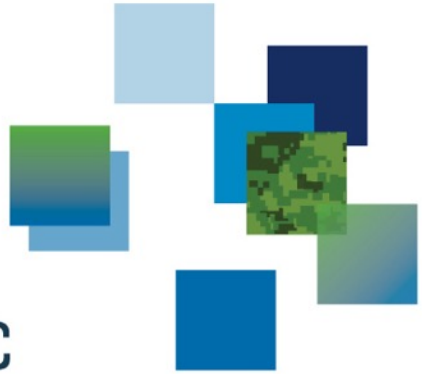
Defence Research and Development Canada | Recherche et développement pour la défense Canada

Psychological, Physiological, and Neurological Effects of Repeated Low-level Blast Exposure: Data from the Canadian Armed Forces

Oshin Vartanian, Ph.D.

Shawn Rhind, Ph.D.

Defence Research & Development Canada



DRDC | RDDC

Canada

VA HSR&D CYBERSEMINARS

Jan 27, 2022

Overview

- Brief overview of recent DRDC research on blast:
  1. Vartanian et al. (2020, 2021),
  2. Nakashima et al. (2021).
- Review latest results from ongoing research involving CAF operators (snipers and breachers):
  1. Neuropsychological effects (post-concussive symptoms),
  2. Brain imaging results (task-related fMRI activity).
- Blast exposure and neurotrauma:
  1. Multi-omics lab approaches,
  2. Neurological biomarkers of blast injury.
  3. PET-Tau imaging for chronic neurodegeneration
- Future directions.

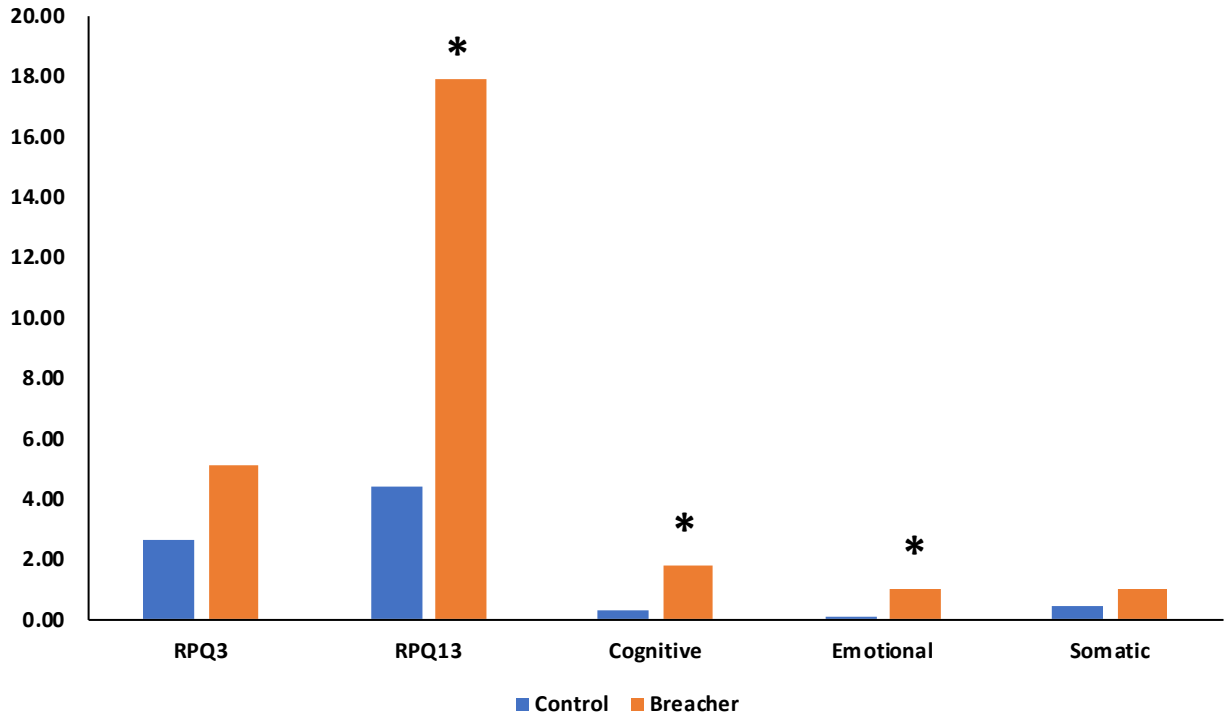
Blast effects (2011-2018):

- Repetitive exposure to low-level blast has been associated with:
  1. Greater levels of post-concussive symptoms,
  2. Greater reports of musculoskeletal difficulties,
  3. Lower levels of self-reported health (e.g., energy, physical health),
  4. Higher rates of self-reported tinnitus,
  5. Difficulty in visuomotor integration,
  6. Less grey matter volume in prefrontal cortex measured with MRI,
  7. Alterations in neurological biomarkers profiles.

Ongoing research (2018-present):

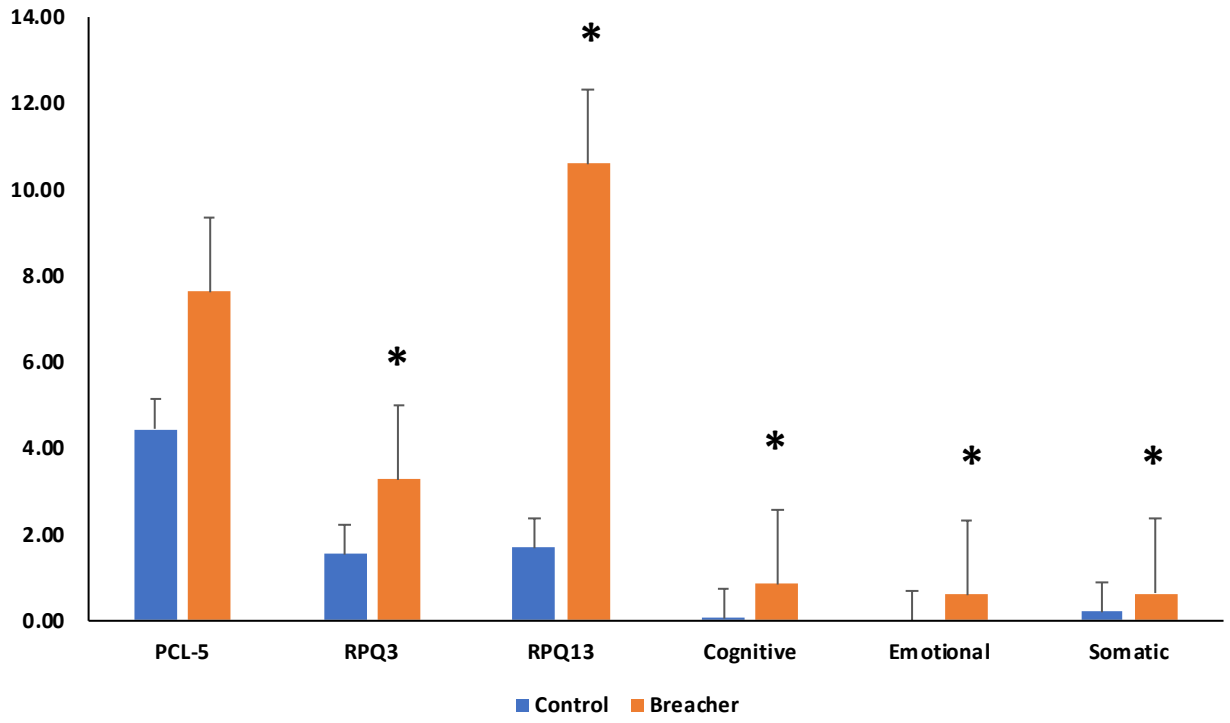
- *N* = 90 (operators + sex- and age-matched CAF controls).
- Measures:
  1. Background history (injury, health and occupation),
  2. Neuropsychological testing,
  3. Neurocognitive testing,
  4. Balance and ataxia,
  5. Hearing,
  6. Brain imaging:
     1. Structural MRI.
     2. Resting-state fMRI,
     3. Task-based fMRI.
  7. Biomarker analysis:
     1. Blood,
     2. Saliva.

Post-concussive Symptoms: Special Ops Breachers (2011-2015):



Vartanian et al. (2021)

Post-concussive Symptoms: CFSME breachers (2015-2018)



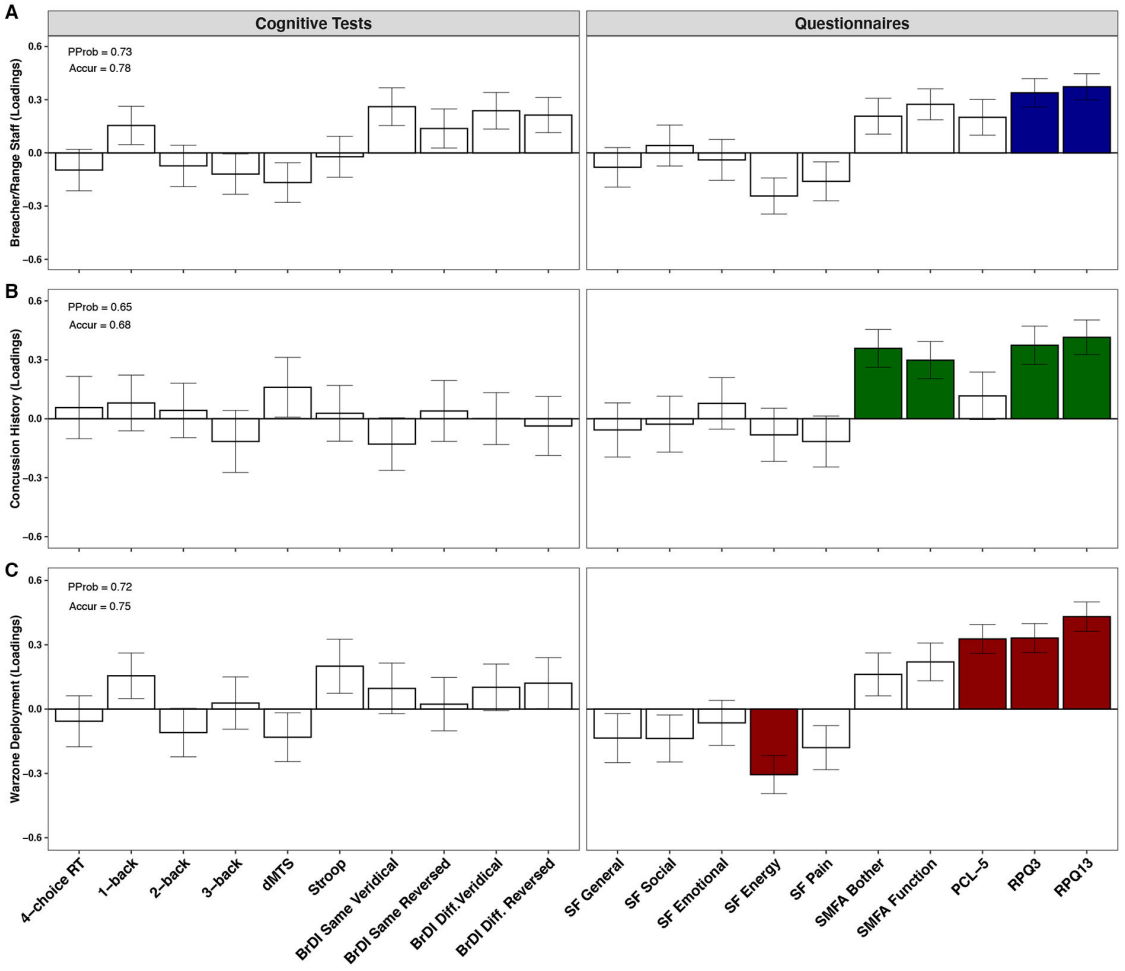
Vartanian et al. (2020)

CFSME breachers (2015-2018): Multivariate analysis

Breaching

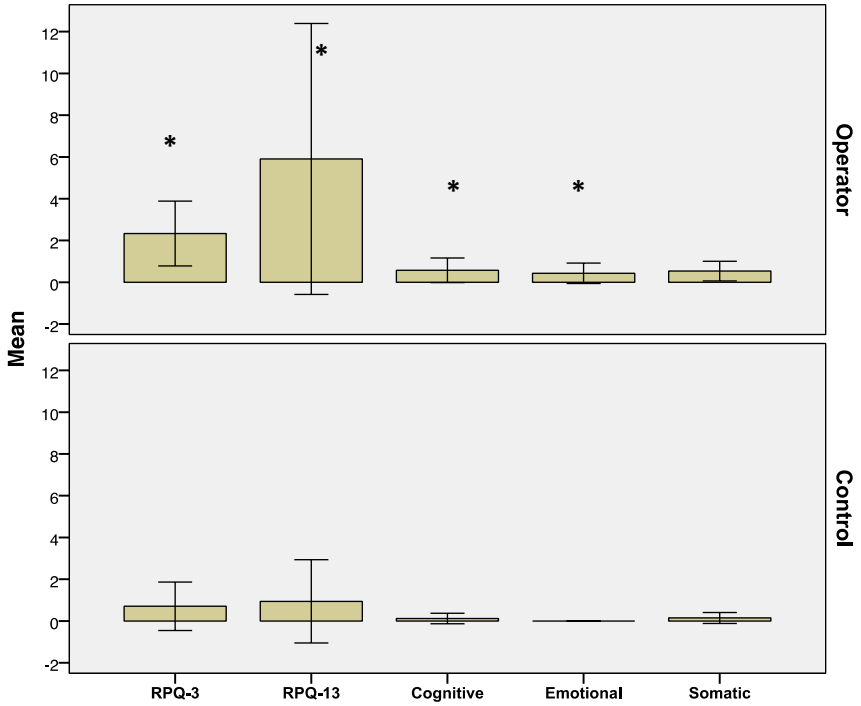
Concussion

Warzone deployment

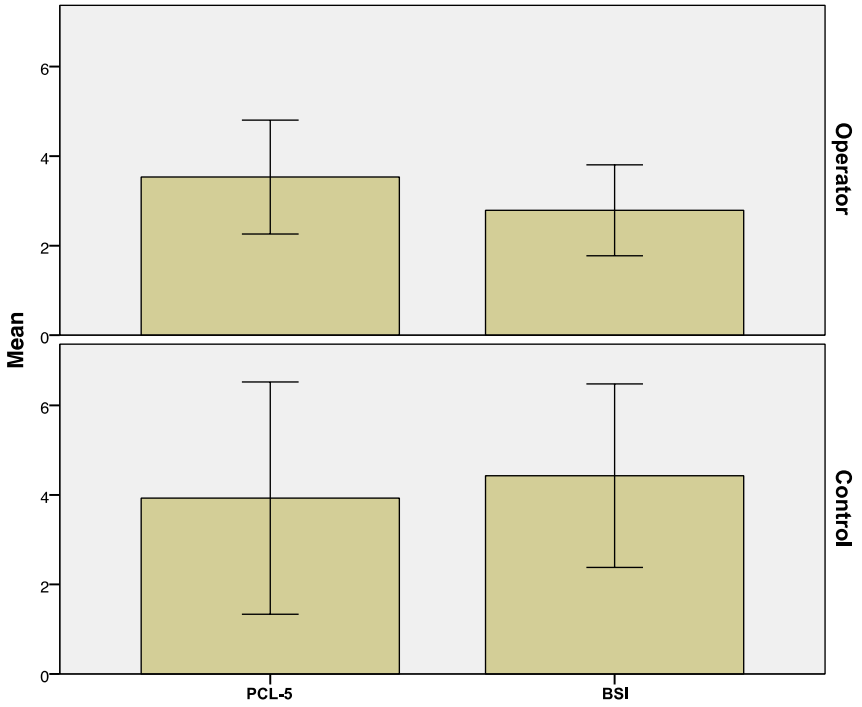


Vartanian et al. (2020)

Post-concussive symptoms: Rivermead

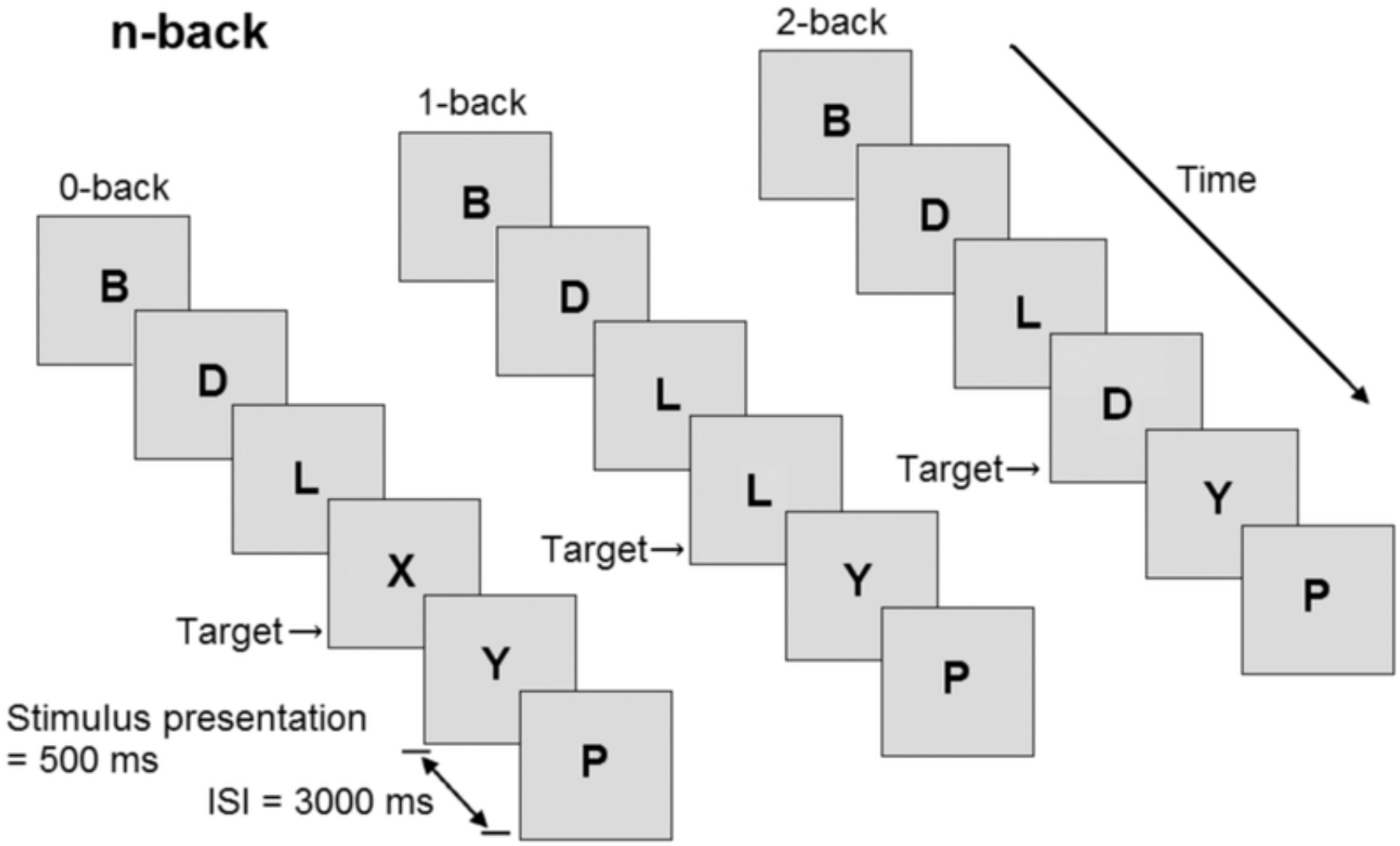


Mental health: PCL-5 and BSI

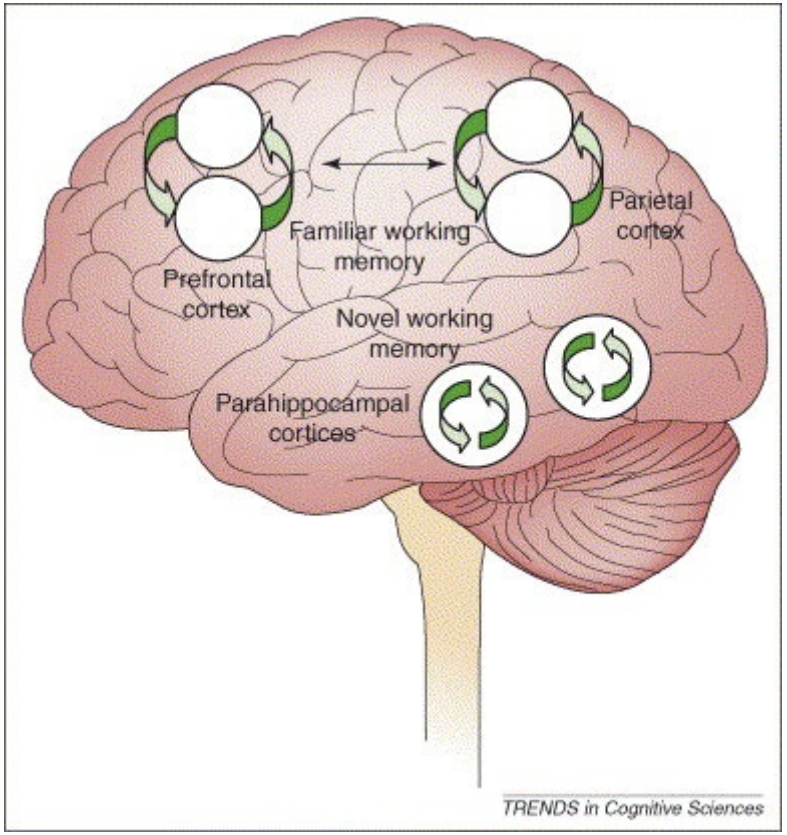


Neuroimaging at York University + The Royal Hospital

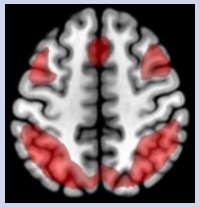
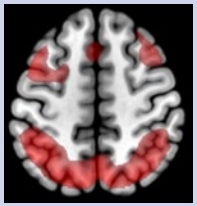
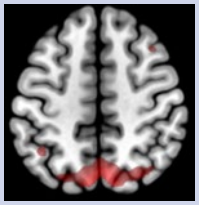
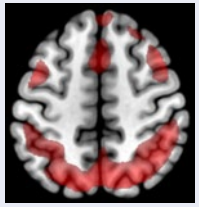
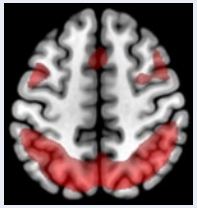
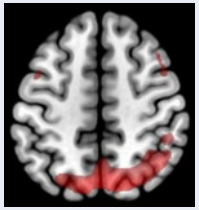
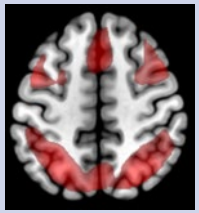
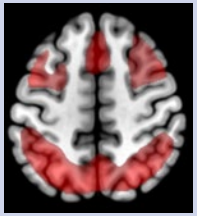
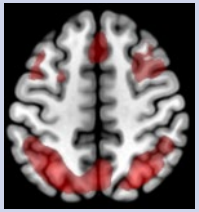
Task-based fMRI: Working Memory



Working Memory System



Working Memory: Neural Activation

	1-back	2-back	3-back
New recruits			
CAF Control			
Operators			

Scope of the Problem

- Exposure to low-level occupational blast overpressure (BOP) is common for military members during training and operational deployments.
- Current Findings: from *experimental animal models* of blast-induced neurotrauma and human studies of subconcussive brain trauma link repeated BOP to measurable performance decrements and health symptomologies; including development of *long-term neurological disease and/or psychiatric disorders*.
- The physiological and neurological manifestations from cumulative exposure to repetitive low-intensity BOP events are distinct, but not currently well understood in humans.
- Available evidence suggests repeated exposure to BOP may lead to *persistent and progressive subconcussive neurological deficits* that are reflected by alterations in fluid biomarkers in the absence of clinically diagnosed injury.
- Blast intensity and frequency matter – yet, *lower limit thresholds for injury are not well defined*. Need for studies to in target populations to report health & performance outcomes concurrently with BOP measurements to facilitate the establishment of a "*dose-response*" relationship in order to understand what constitutes safe exposure limits and assist in development of evidence-based exposure guidelines/ countermeasures.

Background: *Human Studies on the Effects of Low Level Military Occupational Blast Exposure on the Nervous System*

MILITARY MEDICINE, 00

Case S
Biomarker
Analysis Be

trauma
ctional MRI
-Level Blast

Stephanie E.
Christin

AJ Walter Carr;*
Tate, MD§

Journal of Neurotrauma

DOI: 10.1089/neu.2019.6742

Acute and Chronic Molecular Signatures and Associated Symptoms of Blast Exposure in Military Breachers

Running Title: Chronic & Acute Biomarkers of Blast Exposure

AUTHORS

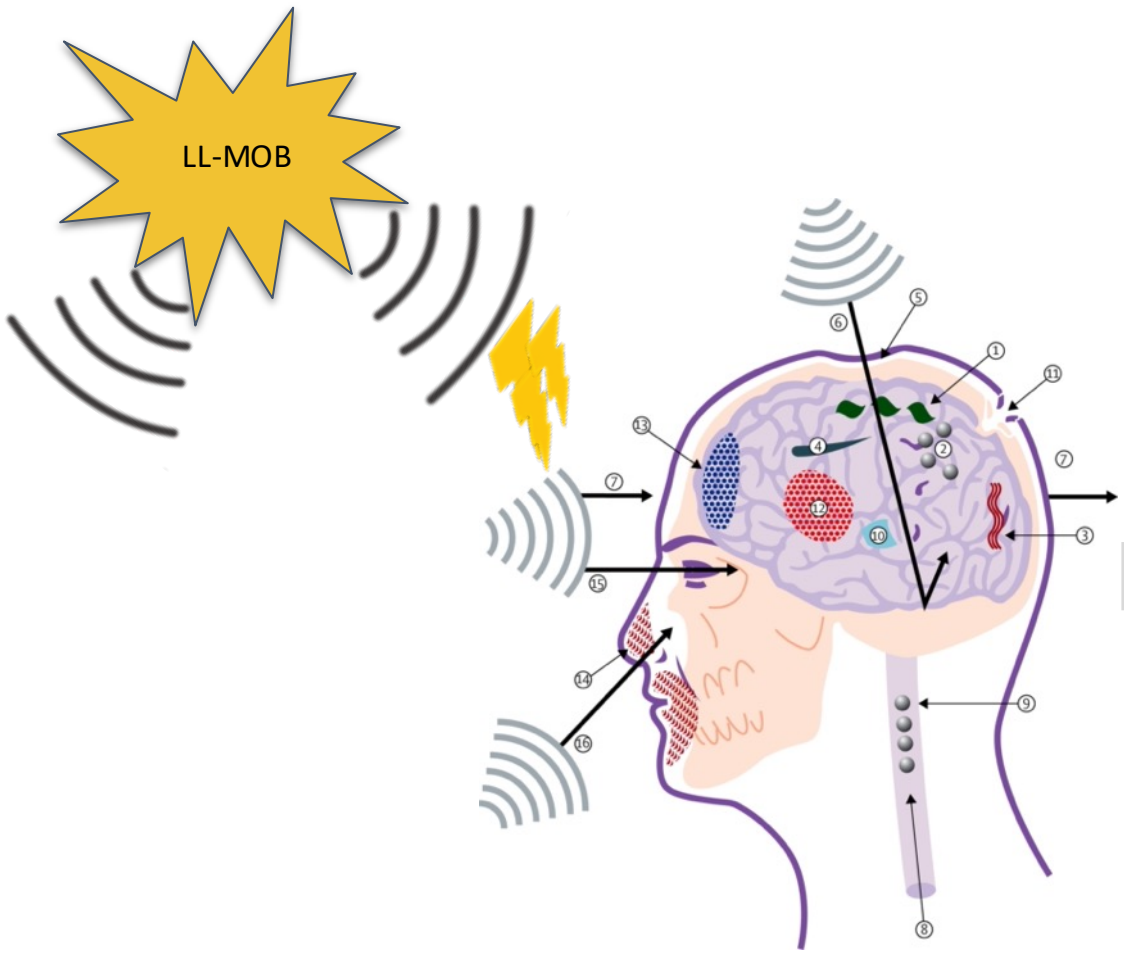
Wang, Zhaoyu[3]*, Wilson, Caroline M[1,3]*, Mendelev, Natalia[1,3], Ge, Yongchao[4], Galfalvy, Hanga[1,6], Elder, Gregory[2,4,5], Ahlers, Stephen[8], Yarnell, Angela M[7], LoPresti, Matthew L[7], Kamimori, Gary[7], Carr, Walter[7,9], Haghighi, Fatemeh[1,3]**

ABSTRACT

exposure duri
sufficient data
symptom prof
Data collectio
Committees o
with no prior l
that completed
held in the m
days, with mu
resonance ima
and ubiquitin
product 150 o

erpressure (OP)
g, which lacked
se a subjective
xposed to blast.
Subjects Review
0-year-old male
er training team
actical training,
ractical training
toms, magnetic
y acidic protein
ived breakdown
ctive markers of
mild TBI remain elusive, but support for serum biomarkers as an early detection mechanism is promising. Additionally, this case study demonstrated an association between OP and high level of neurotrauma biomarker in an individual.

LL-MOB Health & Performance Dimensions



Adverse Outcomes Reported

- ➔ Headaches (fatigue, dizziness)
- ➔ Comorbidities (PTSD, depression, anxiety)
- ➔ Neurosensory Impairment (auditory, visual)
- ➔ Cognitive Impairment (memory, attention complaints)
- ➔ Sleep disturbances
- ➔ Operational effectiveness decrements (deployment)

- Cognition
- Quality of Life
- Mood
- Behaviour

Operational Definitions of Blast

	Acute	Chronic/Cumulative
Exposure	Exposure resulting from a single origin at a specific point in time that is relatively short in duration and transient	Multiple acute exposures sustained over a prolonged period of time
Outcomes	Outcomes that occur in close temporal proximity to the exposure and are short in duration	Outcomes that occur over time, not necessarily within close temporal proximity to the exposure

- **Low-level blast (LLB):** overpressure exposure that results from outgoing (i.e., user directed) munitions being fired at an enemy or target.
- **High-level blast (HLB):** overpressure exposure that results from incoming enemy munitions (e.g., IEDs, rocket-propelled grenades).

Assessments of Low-Level Blast Exposures / Outcomes

	Acute	Chronic/Cumulative
Exposure	Estimated quantification • Shot counts and blast sensor measures taken during discrete training exercises	Estimated relative quantification • Career/service records • Self-reported lifetime/career history
Outcomes	Objective assessments or symptom reporting performed during discrete training exercises	Objective assessment or symptom reporting performed distally from training exercises and/or career exposure Analysis of healthcare utilization or medical diagnoses

Blast Exposure and Neurotrauma

Dimension	Moderate-Severe TBI	Mild TBI	Sub-concussive
Blast Frequency	single event		multiple events
Blast Peak Pressure (psi)	20+	11-20 ?	4-11 ?
Physical Forces	1°, 2° & 3°	1° & 3°	1°
Acute Clinical Manifestations (GCS)	LOC, closed & penetrating head trauma, polytrauma GCS ≤12	closed head injury, LOC/AOC GCS 13-15	None detectible, so far
Clinical Onset	event-related		emergence after multiple exposures
Conventional radiographic findings	CAT/MRI, obvious hemorrhage, edema	negative	Negative, so far
Pathology	obvious hemorrhage, edema, damage to white & gray matter, vasospasm	diffuse	unknown, so far
Biomarkers	N/A	GFAP, UCH-L1, Tau	none, so far
Major Studies	TRACK TBI/TED	TED, TRACK TBI, CENC	Exp. Standards, ESiT, others

DIAGNOSED

Adapted from Ahlers et. al., 2012

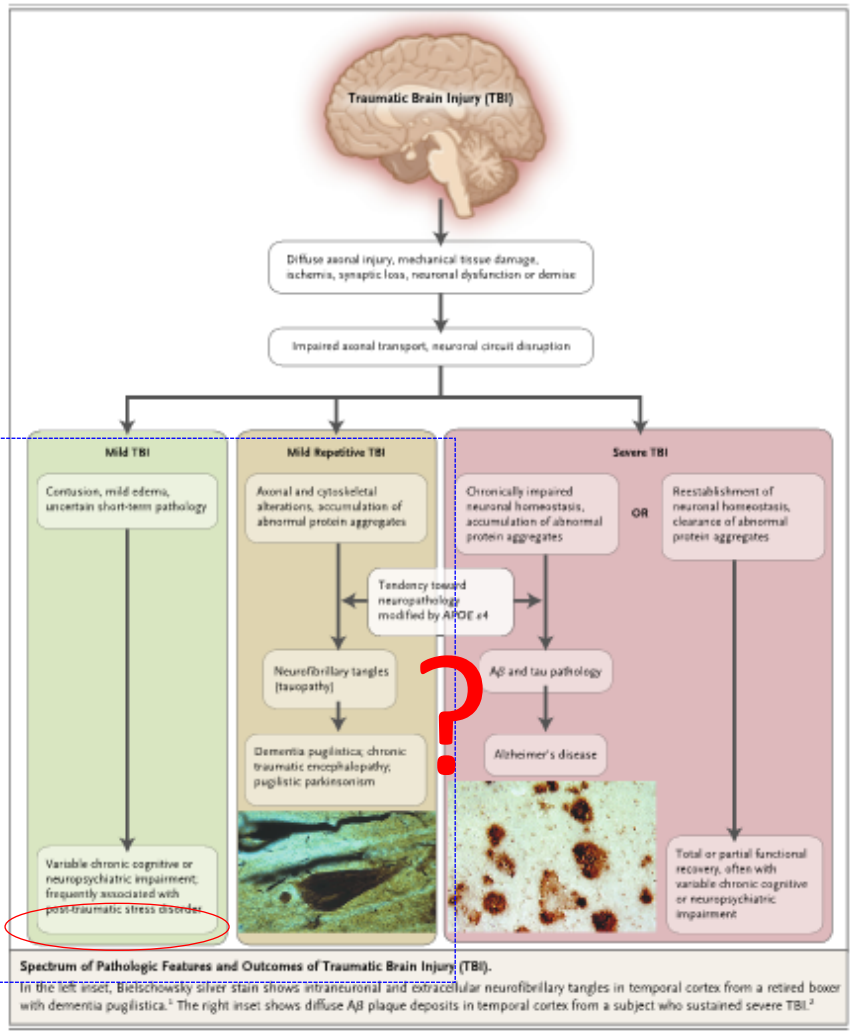
Potential Neuropathological Trajectories

Repetitive exposure to blast or impact concussive or sub-concussive events may result in the manifestation of long-term sequalae such as PCS, CTE, PTSD, and/or related pathologies.

More complex than we thought, still evolving…

Dimension	Moderate-Severe TBI	Mild TBI	Sub-concussive
Blast Frequency	single event		multiple events
Blast Peak Pressure (psi)	20+	11-20 ?	4-11 ?
Physical Forces	1°, 2° & 3°	1° & 3°	1°
Acute Clinical Manifestations (GCS)	LOC, closed & penetrating head trauma, polytrauma GCS ≤12	closed head injury, LOC/AOC GCS 13-15	None detectible, so far
Clinical Onset	event-related		emergence after multiple exposures
Conventional radiographic findings	CAT/MRI, obvious hemorrhage, edema	negative	Negative, so far
Pathology	obvious hemorrhage, edema, damage to white & gray matter, vasospasm	diffuse	unknown, so far
Biomarkers	N/A	GFAP, UCH-L1	none, so far
Major Studies	TRACK TBI/TED	TED, TRACK TBI, CENC	Exp. Standards, ESiT, others

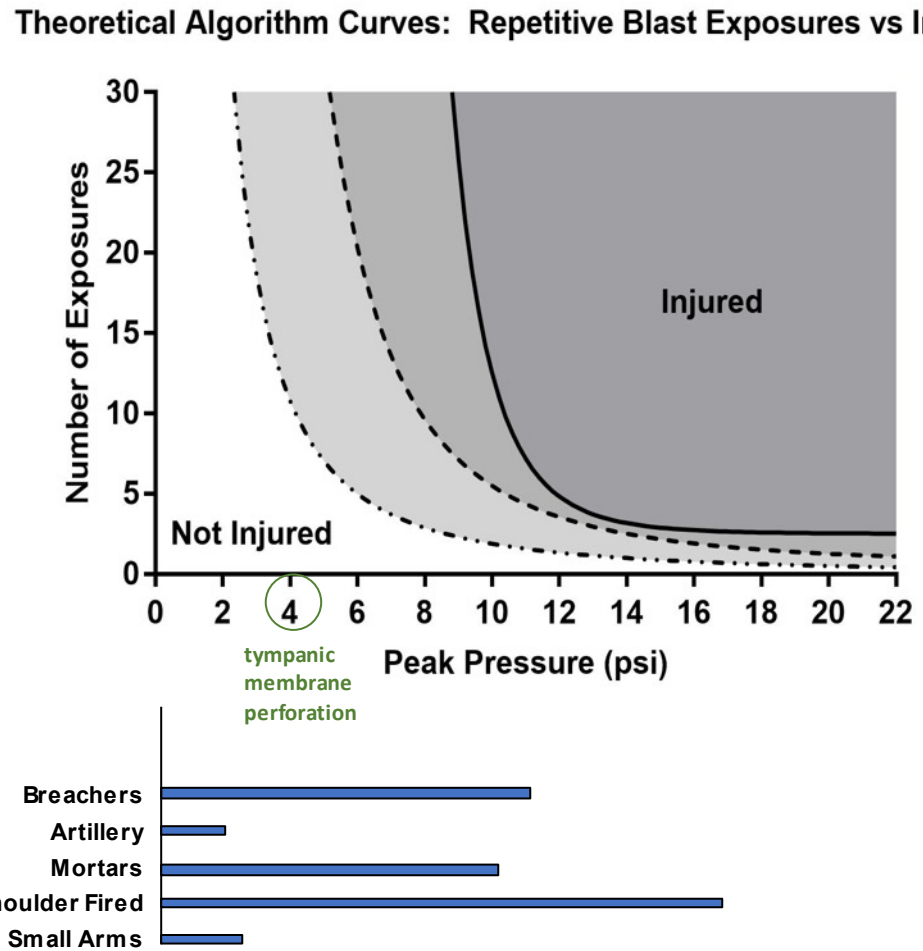
DIAGNOSED

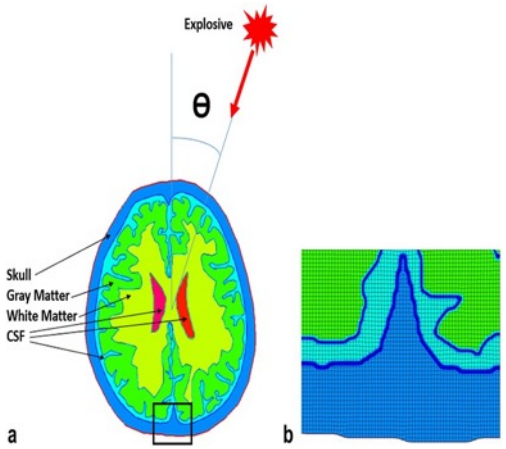


Exposure Standards and Modelling

A Repetitive Blast Exposure Algorithm

Does a repetitive LL-MOE exposure algorithm exten beyond the acute blast exposure standard?





putational analyses of blast mechanics can establish onships between blast sure on the head, internal biomechanical response, and locations of induced brain injury.

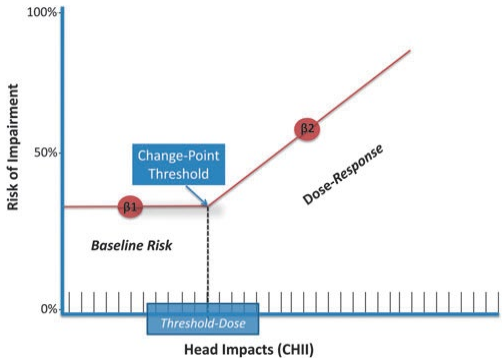
- *This insight is useful in understanding injury mechanisms and designing improvement of protection systems.*

Mil Med, Volume 185, Issue Supplement_1, January-February 2020

Generalized Blast Exposure Value (GBEV)

- Analogous to cumulative head impact index (CHII)
  - Characterize populations
  - Identify and associate with health outcomes
  - Identify threshold for risk

Montenigro et al., 2017



JOURNAL OF NEUROTRAUMA XX: 1–8 (XXXX 00, 2020)
© Mary Ann Liebert, Inc.
DOI: 10.1089/neu.2020.7405

Original Article

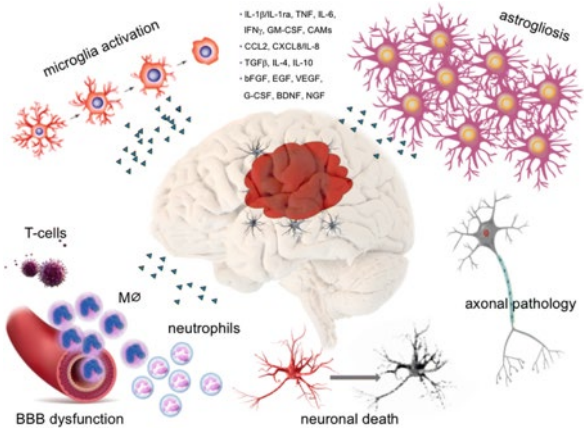
Development of a Blast Exposure Estimator from a Department of Defense-Wide Survey Study on Military Service Members

LT Claire M. Modica,[1] Michael J. Egnoto,[2,3] Jonathan K. Statz,[1,4] Walter Carr,[2,5] and Stephen T. Ahlers[1]

- $\boldsymbol{GBEV} = 0.976 * 1\,BEC + 0.751 * (383 * 2\,BEC) + 0.753 * (55 * 3\,BEC) + 77 * 4\,BEC * (4freq) + 75 * 5\,BEC * (5freq)$

BEC (blast exposure count) = years of experience with a weapon $*$ months of experience per year $*$ days of experience per month $*$ number of exposures per day.

Biological Aspects of Repetitive Exposure to Low-Level Military Occupational Blast Overpressure



Identify Molecular Biomarkers

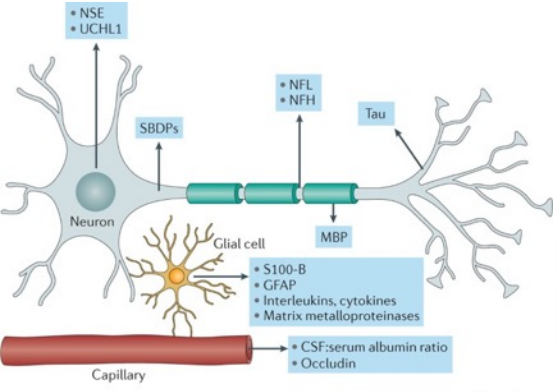
- **NeuroProteomic Discovery Panel** – ~100 blood-based Neuro-inflammatory proteins tested on new Ella system. **TruGenomics Targeted Sequencing** – RNAseq + DNA Methylation + miRNA

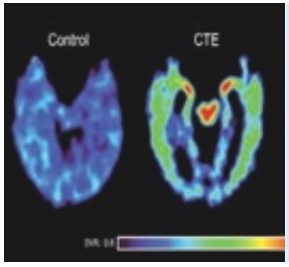
Polaris Genomics

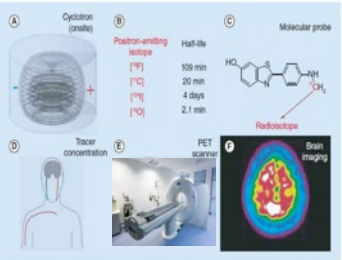
TRUGENOMIX

Assess NeuroInjury Biomarkers

- **MSD and SiMO Brain Injury Panel** – S100b, NSE, UCH-L1, GFAP, NF-L/H, PRDX-6, BDNF, T-tau, pTau-181, A-beta







Optimization of Health & Performance

- Pharmacological/non-pharmacological, treatments (e.g., Omega-3 FA, antioxidants, micro/macronutrients).
- Supplementation Study – RCT v. naturalistic.

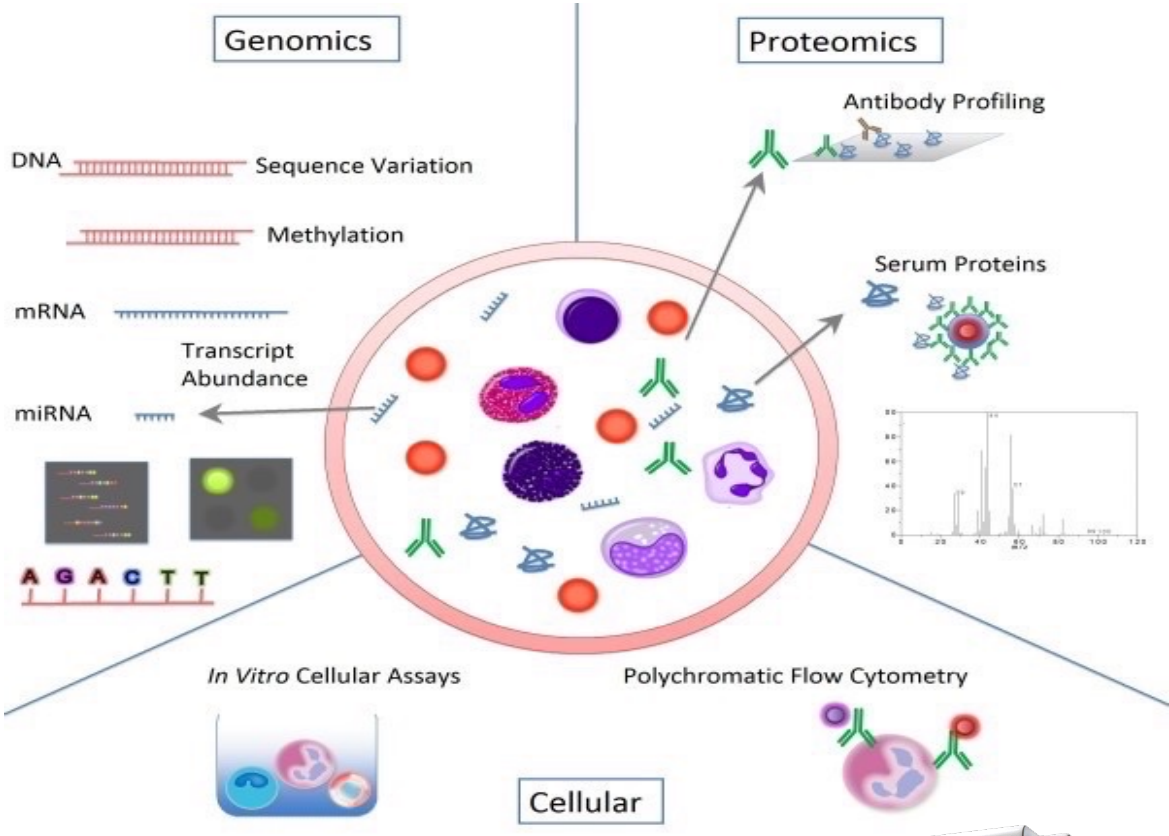
PET-Tau Imaging Study

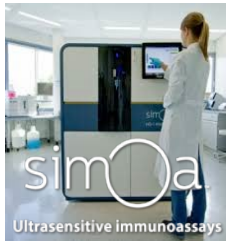
- Clinical investigation in career breachers/assaulters at **CAMH** using novel in vivo PET imaging tracers - [18F]-T807 - **Flortaucipir** to track potential *neurodegeneration;*
- Examine possible Tau-related pathologies or **CTE,** as disease mediator and/or treatment target.

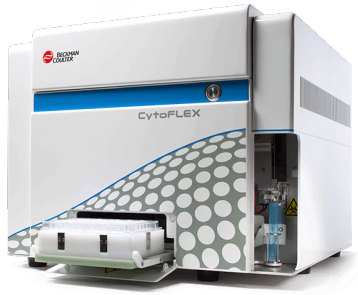
Multi-Omics Lab Approaches

- **Next Gen-Sequencing**
  - RNA-seq/Transcriptomics
  - Epigenetics
  - 30x-Exome Seq/SNPs
  - Salivary miRNA
- **NeuroProteomics**
  - Ella, SimOa, MSD multiplex
  - HPLC, GC-MS
- **Cellular Analysis**
  - Flow/imaging cytometry
  - *Ex vivo* TC functional assays
  - Robotic Liquid Handling

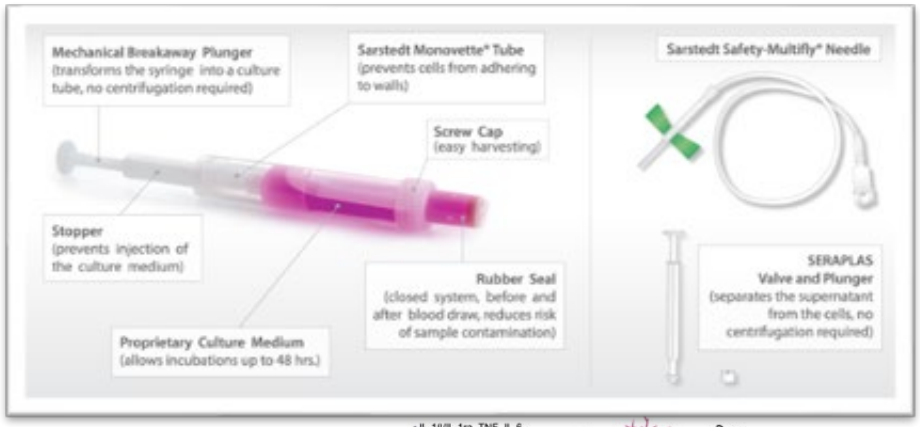
Cellular and Molecular Profiling Tools

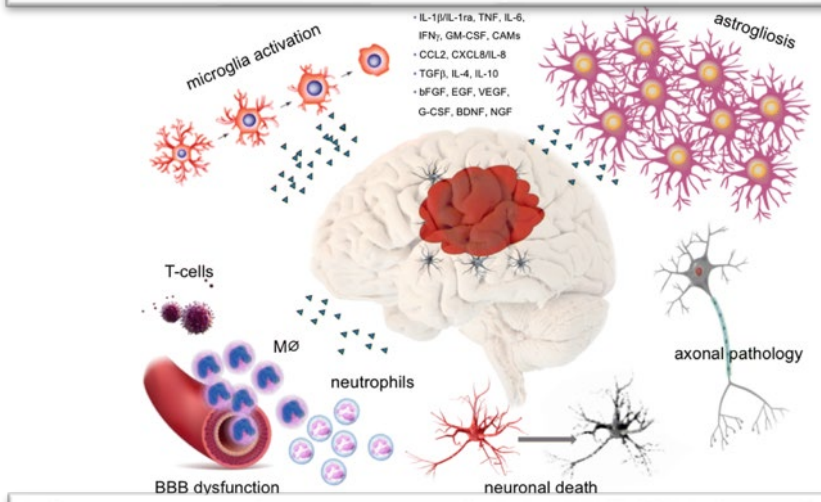




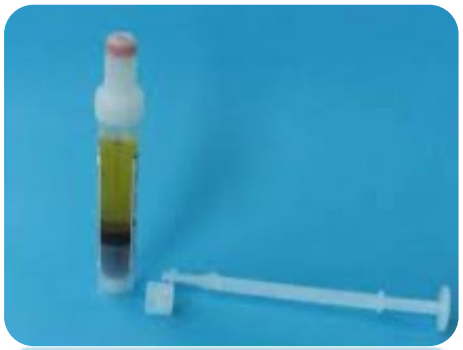


TruCulture - Integrated Blood Collection and Culture System



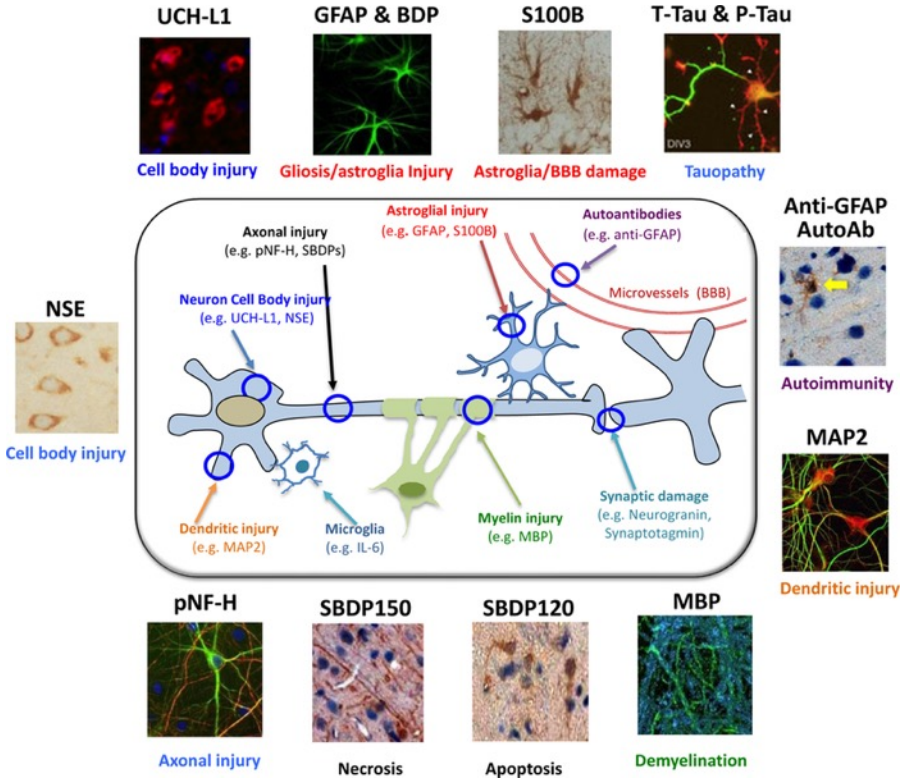


- **TruCulture Advantages**
- TruCulture is simple, reliable, easy to use, reproducible – eliminates need for cell manipulation in sample collection/ analysis.
- Standardized to ensure consistent performance across multiple users/sites.
- Retains all blood components, granulocytes, platelets, red blood cells, soluble factors.
- TruCulture is designed to reproducibly and *accurately capture ex vivo immune cell activity to explore disease states, or develop new diagnostic tests.*



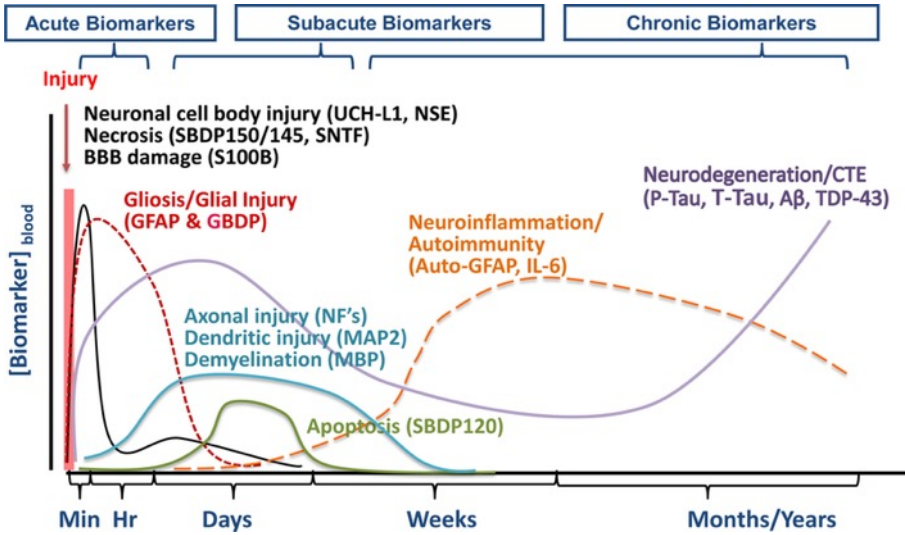
NeuroProteomic Biomarkers

Major brain biomarkers linked to different pathophysiologic processes in TBI.



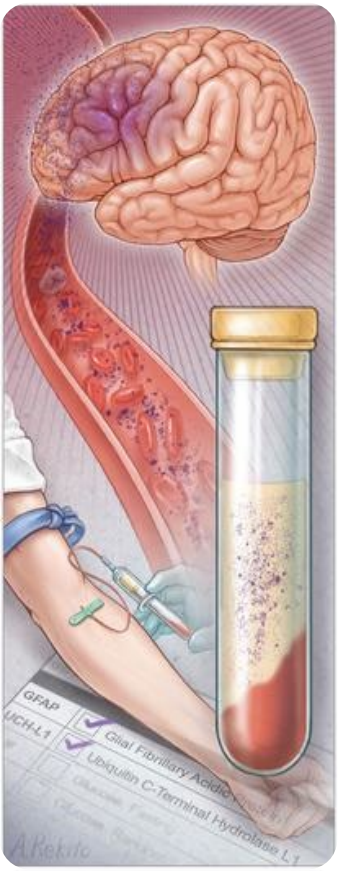
Wang, K.K. et al. *Expert Rev Mol Diagn* 18, 165-180; 2018.

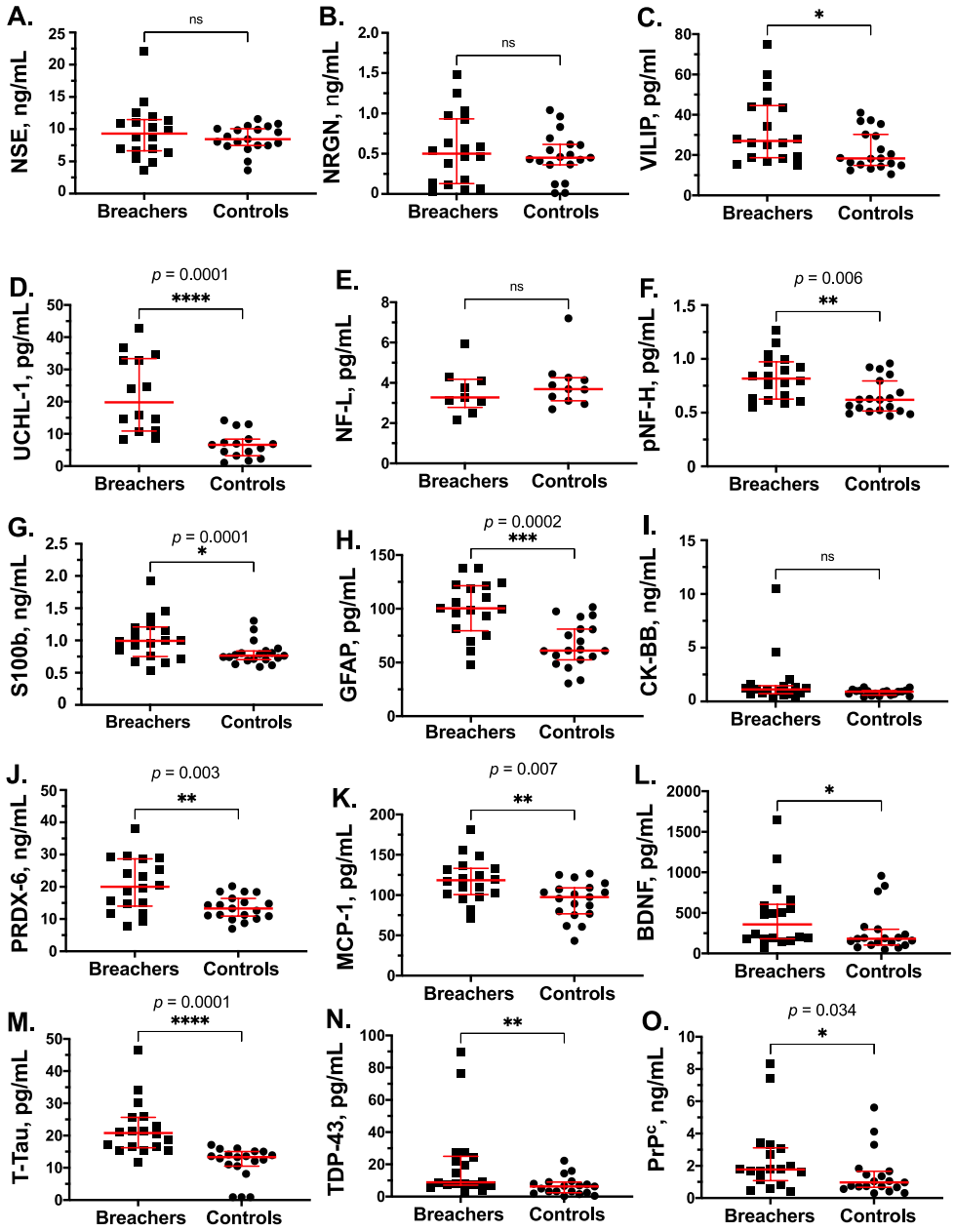
A continuum of protein biomarkers in tracking different phases of TBI.



ImmunoAssay Platforms

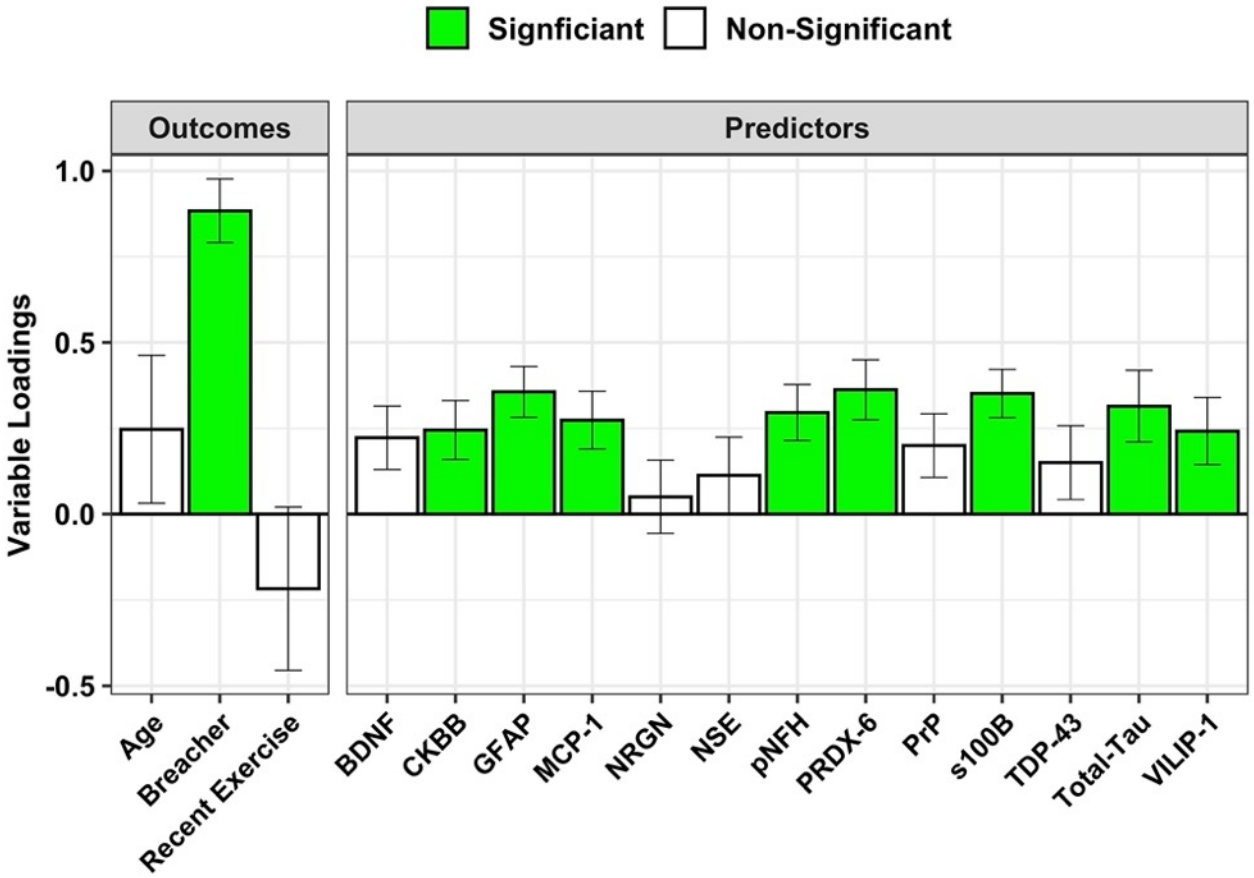
Neurological Biomarker Profiles in CFSME Breachers



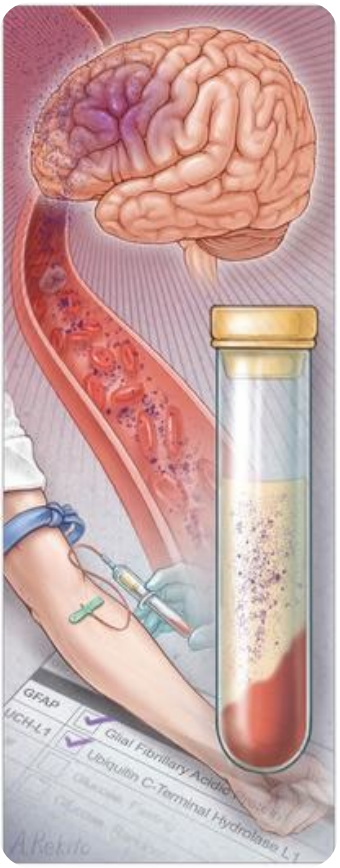


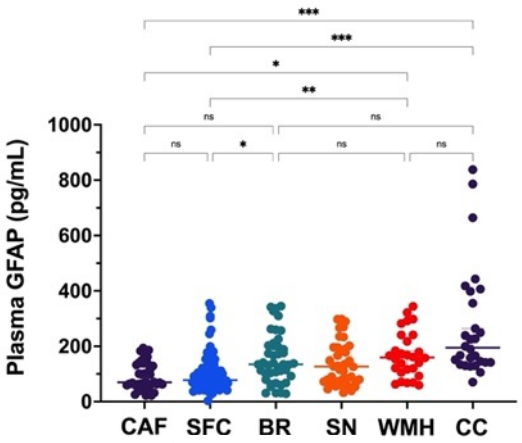
Relationship between Breaching and Blood Biomarkers

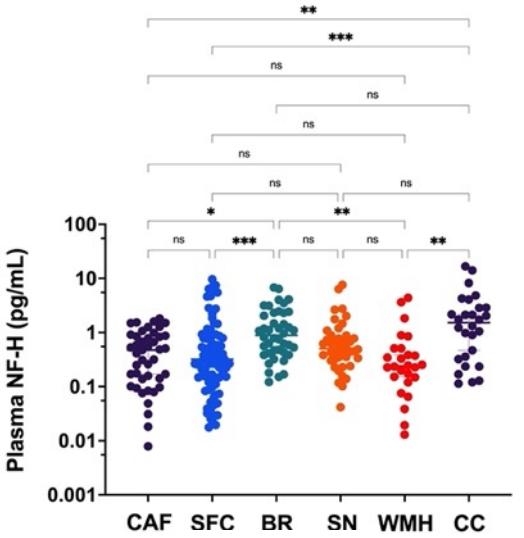
- A PLS regression analysis shows that breaching is associated with higher blood concentrations of many neurological biomarkers

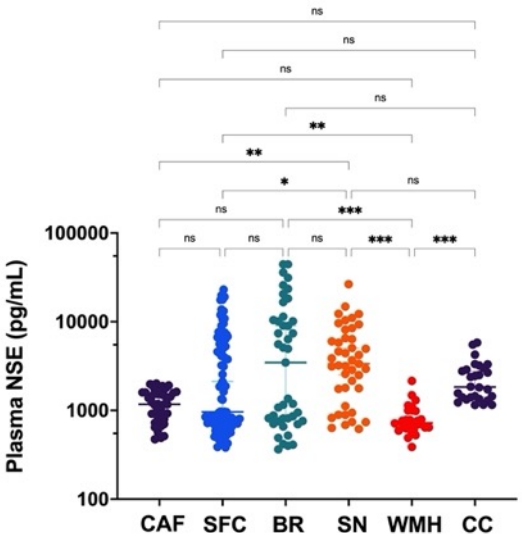


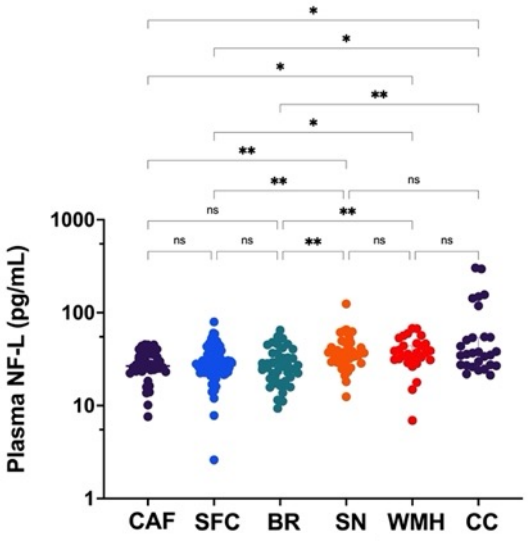
Neurological Biomarker Profiles in CAF Operators







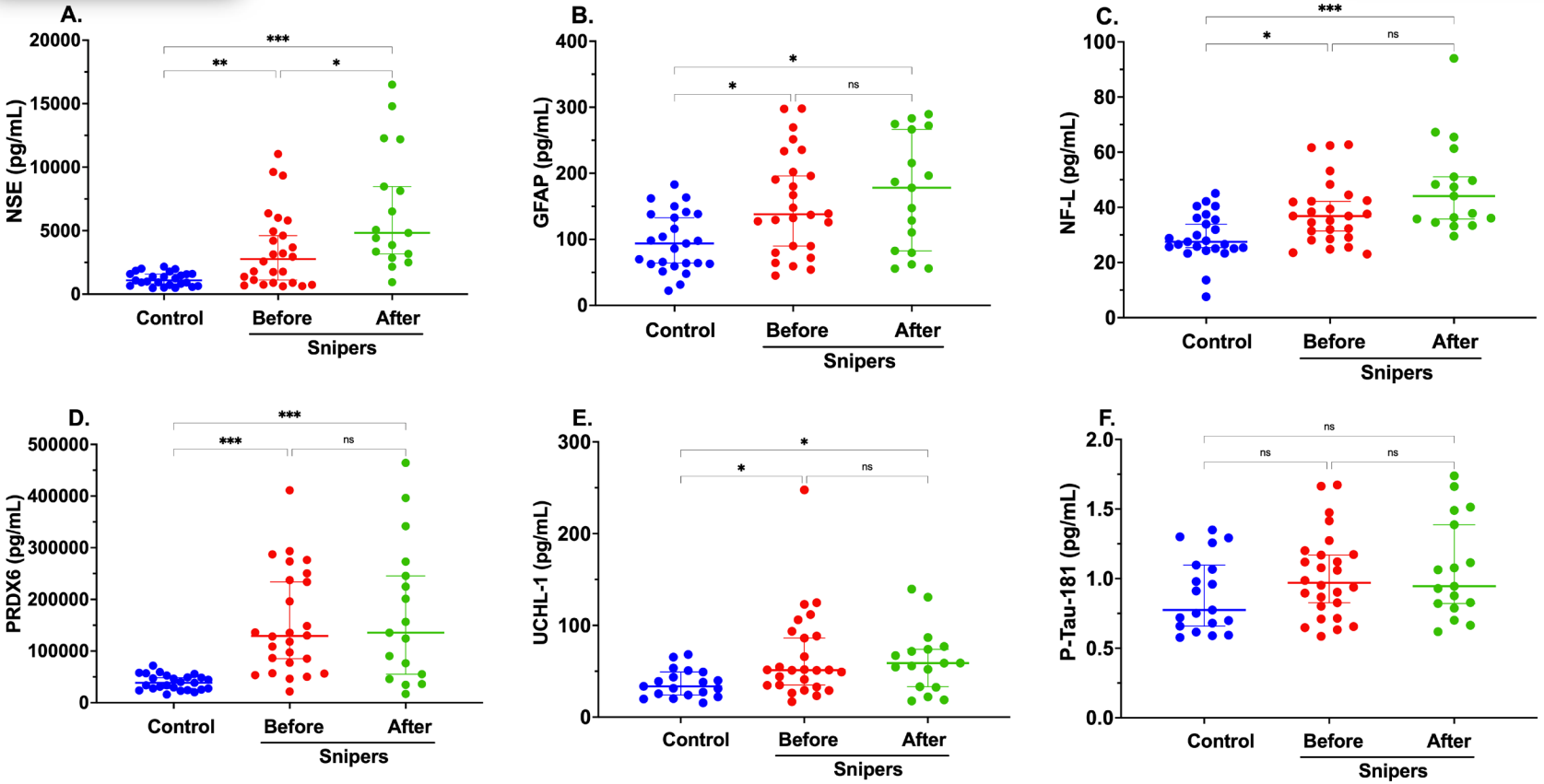




*P< 0.05 by Kruskal-Wallis

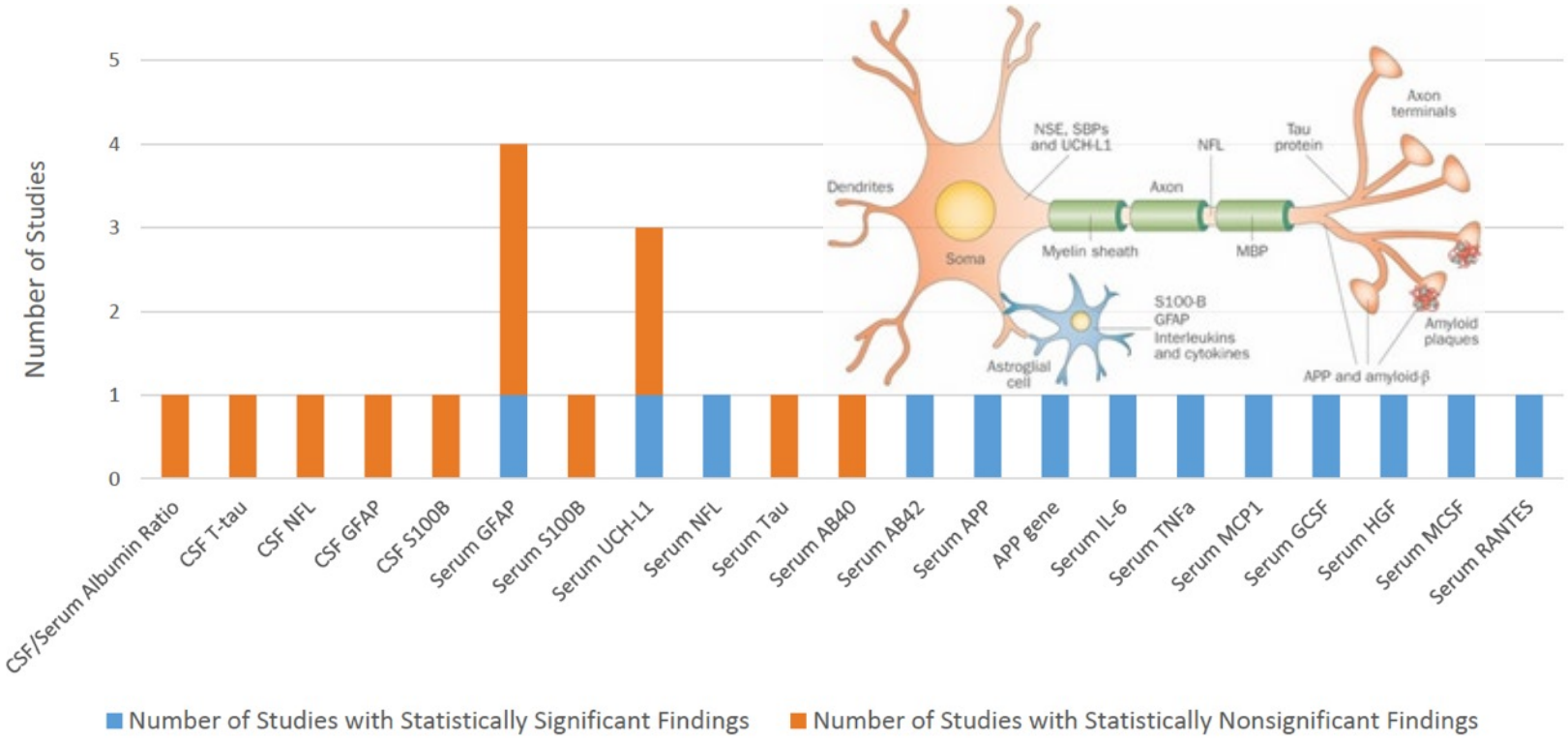
TBD - UCHL-1, T-Tau, P-Tau-181, amyloid beta peptides (Aβ-40 & Aβ-42)

Blood Neurological Injury Biomarker Profiles in CAF Snipers Following Heavy Weapons Training



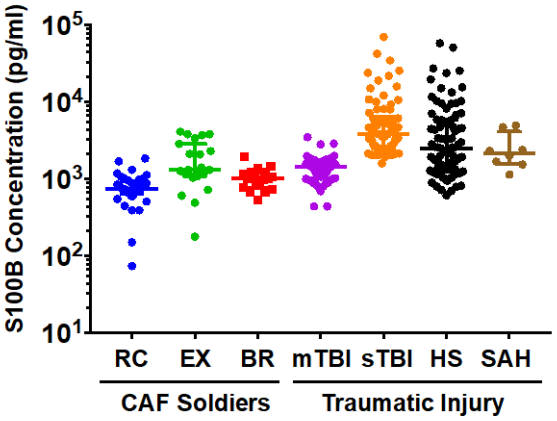
Brain biomarker Concentrations (pg/mL) in plasma from healthy *controls and snipers* before and after exposure to blast OP during training plotted for NSE (**A**), GFAP (**B**), NF-L (**C**), PRDX-6 (**D**), UCHL-1 (**E**), P-T-tau-181 (**F**). Each dot represents biomarker values for an individual subject, solid lines show medians. Significant differences *p<0.05, p<0.01, p<0.001 for Kruskal-Wallis one-way ANOVA are displayed for each marker.

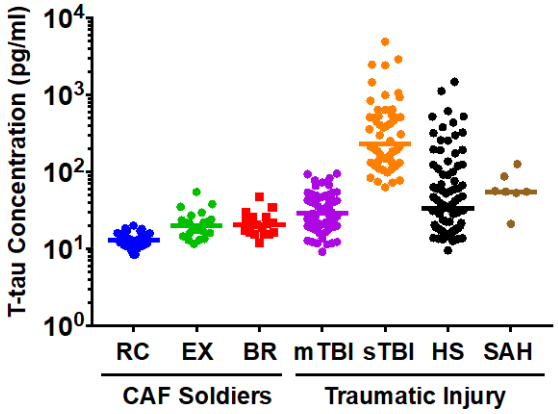
Literature Findings on LL-MOB Blood Biomarkers

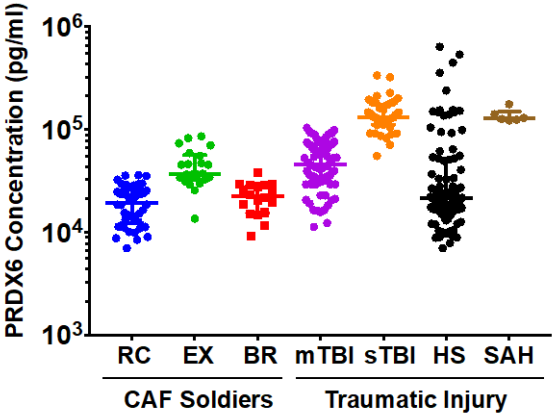


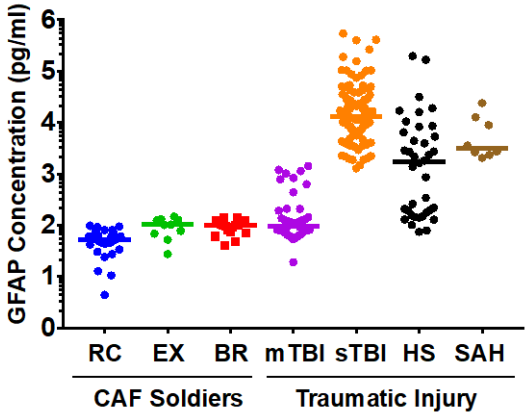
- Despite a growing number of pre-clinical studies (30+ to dates) showing significant differences in fluid biomarkers with blast exposure, there are few consistent trends and objective biomarkers of LL-MOB remain elusive.
- Need to harmonize (pre)analytical assay methods and other common data elements across studies platforms and conduct multi-site studies.

Relative Blood Neurological Biomarkers



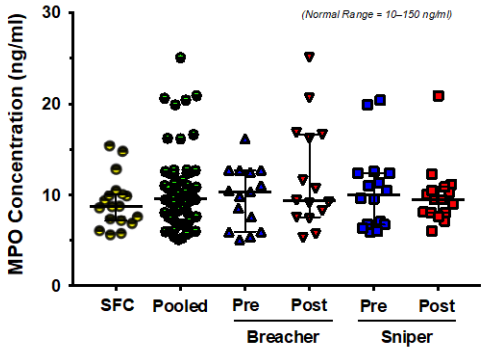


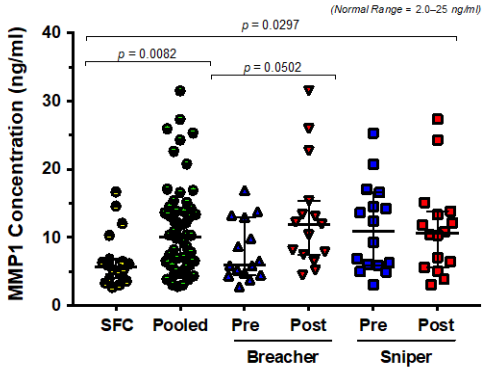


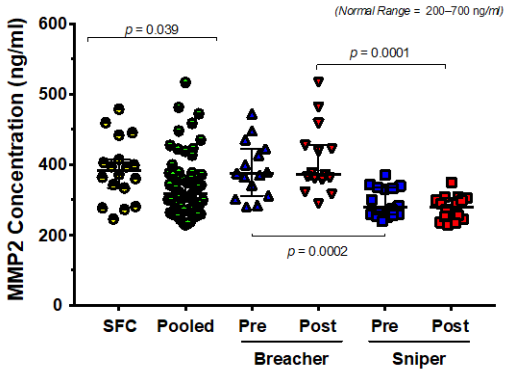


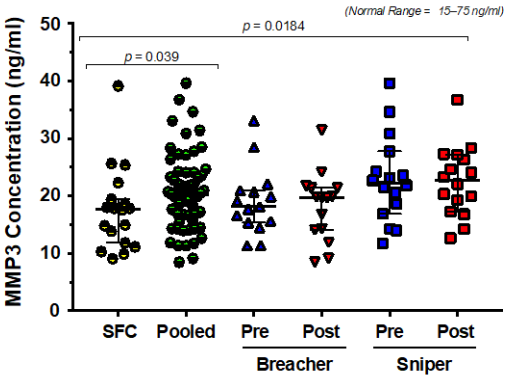
- Increases in blood neuroinjury biomarkers in breachers are modest compared to *moderate to severe brain injury,* hemorrhagic shock (HS) and subarachnoid hemorrhage (SAH).
- *Physiological stressors*, including high intensity exercise can also influence biomarker levels.
- Need to interpret blood biomarkers in context of a comprehensive *multi-dimensional test battery*, incorporating baseline assessment information into a suite of neurocognitive functional tests (memory, balance, postural), mental health status, and neuroimaging findings and other demographic and medical risk modifiers (age, sex, previous number of concussions, etc.) and self-reported symptoms.

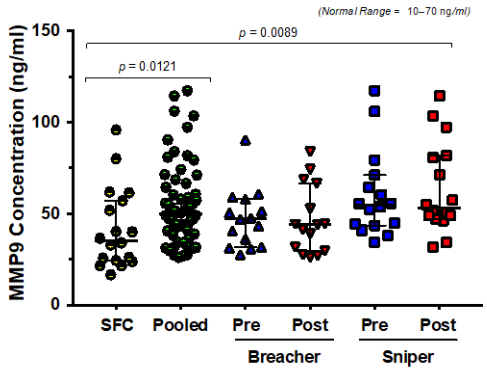
Myeloperoxidase (MPO) and Matrix Metalloproteinases (MMPs) in Breachers and Snipers

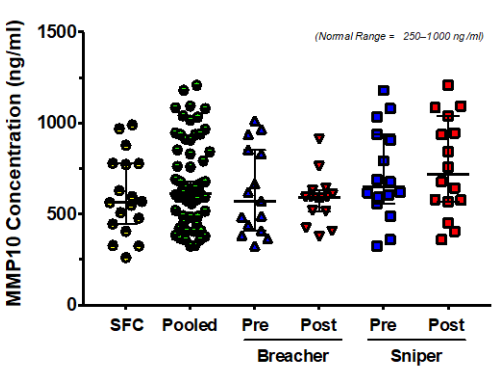


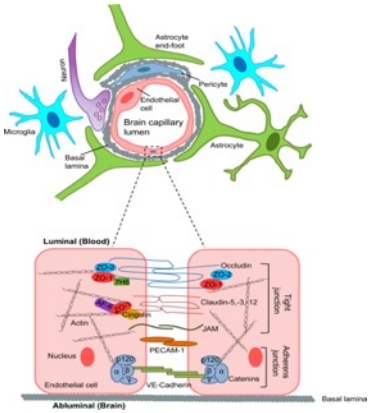


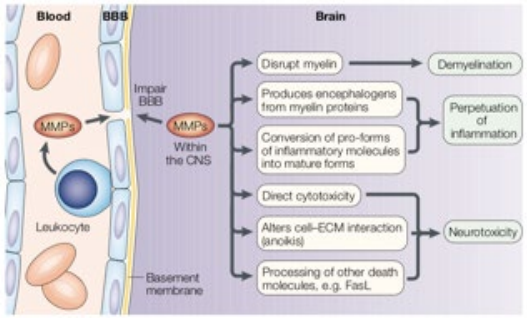








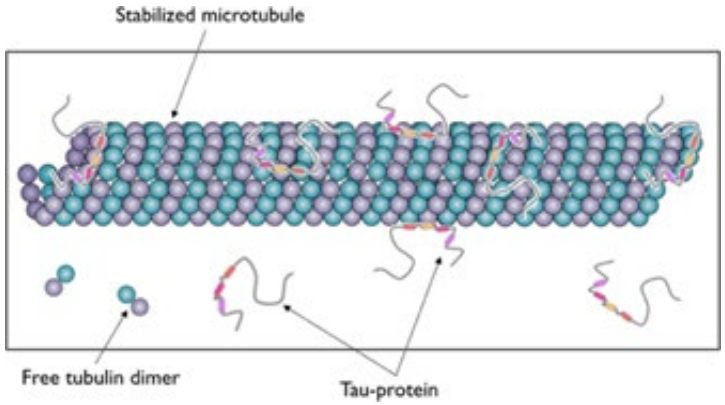


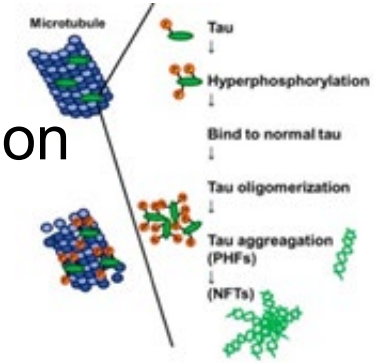


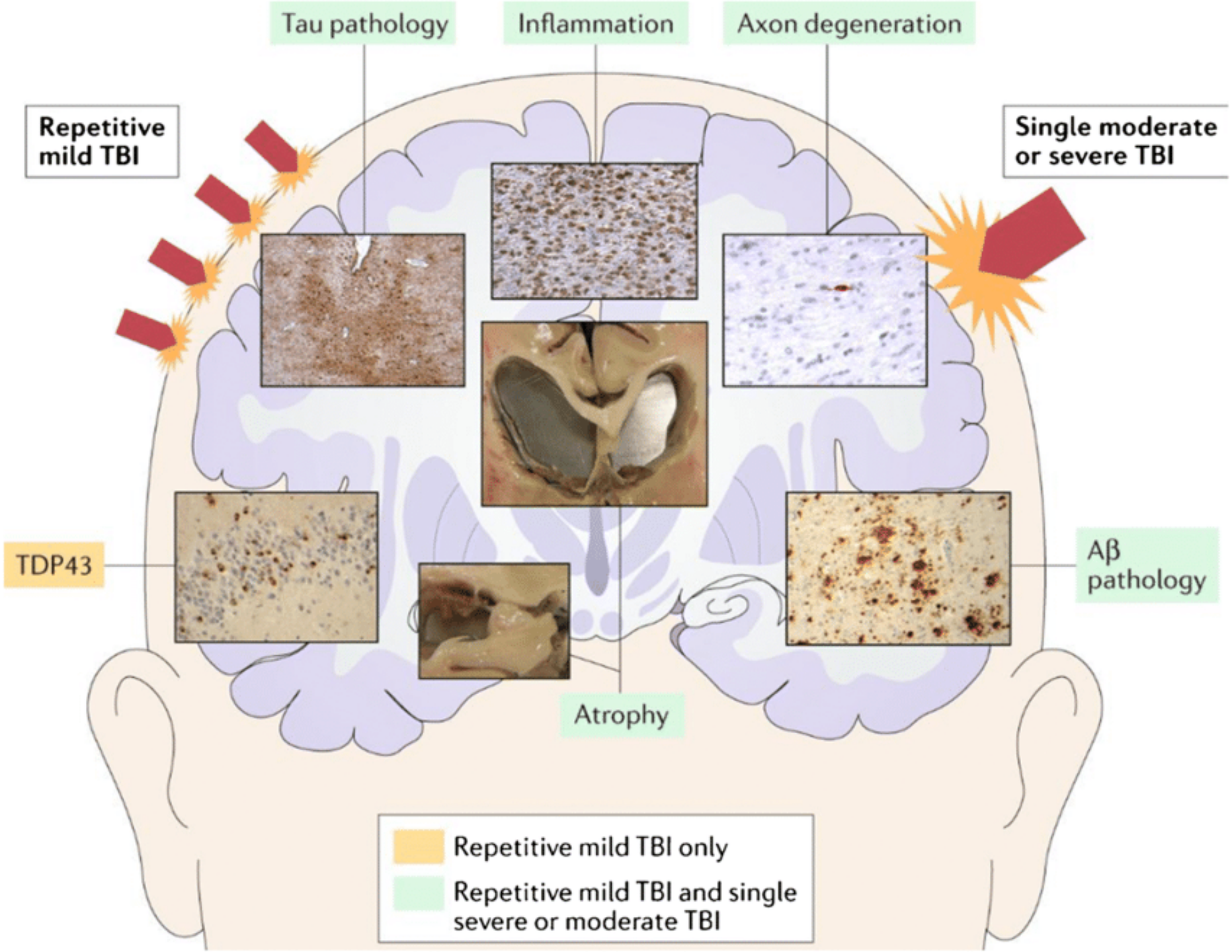
TAU as a marker of ….

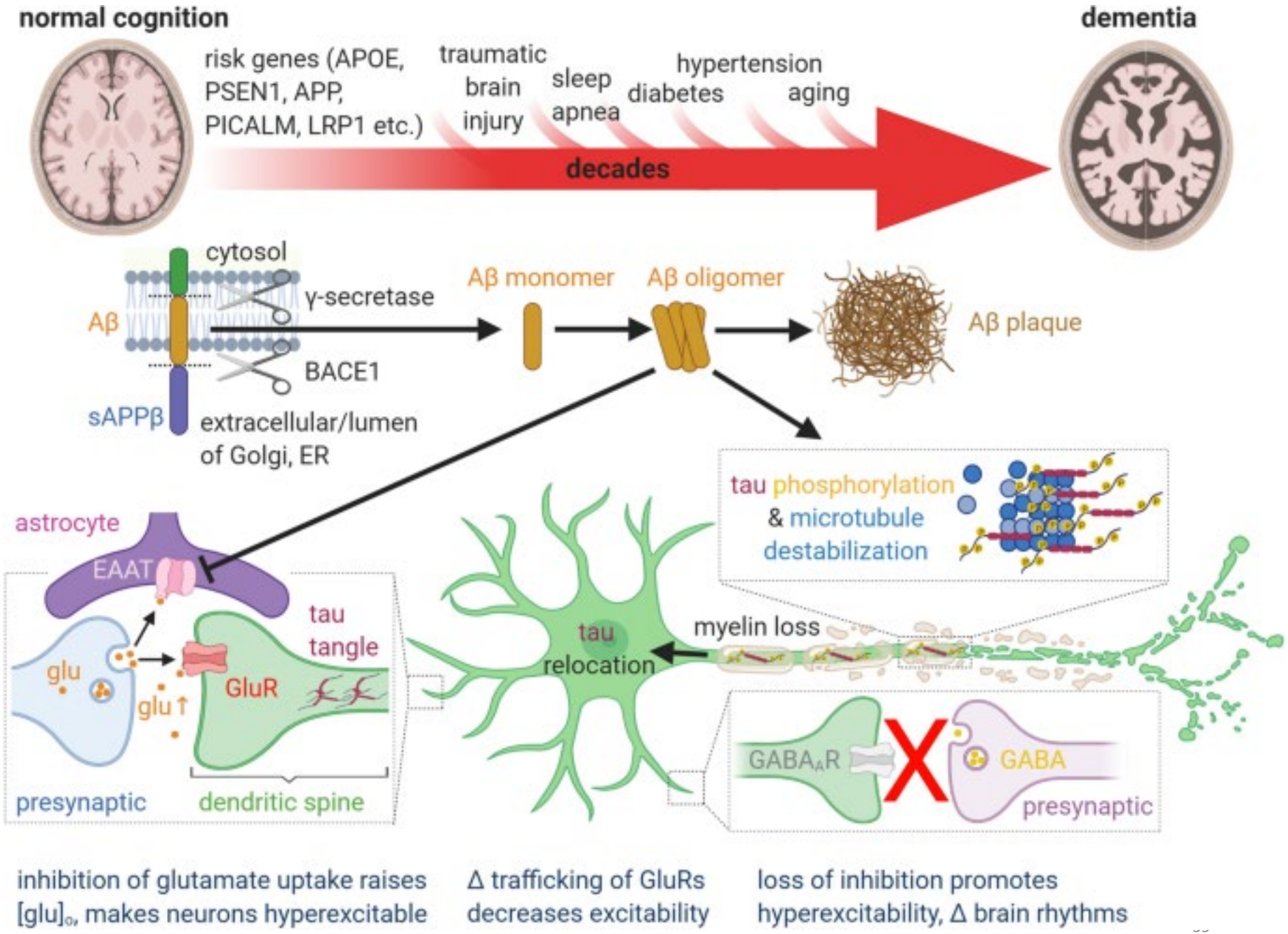
Mechanism

- ↑ phosphorylation
  - ↓microtubule binding
  - ↑ free tau
- Fibrillation
- Mediator of β-amyloid induced neurodegeneration
- Axonal filament protein
- Stabilizes microtubules to support axons

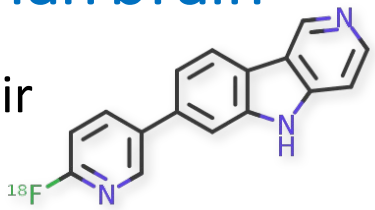




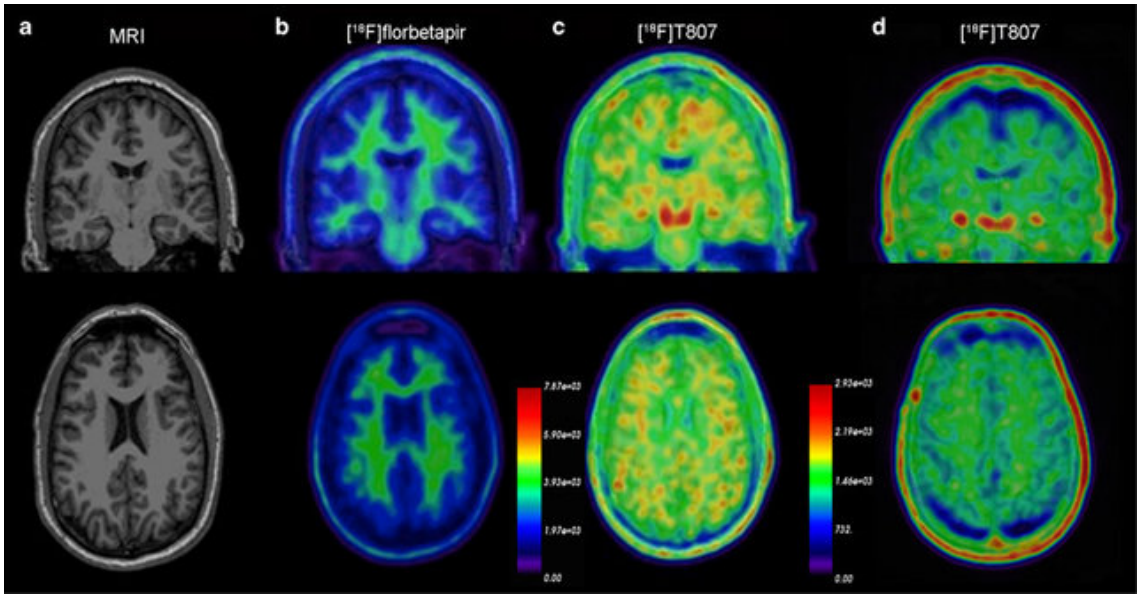

Tau pathology
Inflammation
Axon degeneration
Repetitive mild TBI
Single moderate or severe TBI
TDP43
Aβ pathology
Atrophy
Repetitive mild TBI only
Repetitive mild TBI and single severe or moderate TBI


normal cognition
dementia
risk genes (APOE, PSEN1, APP, PICALM, LRP1 etc.)
traumatic brain injury
sleep apnea
diabetes
hypertension
aging
decades
cytosol
Aβ
γ-secretase
BACE1
sAPPβ
extracellular/lumen of Golgi, ER
Aβ monomer
Aβ oligomer
Aβ plaque
tau phosphorylation & microtubule destabilization
astrocyte
EAAT
glu
glu↑
GluR
tau tangle
presynaptic
dendritic spine
tau relocation
myelin loss
GABA$_A$R
GABA
presynaptic
inhibition of glutamate uptake raises [glu]$_o$, makes neurons hyperexcitable
Δ trafficking of GluRs decreases excitability
loss of inhibition promotes hyperexcitability, Δ brain rhythms

PET [F-18] T807 to measure TAU in living human brain



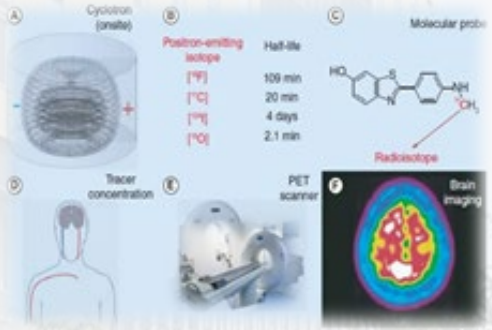
- → [F-18] T807 is a FDA approved, highly selective flortaucupir radiotracer for PHF-tau binding (Xia 2013)
- → Rapid brain penetration (crosses BBB and rapid clearance (Xia 2013)
- → ↑ Lipophilicity
- → Minimal Risks, favourable in vivo
- → Outcome measure for analysis of brain tau levels in ROI is SUVR (Standardized Uptake Value Ratio)

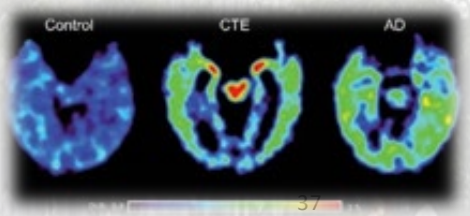


Investigating Tauopathy in Military Blast Exposure: A Positron Emission Tomography (PET) Study with the Tau Tracer [F-18] T807

- **Background:** Chronic Traumatic Encephalography (**CTE**) is a neurodegenerative tauopathy associated with repetitive head impacts or exposure to blast waves.
- **CTE** is characterized by accumulation of hyperphosphorylated **Tau protein** in neurons, astrocytes and cell processes around blood vessels. It is found in athletes (and potentially soldiers), who have sustained repeated brain trauma, and is associated with neurocognitive decline, dementia, mood changes, and aggression.
- **Specific Aims**: To investigate possible Tau accumulation in the brain using Positron Emission Tomography (**PET**) tracer **[F-18] T807 at CAMH**, as an indicator of neurodegeneration in *experienced CAF Operators* to provide *in vivo* evidence of possible CTE as a potential disease mediator and treatment target.
- **Hypothesis**: Greater regional [F-18] T807 uptake will be associated with measures of mood, cognition, greater symptom severity and neurocognitive deficits.
- **Study Design**: Observational cohort study to evaluate three groups: 1) **career breachers** - N=30 experienced at risk CAF members with multi-year exposure to BOP; 2) N=30 age-/sex-matched **healthy CAF controls** without significant blast exposure; 3) historical reference dataset of healthy civilians.
- **Measures**: neurocognitive assessments, neurological injury marker profiles, and PET imaging at CAMH using **[18F]-T807** or ***Flortaucipir*** to track suspected neurodegeneration and examine possible tau-related pathologies or CTE.
- **Deliverables:** Better understanding of *potential long-term neuropathological effects of blast* in operators, in order to enhance safety and health of at risk military members. Provide recommendations for establishing *longitudinal health monitoring* to assess brain health and CTE symptomology across career trajectories.

camh





Preliminary Results - Investigating Tauopathy in Military Blast

Abstract #302 | Oral or Poster presentation

Investigating Tauopathy in Military Occupational Blast: A [^{18}F]flortaucipir Positron Emission Tomography Study in Canadian Armed Forces Members

Shamantha J. Lora[3,2], Sarah E. Watling[3], Jerry Warsh[2], Oshin Vartananian[5], Neil Vasdev[7,2], Iain Vergie[6], Isabelle Vallee[6], Tina McCluskey[2], Carmela Tartaglia[4], Shawn Rhind[5], Isabelle Boileau[2,1]

[1] *University of Toronto, Psychiatry, Toronto, Ontario, Canada*
[2] *Centre for Addiction and Mental Health, Campbell Mental Health Research Institute, Toronto, Ontario, Canada*
[3] *University of Toronto, Institute of Medical Sciences, Toronto, Ontario, Canada*
[4] *University of Toronto, Tanz Centre for Research in Neurodegenerative Diseases, Toronto, Ontario, Canada*
[5] *Toronto Research Centre, Defence Research and Development Canada, Toronto, Ontario, Canada*
[6] *Canadian Armed Forces, Canadian Special Operation Forces Command, Ottawa, Ontario, Canada*
[7] *Centre for Addiction and Mental Health, Azrieli Centre for Neuro-Radiochemistry, Toronto, Ontario, Canada*

Introduction

Chronic traumatic encephalopathy (CTE), a tauopathy, is suspected to occur as a result of repetitive exposure to low-intensity blast overpressure during military training and operations. Although animal models putatively link explosive blast exposure with tau aggregation, studies in humans exposed to repeated low level blasts are limited. We used positron emission tomography (PET) imaging of [^{18}F]flortaucipir (a.k.a [^{18}F]TAUVID™, [^{18}F]AV-1451; [^{18}F]T807) to evaluate tau levels in Canadian Armed Forces (CAF) operators with significant career exposure to blast.

Methods

CAF members (5 males; 44.6 ± 6.2 years old) exposed to blast completed an MRI and a PET [^{18}F]flortaucipir scan. Standardized Uptake Value ratio (SUVr) were calculated with the cerebellum as reference tissue. Participants performed a test of executive function (Stroop) and completed mood and clinical questionnaires.

Results

[^{18}F]flortaucipir uptake was highest in midbrain/substantia nigra (SUVr range: 0.8 to 1.6), basal ganglia (SUVr range: 1.0 to 1.3), temporal (SUVr range: 0.8 to 1.13) and frontal cortices (SUVr range: 0.8 to 1.11). [^{18}F]flortaucipir SUVr values were positively correlated with years of exposure to explosives and to years of breaching (r = 0.9; p-uncorrected<0.05). Greater [^{18}F]flortaucipir SUVr values in prefrontal regions were related to poorer performance on the Stroop test of executive function (r = 0.9; p<0.05). [^{18}F]flortaucipir SUVr did not correlate with mood or clinical symptoms.

Conclusion

These preliminary results suggest that while [^{18}F]flortaucipir uptake in CAF operators regularly exposed to low-intensity blast is within the range reported for normal mid-aged controls [1], our study found that

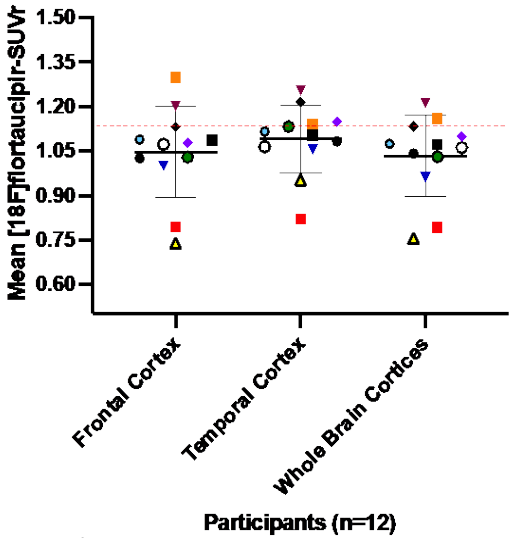


Figure 1. Regional [^{18}F]flortaucipir SUVr in CAF exposed to Low-level Military Blast

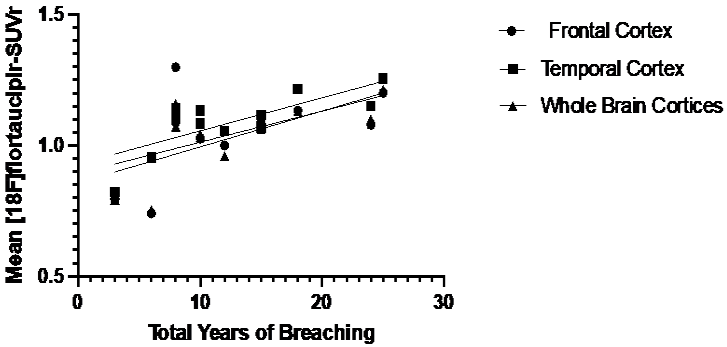


Figure 2. Pearson correlation revealed significant positive associations (r > 0.88) between mean [^{18}F]flortaucipir SUVr in ROIs and total years of breaching in the CAF.

CONCLUSIONS: In line with an earlier PET study linking tau deposition with dose exposure to blast[3], our study finds a positive correlation between blast exposure and tau deposition – suggesting that repeated LL-MOB exposure could potentially increase tau deposition. Participant enrolment is continuing, with a current sample size of 25 and target N =50 blast exposed breachers.

Overall Conclusions & Future Directions

- **Conclude**: there are several psychological and physiological health & performance measures that exhibit sensitivity to effects of repeated LL-MOB in the context of breaching and sniping.
- Valid and reliable quantification of blast effects necessary for linking exposure to clinical outcomes.
- Breaching appears to be related to sub/post-concussive symptoms, but not consistently to mental health outcomes (PCL-5, BSI).
- Necessary to operationalize research to better relate variations in clinical outcome measures to job-specific functional targets.
- We advocate for a holistic approach – that accounts for the larger occupational and operational environment within which blast is experienced for longitudinal health assessment programs.
- **Future Research**: focus on completion of existing blood and salivary proteo-genomic/epigenomic sample analyses for neurological and inflammatory biomarker profiles.
- Address capability gaps precluding incorporation of individual factors (i.e., genetic indicators of risk/resilience) into predictions of LL-MOB exposure effects.
- Completion of Flortaucipir T807 PET imaging study using to examine CTE risk in career breachers.
- Integrate multidimsional health & performance data into an AI-driven ML predictive algorithm/tool to better inform risk assessment within the operational community.

Acknowledgments

- Oshin Vartanian
- Ann Nakashima
- Catherine Tenn
- Maria Shiu
- Tim Lam
- Doug Saunders
- Kristen King
- Norleen Caddy
- Michelle Garrett
- Alexi Natale
- Mark Rutley
- Al Taylor
- Mike Crouzat
- Al Crawford
- Isabelle Vallee
- Rakesh Jetly
- Alex Di Battista
- Isabelle Boileau
- Neil Vasdev
- Sarah Watling
- Shamantha Lora
- Tina McCluskey
- Ben Dunkely
- Michael Hutchison
- Lauren Sergio
- Angela Colantonio
- Kevin Wang
- Zhihui Yang
- Greg Mueller

- **CAF Members**

Thank you.

DRDC | RDDC

SCIENCE, TECHNOLOGY AND KNOWLEDGE FOR CANADA'S DEFENCE AND SECURITY

SCIENCE, TECHNOLOGIE ET SAVOIR POUR LA DÉFENSE ET LA SÉCURITÉ DU CANADA

Questions?