability in learning style among resident trainees. Based on audit results, proper intraoperative management increased from 33% to 75% following intervention. Our hope is that with time and continued education and instruction, this number will continue to increase, while CLABSI rates and their devastating consequences will fall.

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POSTER PRESENTATION

Erebosis, A New Cell Death Mechanism, May Be Involved in the P-tau-mediated Neuronal Cell Death in Alzheimer's Disease

Jun Li, PhD; Zhiyi Zuo, MD, PhD

Background

Alzheimer's disease (AD) is a chronic neurodegenerative disease often occurring in elderly people. It has been reported that multiple forms of regulated cell death are involved in the neuropathological process, which leads to the gradual decline of memory and cognitive function. One of the pathological hallmarks of AD is the accumulation of neuro-fibrillary tangles formed by the abnormally hyperphosphorylated tau (P-Tau) proteins. It is believed that the pathogenic aggregation of P-tau is an intracellular stressor resulting in aberrant activation of regulated cell death but how it can induce neuronal cell death is less studied [1]. Recently, erebosis, a new type of regulated cell death for tissue homeostasis, has been described. This form of death does not show the characteristic features of apoptosis, necrosis, or autophagic cell death. Erebosis-positive cell is characterized by increased intracellular accumulation of angiotensin-converting enzyme [2]. It has been shown that angiotensin-converting enzyme 2 (ACE2) in the brain of individuals with AD is up-regulated and positively associated with P-tau [3]. Hence, we hypothesize that erebosis is a cell death mechanism in the pathological process of AD and is related to the P-tau accumulation.

Methods

Brain sections of sixteen-month-old female 3xTg-AD mice (B6;129-Tg (APPSwe, tauP301L) 1Lfa Psen1tm1Mpm/Mmjax, Jackson Lab) and the same age and gender control mice (B6129SF2/J, Jackson Lab) were used for immunostaining study.

Results

There was a significant immunoreactivity to P-tau-231 and P-tau-396 throughout the hippocampus in AD mice as compared to the AD control mice. ACE2 immunosignal was strong in the hippocampal regions in AD mice as compared to the AD control mice. Interestingly, cells with high P-tau-231 expression and high P-tau-396 expression in the hippocampus had intense positive immunostaining signals of ACE2. The ACE2-positive cells were large and had abnormal morphology. Some of these cells did not have nuclei.

Discussion

Our results suggest that erebosis may occur in the brain with AD and be a form of P-Tau-induced cell death. In the future, we will detect if there are any subcellular changes in the cytoskeleton, cell adhesion, and organelles in these ACE2-positive cells to provide additional evidence for the existence of erebosis. We will also determine if this ACE2-positive cell represents the distinctive erebotic neuron cell death in the brain with AD.

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POSTER PRESENTATION

Intraoperative Severe Anaphylactic Shock to Sugammadex in an Anesthesia-Naive Patient

Alisa Wilkinson, MD; Ziyad Knio, MD; Alexander Metzger, MD; Nabil Elkassabany, MD; Jenna L Leclerc, MD, PhD

Background

Sugammadex is a modified gamma cyclodextran which works by directly binding and inactivating nondepolarizing neuromuscular blockers. It has been reported in the literature to have side effects including hypotension, tachycardia, dry mouth and dizziness. There are also rare reports of anaphylaxis (estimated incidence, 0.01% to 0.08%) [1]. The present case describes one such presentation of anaphylaxis to sugammadex. A 38 y.o. male with history of type 2 diabetes mellitus and no prior anesthetic exposure presented for inguinal hernia repair. He was hemodynamically stable throughout the case. Within minutes of sugammadex administration, he developed severe hypoxia (nadir SpO2, 74%) and hypotension (nadir mean arterial pressure, 42mmHg) refractory to increased fresh gas flows and FiO2, alveolar recruitment, intravenous fluids, and high-dose vasopressors (Figure 1). ST elevations, an erythematous truncal rash, angioedema, and increased airway pressures were subsequently noted. Differential was narrowed from undifferentiated shock to suspected anaphylaxis and targeted treatment stabilized his hypoxia and hemodynamics. Serum tryptase drawn at one hour confirmed anaphylaxis (83.8ng/mL). The patient was extubated and discharged on postoperative day one and two, respectively, without further complications.

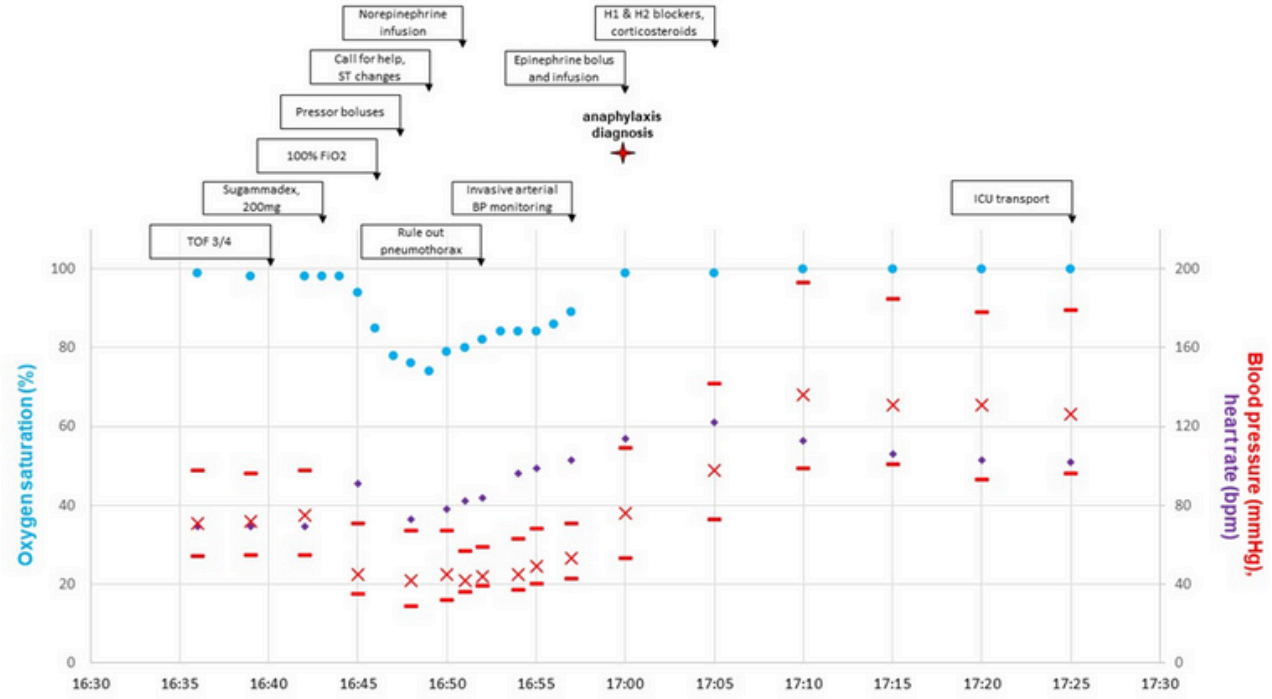
Methods

A written Health Insurance Portability and Accountability Act (HIPAA) authorization to use and disclose existing protected health information was obtained from the subject of this case report. This singleton case report did not require Institutional Review Board approval and it adheres to the applicable EQUATOR guideline (CARE guidelines for clinical case reporting).

Conclusion

Currently, while anaphylaxis to sugammadex is a rare occurrence, there are conflicting reports of incidence rates in the available literature [2-3]. There are also inconsistencies in how the current studies evaluating sugammadex anaphylaxis were conducted and how they classified anaphylactic reactions. Therefore, given the potential for patient harm, further study in larger and more diverse populations is warranted. It is notable that like the case presented here, many of the patients that have been reported to develop anaphylaxis to sugammadex in the literature had no prior exposures [4-5]. This highlights the need for anesthesiologists to remain vigilant for signs of anaphylaxis after administration of sugammadex, possibly even more so in sugammadex-naive patients.

Figure 1.



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POSTER PRESENTATION

Isoflurane and Propofol Differentially Modulate Hepatic Cancer-associated Genes in a Rat Model of Abdominal Sepsis

Hari Prasad Osuru, PhD; Nanda Kumar Yellapu, PhD; Jinny Park, BA; Keita Ikeda, PhD; Navya Atluri, PhD; Nadia Lunardi, MD, PhD; Robert Thiele, MD

Background

Hepatic dysfunction significantly contributes to the adverse outcomes associated with sepsis (1-3). General anesthetics are integral components to many surgeries, as well as diagnostic imaging and testing procedures. However, anesthetics have been implicated in physiological and metabolic disruptions that may contribute to cancer propagation by impacting immunosurveillance and inflammatory responses (3-5). The aim of this project was to investigate the effect of the volatile anesthetic isoflurane or intravenous anesthetic propofol on key genes associated with liver cancer during sepsis.

Methods

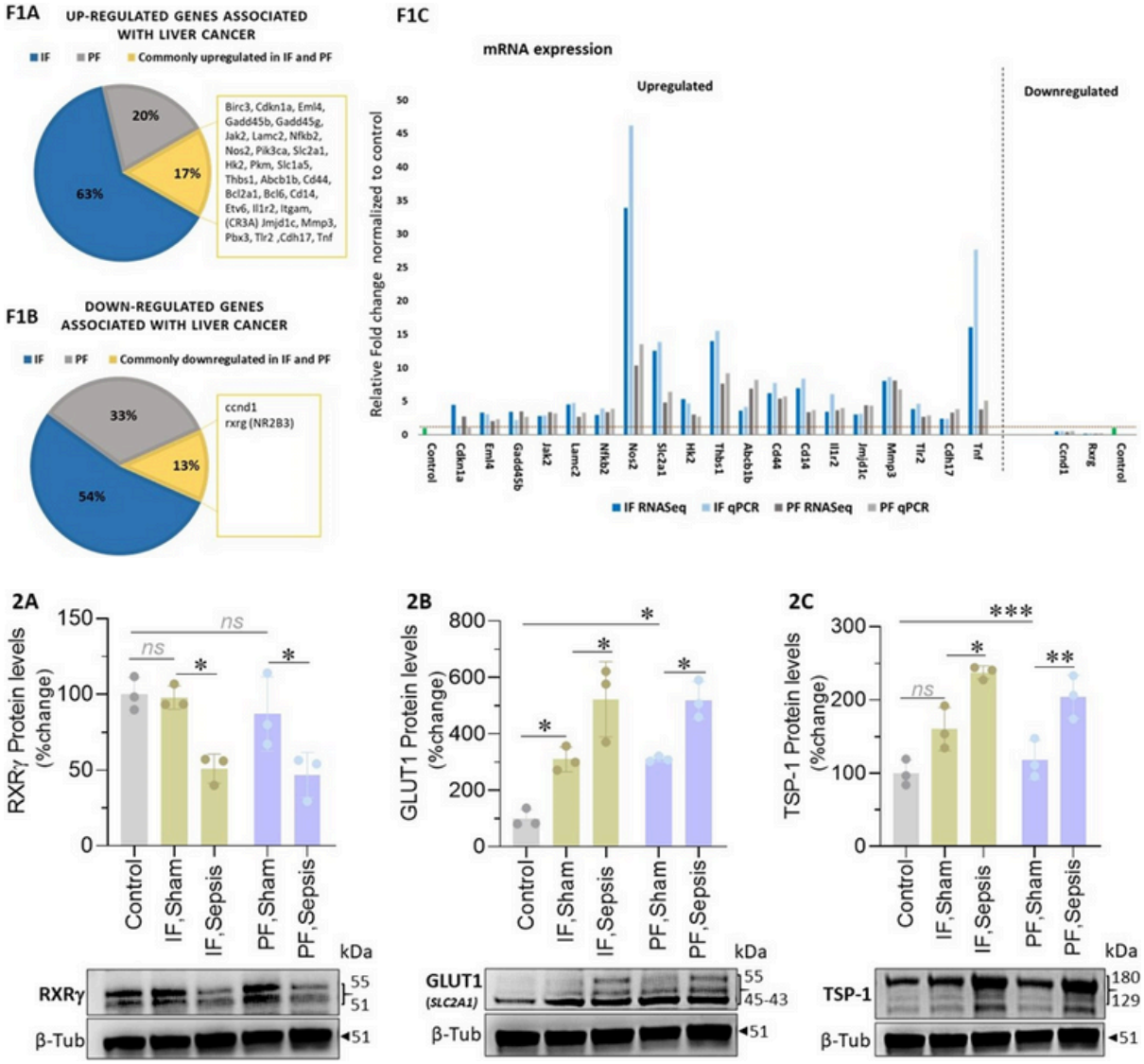
Ten-week-old male Sprague-Dawley rats (forty-eight) were randomized to either a celiotomy and closure group (Sham, non-septic) or a cecal ligation and puncture group (CLP, septic), undergoing anesthesia with either propofol or isoflurane for an 8-hour duration. Endotracheal intubation was performed, and continuous monitoring of oxygen saturation, end-tidal carbon dioxide, and blood pressure was conducted throughout the anesthesia period. Liver mRNA expression profiles were measured using RNA-sequencing and differentially expressed genes associated with hepatic cancer were identified using The Cancer Genome Atlas (TCGA). Validation of mRNA expression levels was performed via qPCR analysis, followed by protein quantification using western blotting for key identified genes. Statistical analysis (GraphPad Prism 8.0.1) was conducted using one way Analysis of Variance with multiple comparisons.

Results

RNA-seq and qPCR expression analysis revealed notable differences in the expression levels of hepatic cancer-associated genes between septic rats anesthetized with isoflurane and septic rats anesthetized with propofol, relative to sham rats. In septic rats, isoflurane led to upregulation of 63% of screened genes associated with hepatic cancer, while only 20% were upregulated in septic rats anesthetized with propofol. Concurrently, 17% of genes showed upregulation during sepsis under both anesthetic conditions. Conversely, under isoflurane, 54% of genes were downregulated in septic rats, while 33% were downregulated in propofol sepsis, with 13% downregulated under both conditions. Among the highly differentially express genes, Solute carrier family 2 member 1 (Slc2a1), known for promoting tumor growth and metastasis, exhibited a 12.6-fold increase in expression in isoflurane-anesthetized septic rats and a 4.8-fold increase in propofol-anesthetized septic rats. Thrombospondin 1 (Thbs1), a gene associated with inflammation and angiogenesis, showed a 14.0-fold increase in septic rats anesthetized with isoflurane and a 7.6-fold increase in rats anesthetized with propofol. Retinoid X Receptor Gamma (RXR□), a tumor-suppressing gene, was significantly downregulated in both isoflurane and propofol-anesthetized septic rats (Fig1). Corroborating the gene expression findings, protein levels of Slc2a1 and Thbs1 were elevated in both anesthetic groups (Slc2a1: 213% increase in isoflurane; 208% increase in propofol; Thbs1: 77% increase in isoflurane; 86% increase in propofol) compared to the sham group. Conversely, protein levels of RXR□ were reduced (46% decrease in isoflurane; 40% decrease in propofol) relative to sham-operated rats (Fig2).

Conclusion

Volatile isoflurane and intravenous propofol exert distinct modulatory effects on the expression of critical hepatic cancer-associated genes in rats during sepsis initiated by cecal ligation and puncture. Notably, isoflurane anesthesia elicited more pronounced alterations in genes governing tumor growth, inflammation, angiogenesis and metastasis compared to propofol anesthesia in septic rats. Further studies are warranted to discern how these findings in an animal model of cecal ligation and puncture-induced sepsis align with other animal sepsis models and their potential implications for clinical translation to human patients.



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POSTER PRESENTATION

Quality Improvement: Standardizing Pulse Oximetry Tone to Improve Responsiveness to Desaturation When Using Transport Monitors

Mark Pressler, MD; Shahroze Ranjha, Medical Student; Sunny Chiao, MD; John McNeil, MD

Background

The ASA outlined in their 2020 standards for basic monitoring, "During all anesthetics, a quantitative method for assessing oxygenation such as pulse oximetry shall be employed. When a pulse oximeter is utilized, the variable pitch pulse tone and the low threshold alarm shall be audible to the anesthesiologist or anesthesia care team personnel 1." Considering the anesthetic ends after the patient is transferred to the PACU team, noted in paperwork as Anesthesia Stop Time, transport from the OR with the travel monitor should include pertinent tones to maximize early identification of hypoxia or changes in heart rate.

Sonification is defined as an auditory signal where qualities of the sound are related to the information it is communicating, such as a Geiger counter "click" and a pulse oximeter change in tone 2. Task performance literature noted that advanced sonification helped distracted anesthesiologists monitor changes 3. Divided attention can lead to mistakes, however there is improved performance with multisensory cues, i.e. both auditory and visual 4,5. Considering the number of tasks for an anesthesia provider are great during awakening/transfer, ensuring an auditory pulse oximetry tone in addition to the visual travel monitor would improve early detection of desaturation.

Pulse oximetry's value lies in early identification and reduction of hypoxemia 6–8. Dual wavelength non-invasive pulse oximetry was introduced more widely in the 80s, after improvements were made to calibration and reliability 8. Pulse oximetry was adopted by the ASA in 1986, prior to outcome studies. One study looking at transport to PACU with room air versus supplemental oxygen quoted previous literature that found a significant incidence of O2 desaturation when transporting patients from the OR to the PACU 9. Risk factors such as age >60, weight >100kg, duration of anesthetic, history of smoking, higher qualitative sedation scores, lower SpO2 when leaving OR (<96%) 9–11. Pediatric patients have a higher oxygen consumption and thus a shorter time to desaturation, placing them at higher risk for desaturation during transport 12.

Methods

The University of Virginia (UVA) Institutional Review Board did not require review for this study. One investigator collected how many monitors had variable pulse oximetry audible during transport to the Post Anesthesia Care Unit (PACU). Data was collected for one week. With this prevalence data, the investigators will reach out to committees at UVA to discuss a rule change. After the rule change, the investigators will perform a post-test of equal data collection to measure the improvement in use of audible variable pulse oximetry.

Results

A single data collector tallied the prevalence of the use of audible pulse oximetry. Data was collected in 2022. The pre-rule change rate of audible variable pulse oximetry was 63%. The investigators met with the institution's Alarms Committee, Critical Care Subcommittee, and Patient Care Committee.

Conclusion

The risk factors for desaturation, and the benefit of multisensory cues, support utilization not only of SpO2 monitoring during transport but also standardizing the volume of the travel monitor. The data gathered by this QI project found a low prevalence of auditory SpO2 monitoring during transport. The authors have presented this QI project to the institution's Alarms Committee, Critical Care Subcommittee, and Patient Care Committee. The Patient Care Committee and Critical Care Subcommittee voted in favor of default volume 'on' for the variable pitch pulse oximetry. The post test has not yet been performed because the travel monitors are still in process of being updated based on the rule change.

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POSTER PRESENTATION

Vasoactive Intestinal Peptide-expressing Interneurons Are Impaired in SCN8A Epileptic Encephalopathy

Raquel Miralles, BS; Shrinidhi Kittur; Alexis Boscia, BS; Manoj K. Patel, PhD

Background

SCN8A Epileptic Encephalopathy (SCN8A EE) is a severe epilepsy syndrome caused by gain-of-function mutations in the SCN8A gene which encodes the voltage gated sodium channel Nav1.6. Nav1.6 is expressed in both excitatory and inhibitory neurons, and the balance of excitation and inhibition is critical in understanding seizure networks. There are three main subtypes of inhibitory neurons: parvalbumin (PV), somatostatin (SST), and vasoactive intestinal peptide (VIP) interneurons. Previous work from our lab shows that PV and SST inhibitory interneurons are impacted by Scn8a mutations and contribute to the seizure phenotype of SCN8A EE. RNASeq data shows that Scn8a is also expressed in VIP interneurons, which inhibit other inhibitory interneurons and have a disinhibitory influence on the cortical network, yet they have not been studied in the context of SCN8A EE. Disinhibition leads to decreased inhibitory drive in cortical networks, and aberrant disinhibition may lead to excessive cortical excitation consistent with the seizure phenotype seen in SCN8A EE.

Methods

Electrophysiology experiments were performed using a mouse model of SCN8A epileptic encephalopathy that globally expresses a patient-derived SCN8A mutation (Scn8aD/+). Brain slices were prepared and recordings of VIP interneurons were collected using whole-cell patch clamp techniques. Recordings of sodium currents and cell excitability were obtained from WT and Scn8aD/+ mice.

Results

We observe an increased persistent sodium current in Scn8a mutant VIP interneurons, a hallmark of gain-of-function SCN8A mutations that may underlie hyperexcitability. Subsequently, we found that VIP interneurons from Scn8aD/+ mice are intrinsically hyperexcitable and exhibit significantly greater spontaneous firing frequencies than their wild-type counterparts. Additionally, we identified two distinct electrophysiological populations of VIP interneurons based on firing patterns and show that they are differentially impaired in Scn8a mutant mice.

Conclusion

These findings indicate an increase in disinhibition in the cortical network in SCN8A EE, leading to a potential decrease in overall inhibitory drive. This highlights a potential role for VIP interneurons in the network dysfunction of this disorder.

Figure 1.

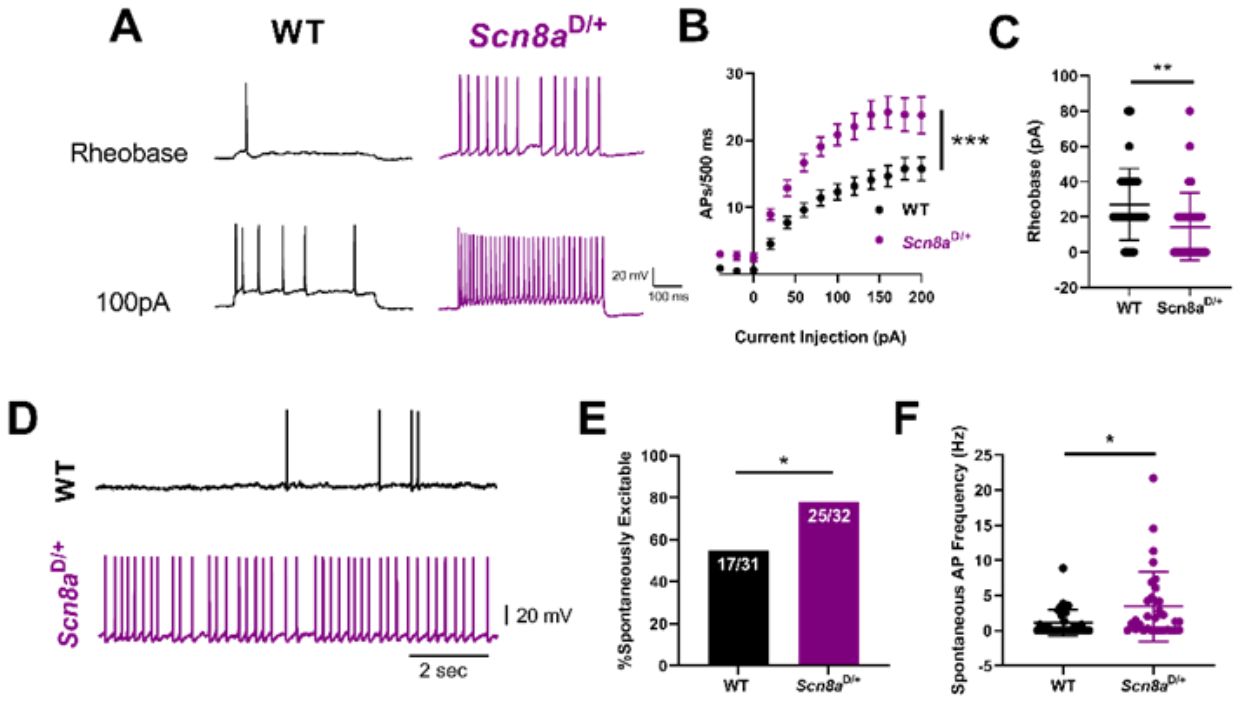
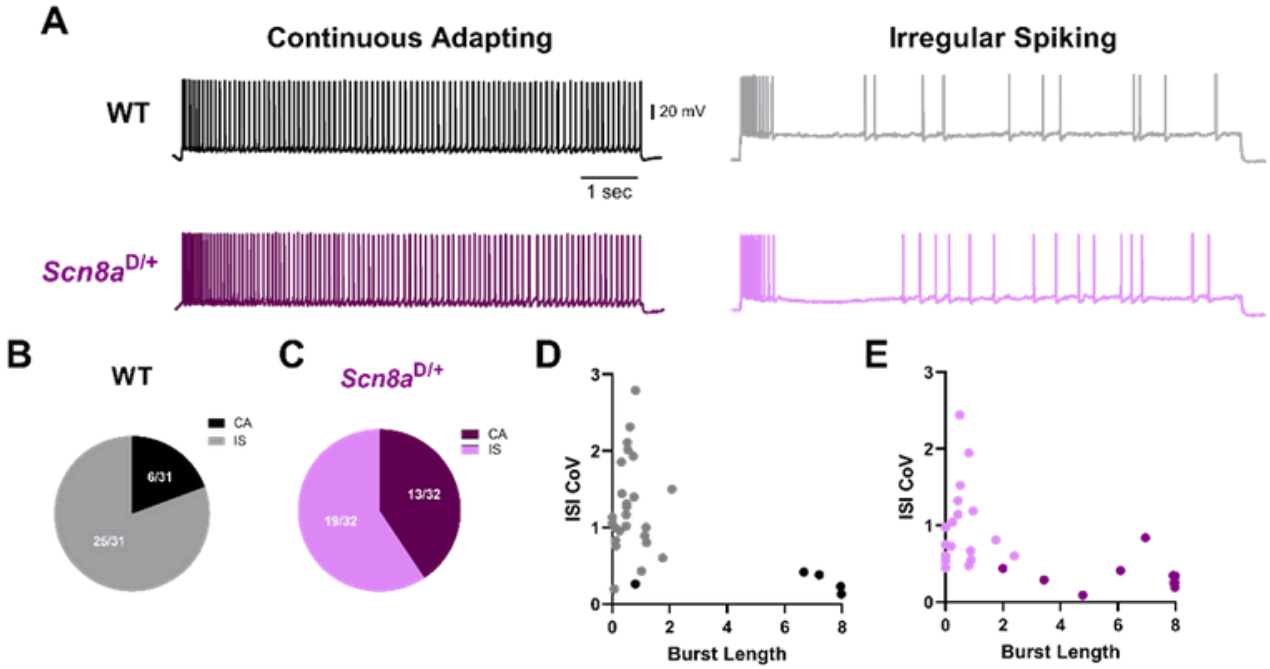


Figure 2.



POSTER PRESENTATION

Assessing Attitudes and Workflow Impact of ACT Testing Among Anesthesia Residents and Technicians

Jason Scafidi, DO; Ali Seferovich, MD; Alex Bredenkamp, MD

Background

Anesthesia management often involves the monitoring of activated clotting time (ACT) to ensure patient safety during surgical procedures. However, the integration of ACT testing into clinical practice requires efficient workflow management and appropriate training for anesthesia team members. This study aimed to evaluate the attitudes of anesthesia residents towards ACT testing training, assess the workflow disruption perceived by anesthesia technicians during high-volume ACT testing cases, quantify the response time of anesthesia technicians to ACT tests, and measure the impact of resident-led ACT testing in the operating room.

Methods

Surveys were distributed to anesthesia residents to gauge their opinions regarding the necessity and efficacy of ACT testing training. Additionally, anesthesia technicians were surveyed to evaluate the disruption of workflow during high-volume ACT testing cases. Response time to ACT tests in the OR was recorded randomly over a one-month period to assess efficiency. Subsequently, training sessions were organized to qualify residents in conducting ACT tests independently in the OR setting.

Results

Out of 64 anesthesia residents, 46 (71.8%) responded to the survey. A significant majority (87%) expressed belief in the beneficial nature of being able to perform their own ACT tests in the OR, while an overwhelming majority (93.3%) indicated willingness to undergo training in ACT testing if given the opportunity. Out of the 11 anesthesia technicians who were surveyed, 7 (64%) reported that it is always or often challenging to complete all of their assigned tasks in a timely manner when assigned to a room running ACTs [Fig 2]. All surveyed techs strongly agreed or agreed that having residents trained in running their own ACTs would improve OR workflow and decrease work strain [Fig 3]. The response time of anesthesia technicians to ACT tests was documented as a median response time of 160 seconds (range 60 to 320 seconds).

Conclusion

The results demonstrate that there is significant potential benefit to training anesthesia residents in performing ACT, both for speeding up time to ACT result and for reducing strain on anesthesia technicians. There is significant buy-in from the residents, as demonstrated by the majority of residents that believe it would be beneficial to have residents trained in performing intraoperative ACT. Overall, these results underscore the value in having residents trained in performing point of care ACT.

Fig 1. Anesthesia Technician Survey-1

I am interrupted during other time-sensitive tasks in order to run ACTs

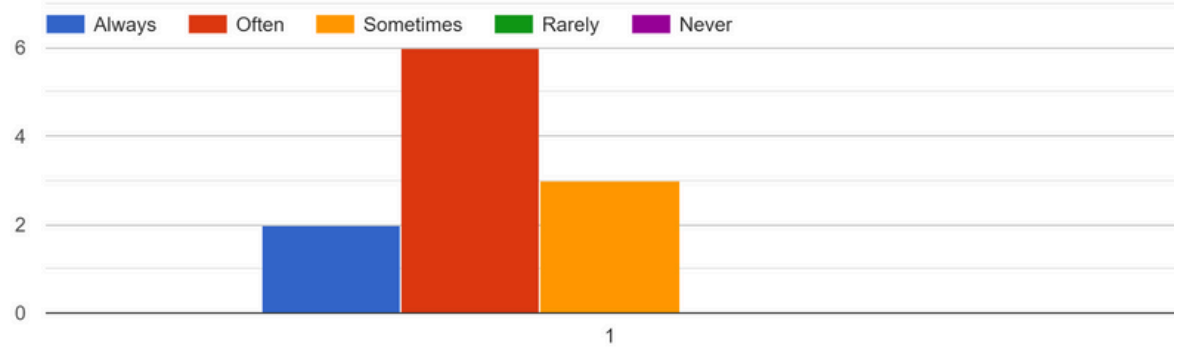


Fig 2. Anesthesia Technician Survey-2

It is challenging to complete all of the tasks required of me when assigned to rooms running ACTs

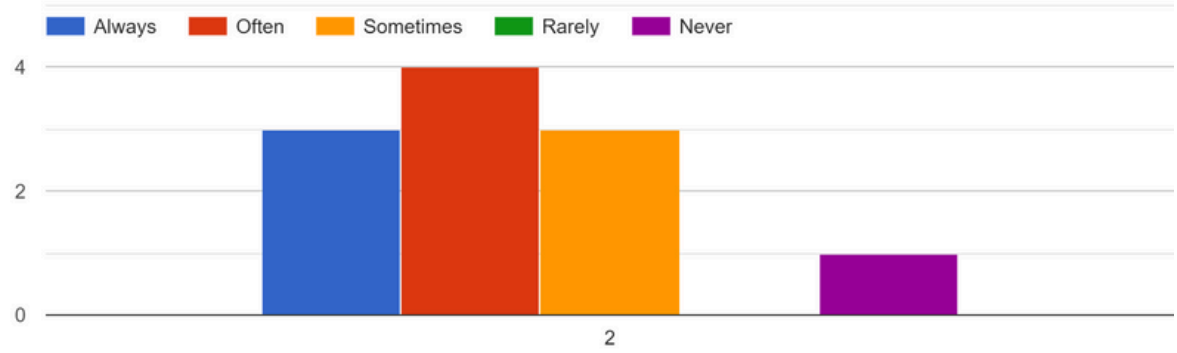
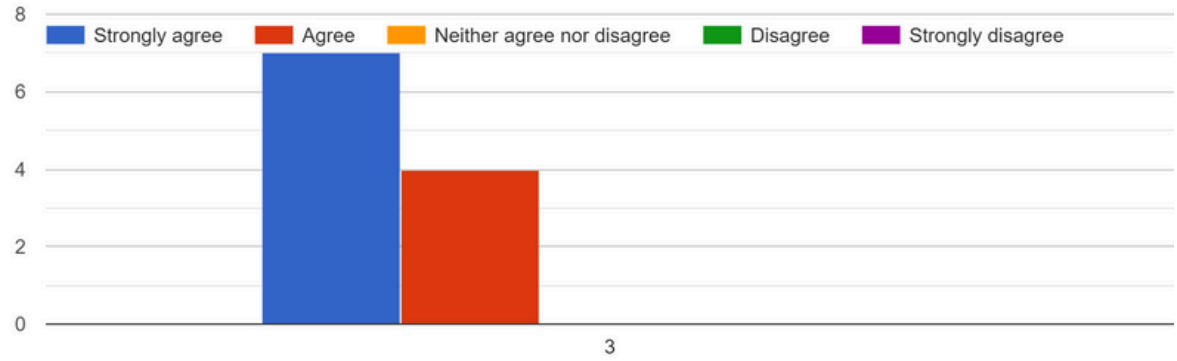


Fig 3. Anesthesia Technician Survey-3

Having residents trained in running ACTs would improve OR workflow and decrease strain on anesthesia techs



POSTER PRESENTATION

Intraoperative Methadone in Cardiac Surgery Patients: A Retrospective Cohort Study

Karen Singh, MD; Siny Tsang, PhD; John McNeil, MD; Jessica Zvara, MD; Michael Mazzeffi, MD

Background

Methadone, a long-acting opioid with NMDA antagonist properties, is increasingly used as a primary intraoperative opioid for volatile-based cardiac anesthetics. A previous randomized controlled trial found that patients receiving methadone had improved pain scores and decreased opioid consumption postoperatively, and small retrospective studies have shown decreased postoperative opioid use in patients receiving intraoperative methadone. The aim of our study was to investigate the association between intraoperative methadone and postoperative opioid consumption, pain scores, and time to extubation. We hypothesized that patients receiving intraoperative methadone would have lower postop opioid administration than patients receiving shorter acting intraoperative opioids.

Methods

We performed a retrospective cohort study of patients having isolated CABG from January 2018 to March 2023 at a single academic center. Demographic characteristics and intraoperative variables were collected for each patient. Study outcomes included time to first postop opioid consumption, total postop opioid consumption in morphine milligram equivalents (MMEs) on POD 0, 1, 2, average and maximum pain scores on POD 0,1, 2, and time to extubation. Linear mixed effects regression models were used to examine the extent to which intraoperative methadone was associated with time to extubation, after controlling for predicted risk of prolonged mechanical ventilation, moderate or severe chronic lung disease, intraoperative rocuronium dosage, use of non-opioids (ketamine, midazolam, and dexmedetomine/propofol), intraoperative MME, CPB time, and LVEF. Linear mixed effects regression models were used to examine the extent to which postop pain and MME use were associated with intraoperative methadone use, after controlling for predicted risk of mortality, history of depression, use of non-opioids intraoperatively and intraoperative MME.

Results

Data on a total of 1338 isolated CABG patients was collected; 1051 patients received intraoperative methadone at a dose of 0.2 mg/kg, and 287 patients received a non-methadone intraoperative opioid. Demographic and intraoperative characteristics are shown in Table 1, and outcome variables are shown in Table 2. Patients who did not receive methadone were more likely to have higher postop MMEs than those who received methadone (OR 1.35, $p < 0.007$). No difference was seen in time to first opioid administration postoperatively between the two groups. There was a statistically significant main effect of methadone use on lower postop average pain score (0.48, $p < 0.001$) and maximum pain score (0.49, $p < 0.001$). While median time to extubation was similar between the methadone and non-methadone groups (4.8 h and 4.6 h), linear regression modeling demonstrated a 25% shorter time to extubation in patients who did not receive methadone (OR 0.74, $p < 0.001$).

Conclusion

Intraoperative methadone use in cardiac surgery is associated with lower postoperative opioid consumption, slightly decreased postoperative pain scores, and a slight increase in time to extubation. The benefits and risks of using intraoperative methadone should be carefully considered when planning enhanced recovery protocols in cardiac surgery.

Table 1. Descriptive statistics of patient characteristics

Variable	Intraoperative methadone N=1051	No intraoperative methadone N=287	P value
Age	66 ± 10	65 ± 10	0.29
Male sex (%)	806 (76.7)	229 (79.8)	0.301
Weight (kg)	91.2 ± 19.4	91.3 ± 20.2	0.89
BMI (kg/m^2)	30.4 ± 6.0	30.0 ± 5.9	0.38
Urgency[1] Elective Urgent Emergent	 489 (46.5) 557 (53.0) 5 (0.5)	 108 (37.6) 169 (58.9) 10 (3.5)	< .001
Current smoker	242 (23.0)	75 (26.1)	.308
Moderate to severe chronic lung disease	84 (8.0)	34 (11.8)	.054
Diabetes mellitus	527 (50.1)	141 (49.1)	.812
Depression	104 (9.9)	47 (16.4)	.003
OSA	312 (29.7)	60 (20.9)	.004
Illicit drug use	33 (3.1)	10 (3.5)	.709
IABP	40 (3.8)	27 (9.4)	<.001
LVEF (%)	53 ± 11	49 ± 14	<.001
Predicted risk of mortality	1.5 ± 1.8	2.1 ± 2.5	<.001
Predicted risk of prolonged mechanical ventilation	6.8 ± 6.5	9.7 ± 9.7	<.001
Methadone (mg)	18.1 ± 4.3	-	-
Ketamine (mg)	110.4 ± 40.5	46.0 ± 62.8	<.001
Midazolam (mg)	2.9 ± 2.0	3.8 ± 3.0	<.001
Hydromorphone (mg)	0.1 ± 0.5	0.1 ± 0.5	.032
Rocuronium (mg)	172.4 ± 52.0	149.6 ± 51.3	<.001
Sufentanil (mcg)	3.0 ± 24.4	150.4 ± 120.4	<.001
MME (mg)	52.0 ± 155.9	152.2 ± 119.6	<.001
Aortic cross clamp time (min)	84.4 ± 31.4	77.0 ± 33.9	<.001
CPB time (min)	107.3 ± 38.7	98.7 ± 40.7	<.001

Note: Linear regression (continuous variable) or Chi-square test (categorical variable) was used to examine differences by group, unless otherwise specified.
1 Fisher's exact test was used due to small sample size.
N=1338

BMI=body mass index, CPB=cardiopulmonary bypass time, IABP=intra-aortic balloon pump, LVEF=left ventricular ejection fraction, MME= morphine milligram equivalents, OSA=obstructive sleep apnea

Table 2. Descriptive statistics of outcome variables between patients with and without intraoperative methadone.

Variable	Intraoperative methadone N=1051	No intraoperative methadone N=287
	Median [IQR]	Median [IQR]
MME POD 0	21.9 [12.0, 34.5]	23.8 [14.9, 38.8]
MME POD 1	15.0 [7.5, 28.8]	16.0 [8.3, 28.8]
MME POD 2	7.5 [2.5, 16.3]	11.7 [5.6, 21.7]
Average pain POD 0	5.3 [3.9, 6.8]	5.9 [4.2, 7.0]
Average pain POD 1	4.2 [2.8, 5.6]	4.5 [3.4, 5.8]
Average pain POD 2	2.8 [1.4, 4.3]	3.1 [1.5, 4.6]
Max pain POD 0	8.0 [7.0, 10.0]	9.0 [7.0, 10.0]
Max pain POD 1	7.0 [6.0, 9.0]	8.0 [7.0, 9.0]
Max pain POD 2	6.0 [4.0, 8.0]	7.0 [4.0, 8.0]
Time to first postoperative MME (h)	3.3 [1.3, 6.7]	3.4 [1.2, 6.2]
Time to extubation (h)	4.8 [3.5, 7.2]	4.6 [3.4, 7.2]

N=1338
MME=morphine milligram equivalent, POD=postoperative day

POSTER PRESENTATION

Susceptible But Not Resilient Mice Develop Learning and Memory Dysfunction after Chronic Social Defeat Stress

Ting Chen, MD; Zhiyi Zuo, PhD

Background

Anxiety and depression are common in patients for surgery. The Chronic Social Defeat Stress (CSDS) model is a well-established paradigm for investigating depression and anxiety disorders, leveraging individual variability in stress sensitivity to yield susceptible and resilient phenotypes. This study aims to examine whether differences in cognitive functions exist after stress among individuals with different stress sensitivities.

Methods

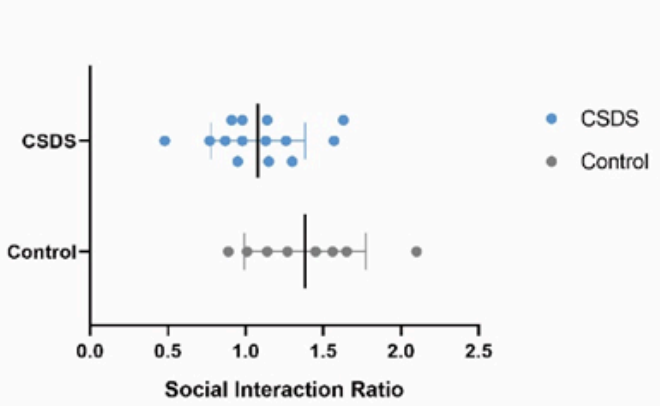
Mice were subjected to prolonged interactions with dominant, aggressive conspecifics to induce a state of continuous stress, mimicking long-term social stress responses. Body weight was measured the day before and after the stressful interactions to assess changes across groups. After the interactions, mice underwent the Social Interaction Test to classify them into susceptible or resilient phenotypes. Anxiety levels were evaluated using the Forced Swim Test, Open Field Test, and Elevated Plus Maze Test. To assess learning and memory, the Novel Object Recognition Test, Barnes Maze Test, and Fear Conditioning Test were conducted.

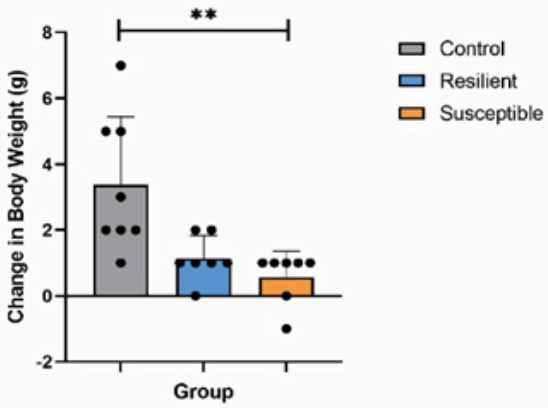
Results

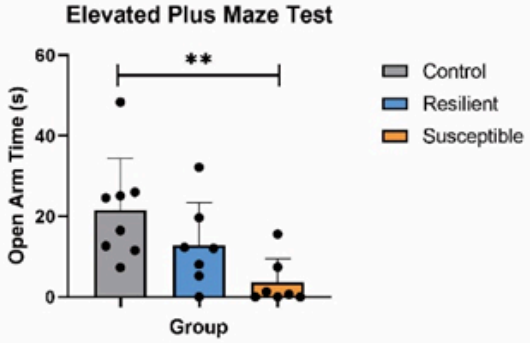
Susceptible mice exhibited significantly less body weight gain compared to the control group ($p < 0.01$). Resilient mice trended to have a reduced weight gain, though the change was not statistically significant. In the Elevated Plus Maze Test, susceptible mice spent significantly less time in open arms compared to controls ($p < 0.01$), with resilient mice showing a non-significant trend. Forced Swim Test results indicated no significant differences in immobility times across groups. Open Field Test outcomes revealed no significant differences in center area time among groups. During the Barnes Maze Test, all groups reduced the time needed to identify target box over four days of training. However, susceptible mice took significantly longer to find the target box than controls on the first day post-training ($p < 0.01$), with no significant difference observed for resilient mice. Eight days post-training, there were no significant differences in the time needed to identify the target box among groups. In the Fear Conditioning Test, both susceptible and resilient mice showed significantly shorter freezing times compared to controls in both context and tone tests ($p < 0.01$ and $p < 0.05$, respectively). The Novel Object Recognition Test revealed no significant differences in novel object discrimination among the groups.

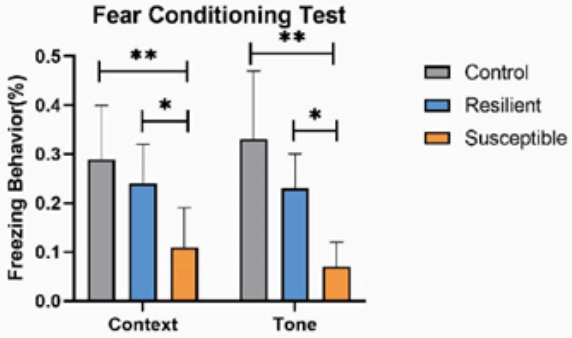
Conclusion

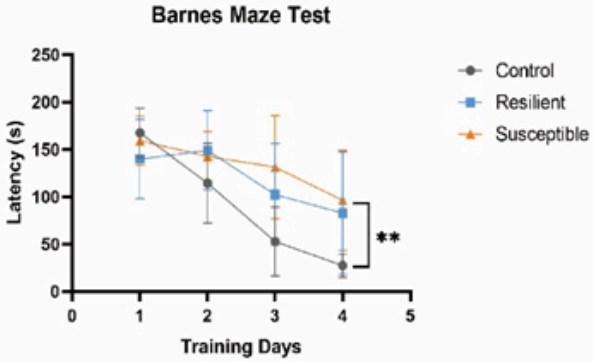
Within the CSDS model, susceptible mice with anxiety after stressful interactions demonstrate a spatial learning and memory impairment.

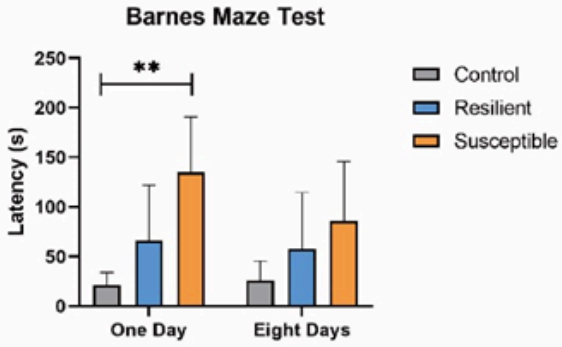

CSDS
Control
0.0
0.5
1.0
1.5
2.0
2.5
Social Interaction Ratio
CSDS
Control


**
Change in Body Weight (g)
8
6
4
2
0
-2
Group
Control
Resilient
Susceptible


Elevated Plus Maze Test
**
Open Arm Time (s)
60
40
20
0
Group
Control
Resilient
Susceptible


Fear Conditioning Test
**
*
**
*
Freezing Behavior(%)
0.5
0.4
0.3
0.2
0.1
0.0
Context
Tone
Control
Resilient
Susceptible


Barnes Maze Test
Latency (s)
250
200
150
100
50
0
0
1
2
3
4
5
Training Days
**
Control
Resilient
Susceptible


Barnes Maze Test
**
Latency (s)
250
200
150
100
50
0
One Day
Eight Days
Control
Resilient
Susceptible

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