Emerging Capabilities for Evaluating Cognitive and Oculomotor Function in Service Members With Traumatic Brain Injury

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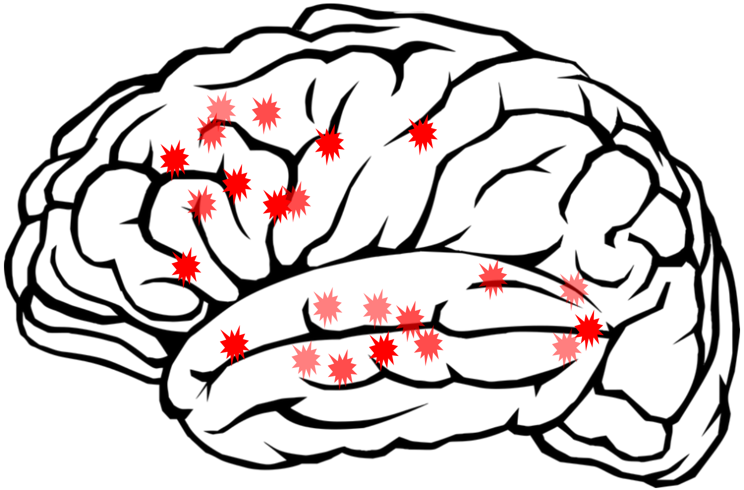
- Technology described in this presentation is included in U.S. Patent Application No. 61/779,801, U.S. Patent Application No. 14/773,987, European Patent Application No. 14780396.9, and International Patent Application No. PCT/US2014/022468. Dr. Ettenhofer is a named inventor on these patents and provides consulting related to this technology to industry partners.

Presentation Overview

- Traumatic Brain Injury (TBI) Basics
  - Common Effects, Prevalence, and Recovery
- Assessment of TBI
  - Current Capabilities and Future Requirements
- Introduction to Eye Movements
  - Oculomotor and Cognitive Networks
- Neurocognitive Eye Tracking
  - Approaches, Scientific Validation, and Ongoing Research
- Summary and Discussion

TBI Basics

- TBI is a traumatically induced change in brain function
- It can be caused by blunt impact, blast, or rapid acceleration/deceleration
- Neural injury can occur in many different places, potentially accumulating across multiple injuries
- To identify TBI effects on an individual, we must evaluate multiple, different cognitive and motor systems



(Image by Brett Robinson, public domain.)

Potential Effects of TBI

- **Cognitive:** Impaired attention, executive functions, psychomotor speed, memory
- **Sensory:** Dizziness, poor balance, abnormal eye movements
- **Physical:** Insomnia, headache
- **Emotional:** Irritability, depression, anxiety
- Reduced operational performance

(U.S. Air Force [USAF] photo by SSgt. Jonathon Fowler.)

Classifying TBI Severity: DoD/Veterans Affair Criteria

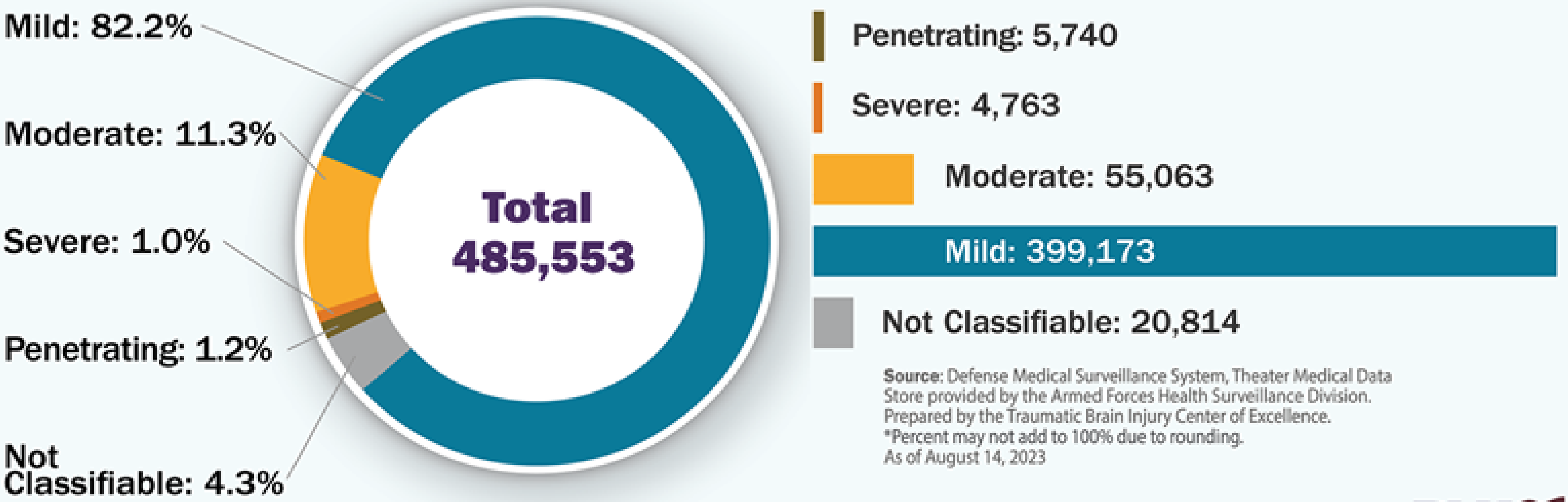
Severity	AOC	LOC	PTA
Mild	≤24 hr	0–30 min	≤24 hr
Moderate	>24 hr	>30 min <24 hr	>24 hr <7 days
Severe	>24 hr	≥24 hr	≥7 days

- **AOC:** Alteration of Consciousness
- **LOC:** Loss of Consciousness
- **PTA:** Post-Traumatic Amnesia

Note: hr = hours, min = minutes

DOD Numbers for Traumatic Brain Injury Worldwide

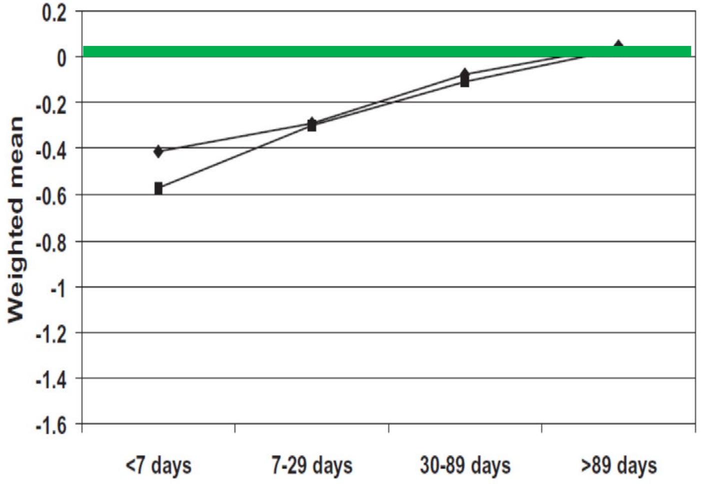
2000–2023 Q2



Source: Defense Medical Surveillance System, Theater Medical Data Store provided by the Armed Forces Health Surveillance Division.
Prepared by the Traumatic Brain Injury Center of Excellence.
*Percent may not add to 100% due to rounding.
As of August 14, 2023

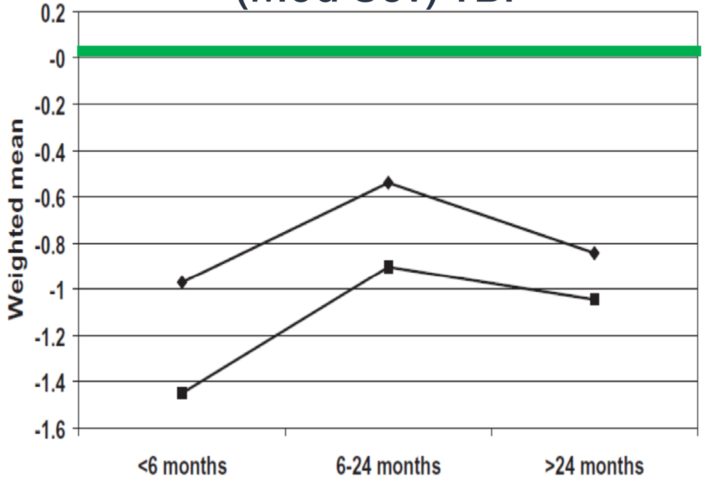
Recovery From TBI: Cognitive Performance

Mild TBI (mTBI)



Mean weighted effects of mild head injury on overall cognitive test performance at four follow-up epochs, ◆ *d (pooled),* ■ *d(control).*

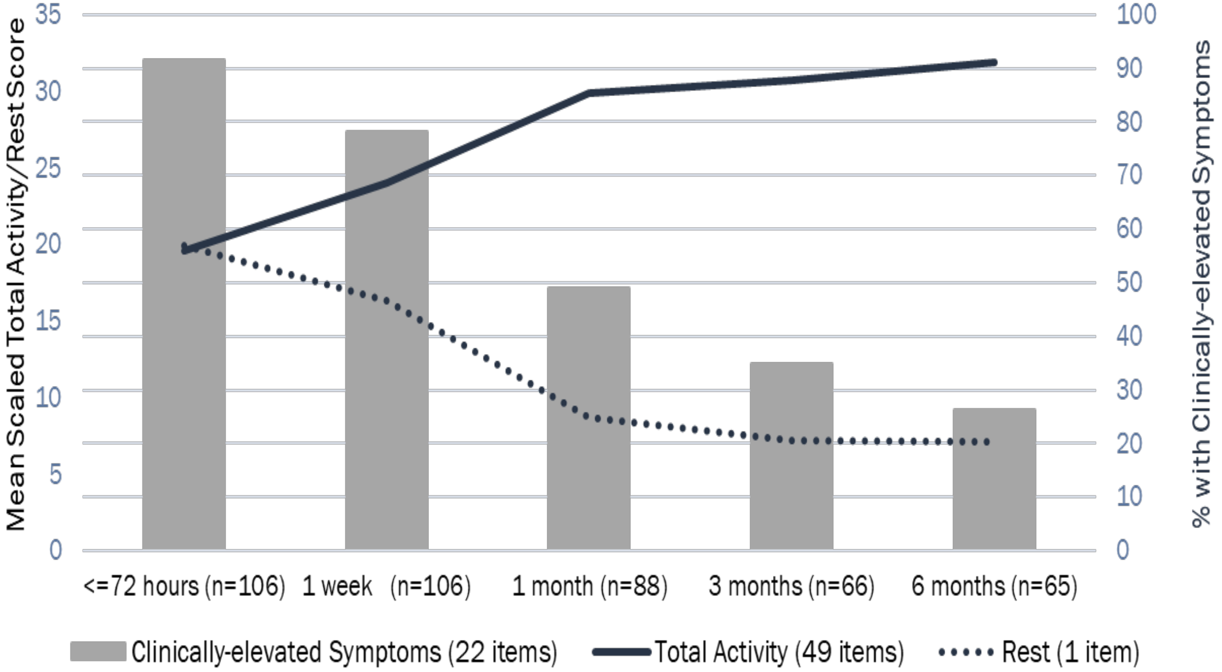
Moderate-to-Severe (Mod-Sev) TBI



Mean weighted effects of moderate–severe traumatic brain injury on overall cognitive test performance at three follow-up epochs, ◆ *d(pooled),* ■ *d(control).*

Meta-Analysis *(Source: Schretlen and Shapiro [1])*

Recovery From mTBI: Symptoms and Activity



Note: N = 106 Active-Duty Military

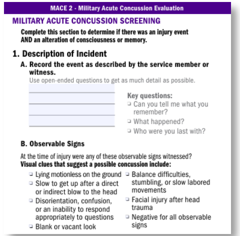
(Source: Ettenhofer et al., 2020 [2])

TBI Assessment: Current Approaches

- **Patient Self-Report** (survey, interview)
  - Strongly influenced by subjective factors
  - Not reliable for detecting injury
  - Still the primary “tool” to determine treatment
- **Screeners** (e.g., MACE-2, ANAM, SCAT)
  - Quick, sensitive for up to 7 days post-mTBI
- **Neuroimaging** (CT, MRI)
  - Typically normal in mTBI
- **Neuropsychological Testing**
  - Current “gold standard” for TBI assessment
  - Lengthy, sensitive for up to 3 months post-mTBI

Note: MACE-2 = military acute concussion evauation-2,
ANAM = automated neuropsychological assessment metrics,
CT = computed tomography,
MRI = magnetic resonance imaging

(USAF photo by Robbin Cresswell.)



MACE 2 - Military Acute Concussion Evaluation

MILITARY ACUTE CONCUSSION SCREENING

Complete this section to determine if there was an injury event AND an alteration of consciousness or memory.

1. Description of Incident

A. Record the event as described by the service member or witness.

Use open-ended questions to get as much detail as possible.

Key questions:
- Can you tell me what you remember?
- What happened?
- Who were you last with?

B. Observable Signs

At the time of injury were any of these observable signs witnessed?

Visual clues that suggest a possible concussion include:
- Lying motionless on the ground
- Slow to get up after a direct or indirect blow to the head
- Disorientation, confusion, or an inability to respond appropriately to questions
- Blank or vacant look
- Balance difficulties, stumbling, or slow labored movements
- Facial injury after head trauma
- Negative for all observable signs

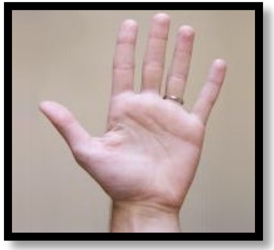
(Image courtesy of Health.mil.)

(Image by Mikael Häggström, public domain.)

Requirements for Next-Generation TBI Assessment

- Sensitive and Specific
  - Detects subtle forms of impairment/decline
- Multimodal/Multidomain
  - Quickly assesses multiple brain systems
- Clinically Feasible and Scalable
  - Mobile, automated, low cost
- Objective and Scientifically Validated
  - Guides treatment and return-to-duty decisions

Somatomotor (Hand) vs. Oculomotor (Eye)



(Photo by Eric Pierce, public domain.)

- Function: Output
- Slower (~250 milliseconds [ms])
- More effortful and conscious
- Strongly impacted by age, intelligence, depression, motivation, etc.

(Photo by Alexander Grey, public domain.)

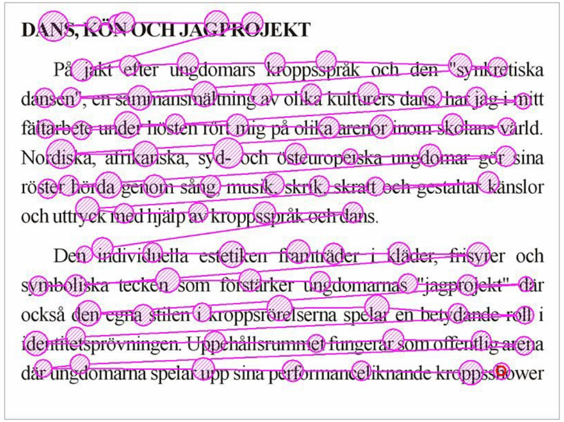
- Function: Input
- Faster (~150 ms)
- More automatic
- Less influenced by many common confounds

(Sources: Ettenhofer, Henshaw, and Barry [3]; Ettenhofer and Barry [4]; Ettenhofer et al. [5]; and Heitger et al. [6])

Eye Movement Basics

Eye-tracking camera measures gaze vector, pupil diameter

- Rapid **saccadic** eye movements acquire visual targets with help from cognitive processing
- Slower **smooth pursuit** eye movements track moving targets
- **Pupil dilates/constricts** in response to light, alertness, cognitive load

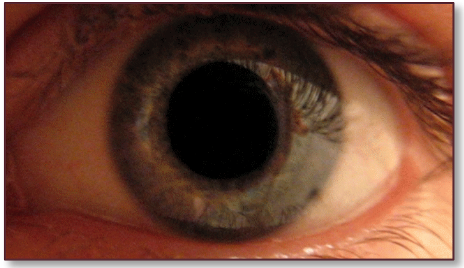


DANS, KÖN OCH JAGPROJEKT

På jakt efter ungdomars kroppsspråk och den "synkretiska dansen", en sammansmältning av olika kulturers dans, har jag i mitt fältarbete under hösten rört mig på olika arenor inom skolans värld. Nordiska, afrikanska, syd- och östeuropeiska ungdomar gör sina röster hörda genom sång, musik, skrik, skratt och gestaltar känslor och uttryck med hjälp av kroppsspråk och dans.

Den individuella estetiken framträder i kläder, frisyrer och symboliska tecken som förstärker ungdomarnas "jagprojekt" där också den egna stilen i kroppsrörelserna spelar en betydande roll i identitetsprövningen. Uppehållsrummet fungerar som offentlig arena där ungdomarna spelar upp sina performanceliknande kroppsshower

(Image by Lucs Kho, public domain.)



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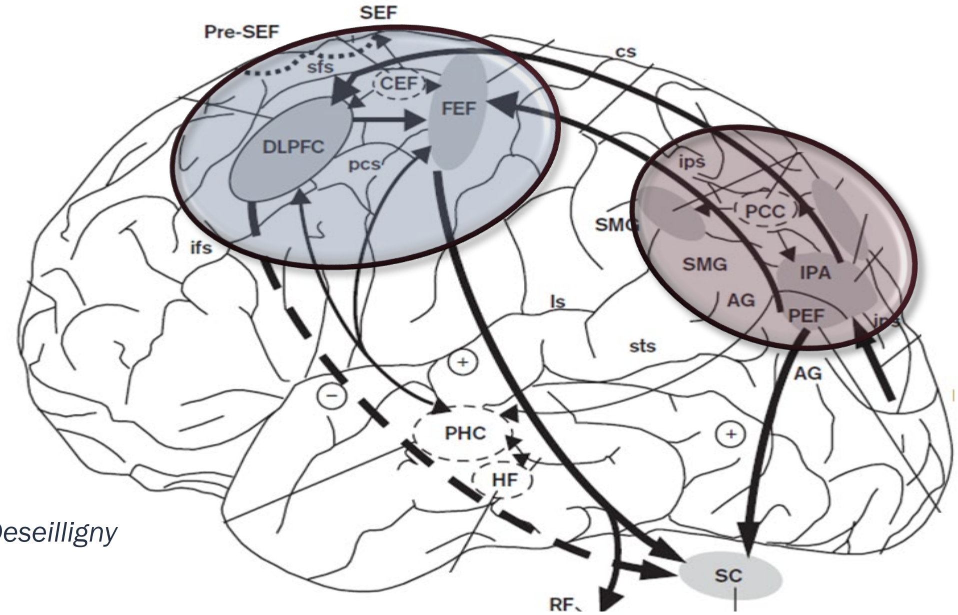
Distributed Neural Pathways of Eye Movement Visual Attention

Top-Down Conscious Control

- ***Decide***
- ***Inhibit***
- ***Predict***



Bottom-Up Automatic Processing

- ***Identify***
- ***Orient***
- ***Alert***

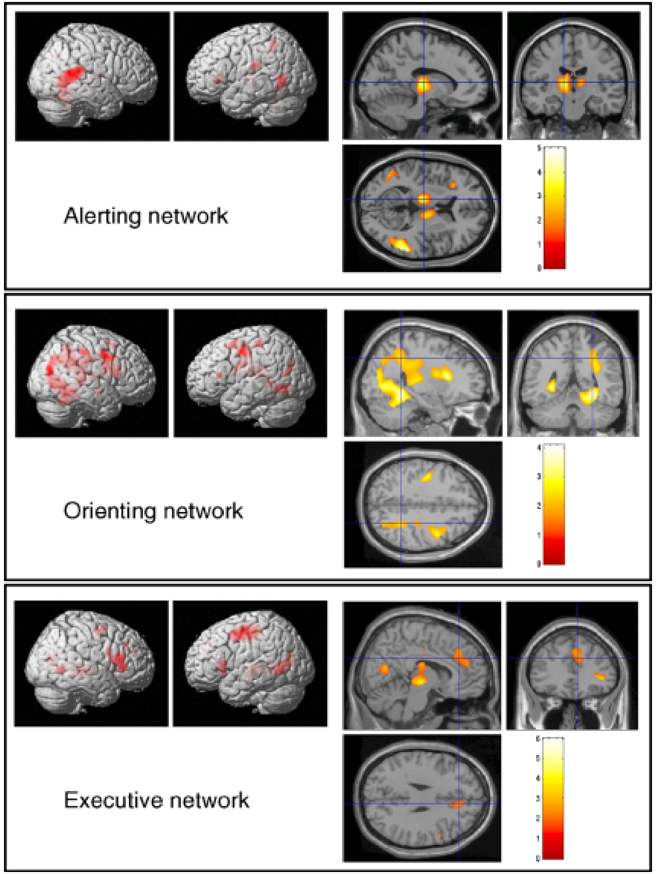
(Source: Adapted from Pierrot-Deseilligny et al. [7])

SEF, supplementary eye field; sfs, superior frontal sulcus; CEF, cingulate eye field; cs, central sulcus; DLPFC, dorsolateral prefrontal cortex; pcs, precentral sulcus; FEF, frontal eye field; ips, intraparietal sulcus; ifs, inferior frontal sulcus; SMG, supramarginal gyrus; PCC, posterior cingulate cortex; SPL, superior parietal lobule; IPA, intraparietal areas; ls, lateral sulcus; AG, angular gyrus; PEF, posterior eye field; sts, superior temporal sulcus; pos, parieto-occipital sulcus; PHC, parahippocampal cortex; HF, hippocampal formation; SC, superior colliculus; RF, reticular formations.

Neuroanatomical Model of Visual Attention

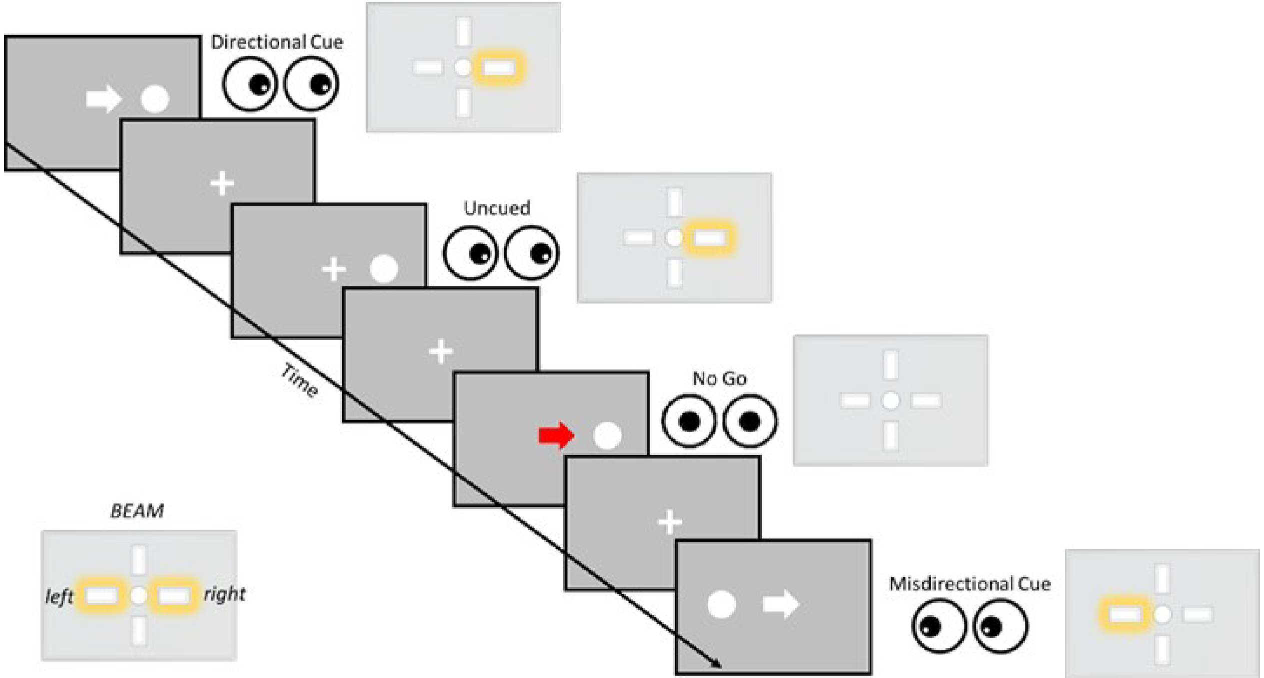
- Approach draws from work previously conducted by Posner and colleagues

- Cues elicit:
  - Time (alerting)
  - Location (orienting)
  - Conflict (executive)



(Source: Fan et al. [8])

Neurocognitive Eye Tracking: Bethesda Eye and Attention Measure (BEAM)



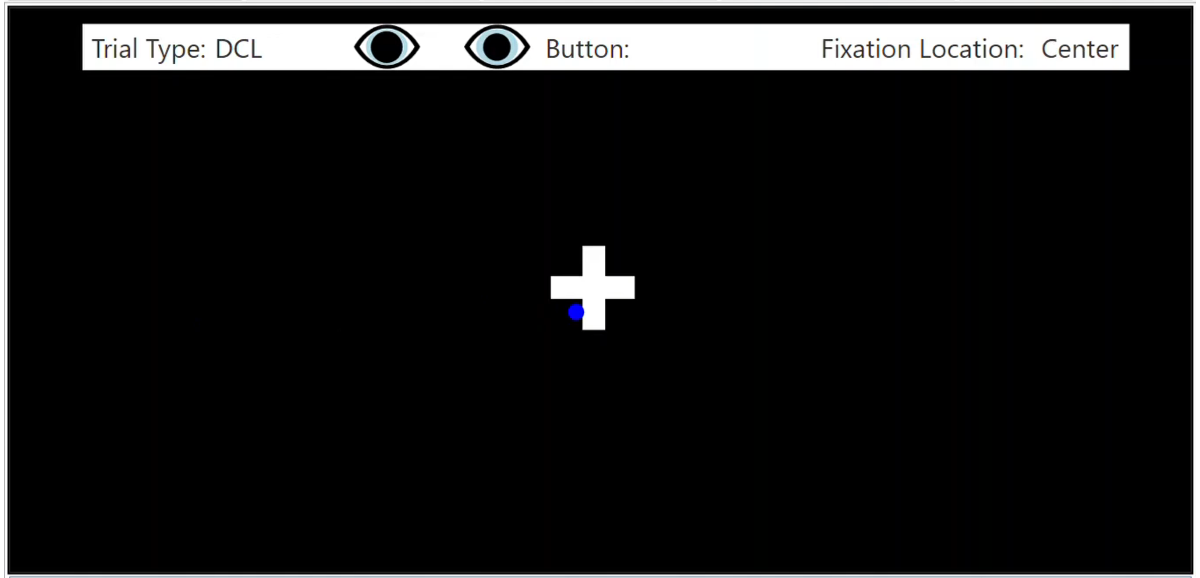
INSTRUCTIONS

Look at the circle and press the correct button as quickly as you can. For circles on the LEFT, press the LEFT button. For circles on the RIGHT, press the RIGHT button.

However, if you see a RED arrow, do not look at the circle and do not press the button.

(Images generated by presentation authors.)

BEAM Test—Raw Gaze Data

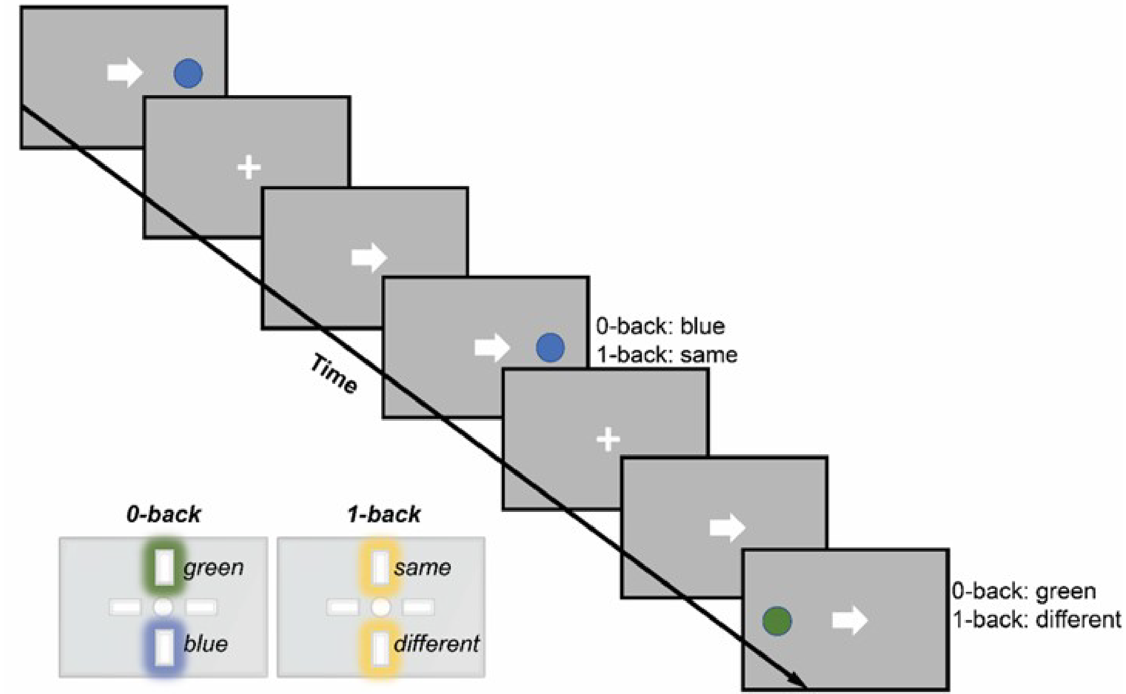


Number	Type	Man Reaction	SAC Reaction	SAC Duration	SAC Latency	Left Pupil Average	Right Pupil Averag	Behavior Codes	Composite Codes	Validity
42	DCL	491.27	437.38	46.88	390.5	21.299	19.526	a (397.16 ms),c (397.16 ms),b (437.38 ms),d (437.38 ms),g (-1306.21 ms),i (491.27 ms),n		n

Automatic analysis of eye movements, pupil response, button presses, and response validity

(Images generated by presentation authors.)

Ramping Up Cognitive Load: *Fusion n-Back*



(Images generated by presentation authors.)

INSTRUCTIONS

Look at the circle and press the correct button as quickly as you can.

0-Back

If the circle is BLUE, press the BLUE button. If the circle is GREEN, press the GREEN button.

1-Back

If the circle is the SAME color as the previous circle, press the SAME button. If the circle is a DIFFERENT color from the previous circle, press the DIFFERENT button.

DoD Fusion System: Prototype Evolution (1/3)

Desktop System (2011)

(Photo by Mark L. Ettenhofer.)

Laptop System (2015-)

(Photo by Mark L. Ettenhofer.)

DoD Fusion System: Prototype Evolution (2/3)

Wired Virtual Reality (VR) System (2018)

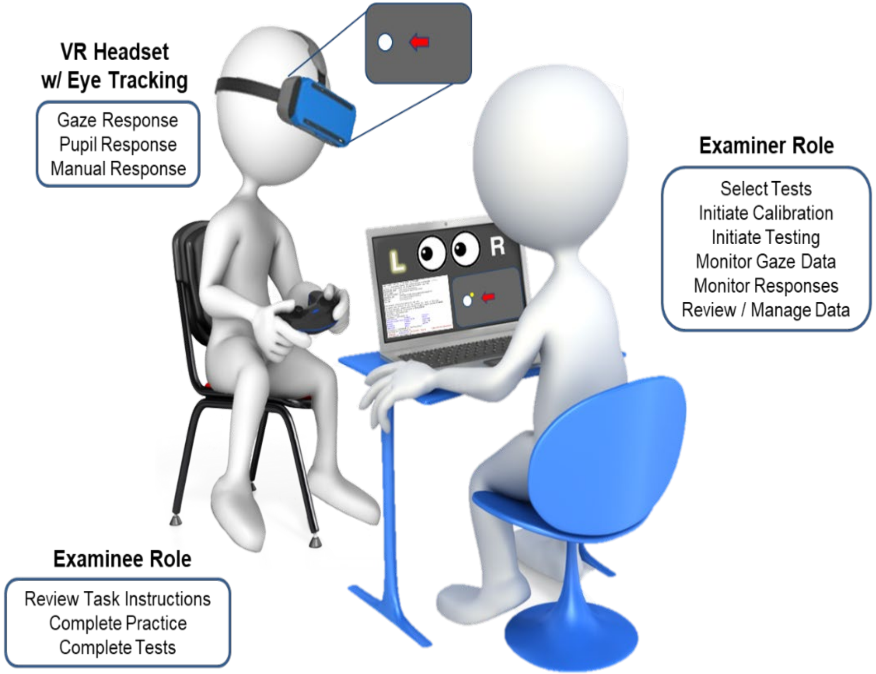
(Photo by Mark L. Ettenhofer.)

CAREN VR System (2019-)

(Photo courtesy of Naval Health Research Center Public Affairs.)

Note: CAREN = computer-assisted rehabilitation environment

DoD Fusion System: Prototype Evolution (3/3)



(Image by Sarah I. Gimbel. Used with Permission)

Wireless Mobile VR (2022-)

(Photo by Jenna K. Trotta, TBICoE)

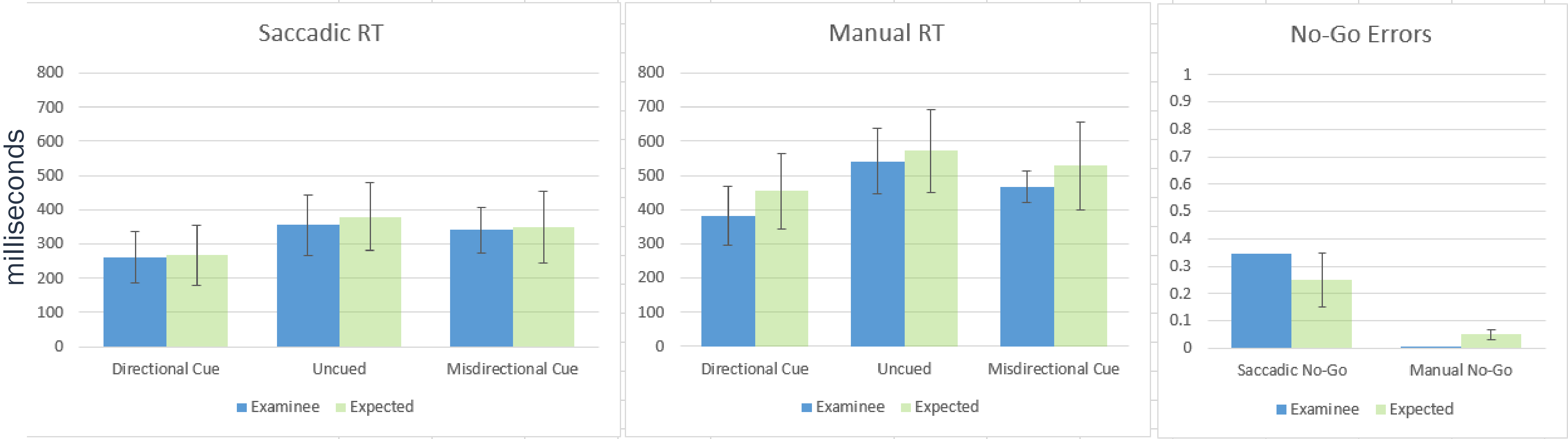
Fusion Eye Tracking: Under the Hood

Data Example:

- **Raw data:** 8 min × 150 hertz (Hz) = ~72,000 rows of data
- **Processed data:** 128 test trials with saccadic and manual response time (RT) and errors and pupil response

Test	Domain	Cue	Metric(s)
BEAM	Psychomotor Speed	+ ●	Uncued speed
BEAM	Inhibition	→ ●	No-go errors
BEAM + n-Back	Visual/Spatial Attention	→ ●	Directional cue speed
BEAM + n-Back	Cognitive Interference	← ●	Misdirectional cue errors, speed & consistency
BEAM + n-Back	Alertness	+ 👁	Pupil diameter (baseline)
n-Back	Cognitive Load	👁 ●	Pupillary response to targets
n-Back	Working memory	All ●	Errors, speed & consistency

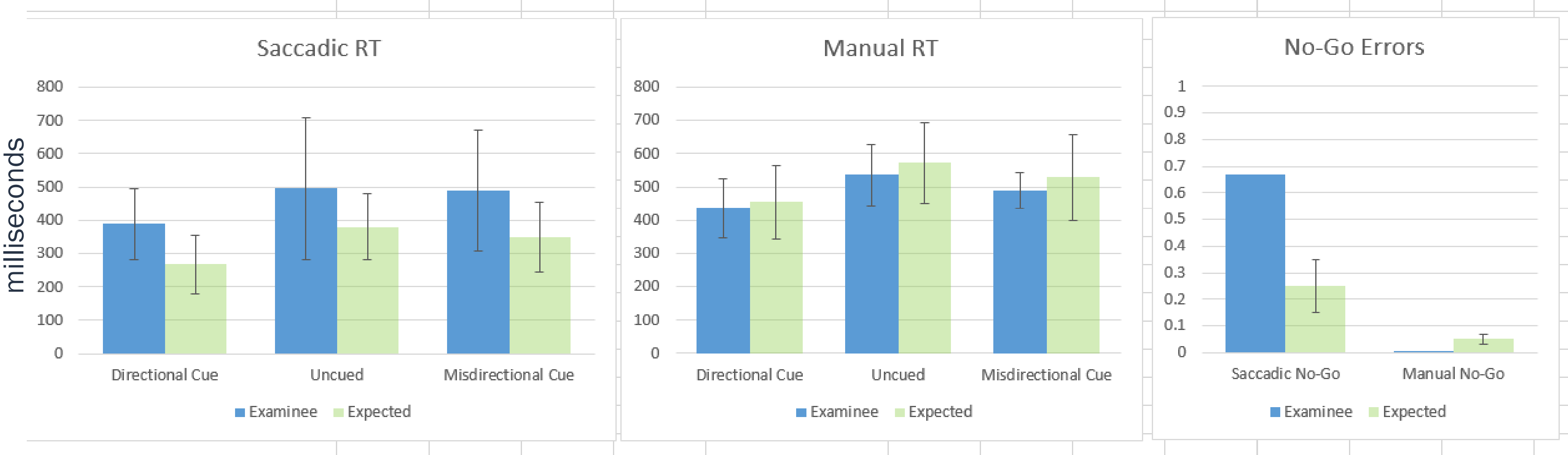
BEAM Score Sheet: Normal Profile (Example)



Fast and consistent, saccadic faster than manual, modest number of errors

(Image generated by presentation authors.)

BEAM Score Sheet: mTBI Profile (Example)

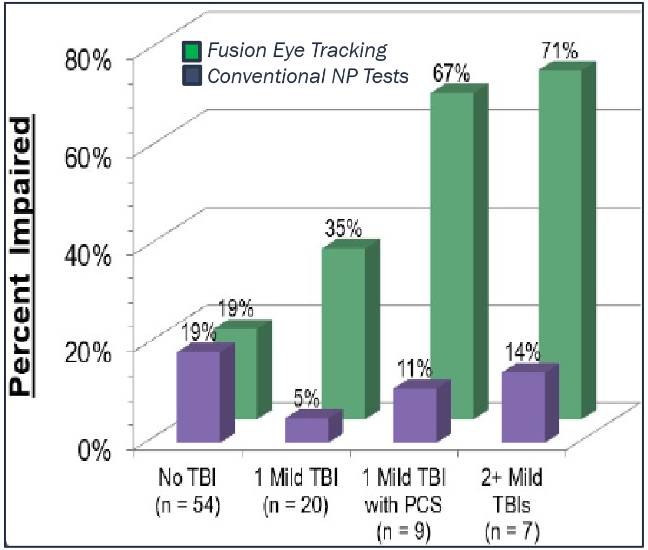


Slow and inconsistent saccadic RT, elevated saccadic errors

(Image generated by presentation authors.)

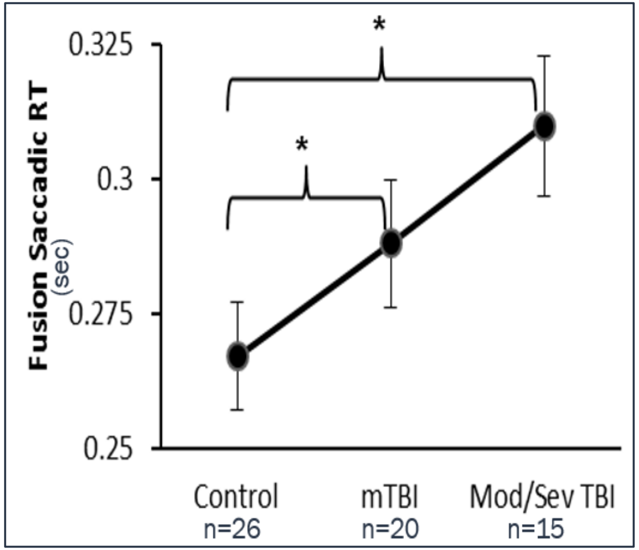
Identifying Persistent Effects of TBI: Validation Studies

Civilian/BEAM



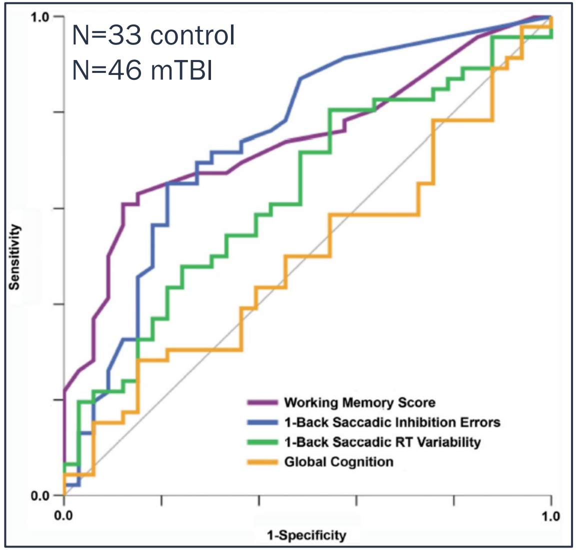
(Source: Ettenhofer, Hershaw, and Barry [3])

Civilian/n-Back



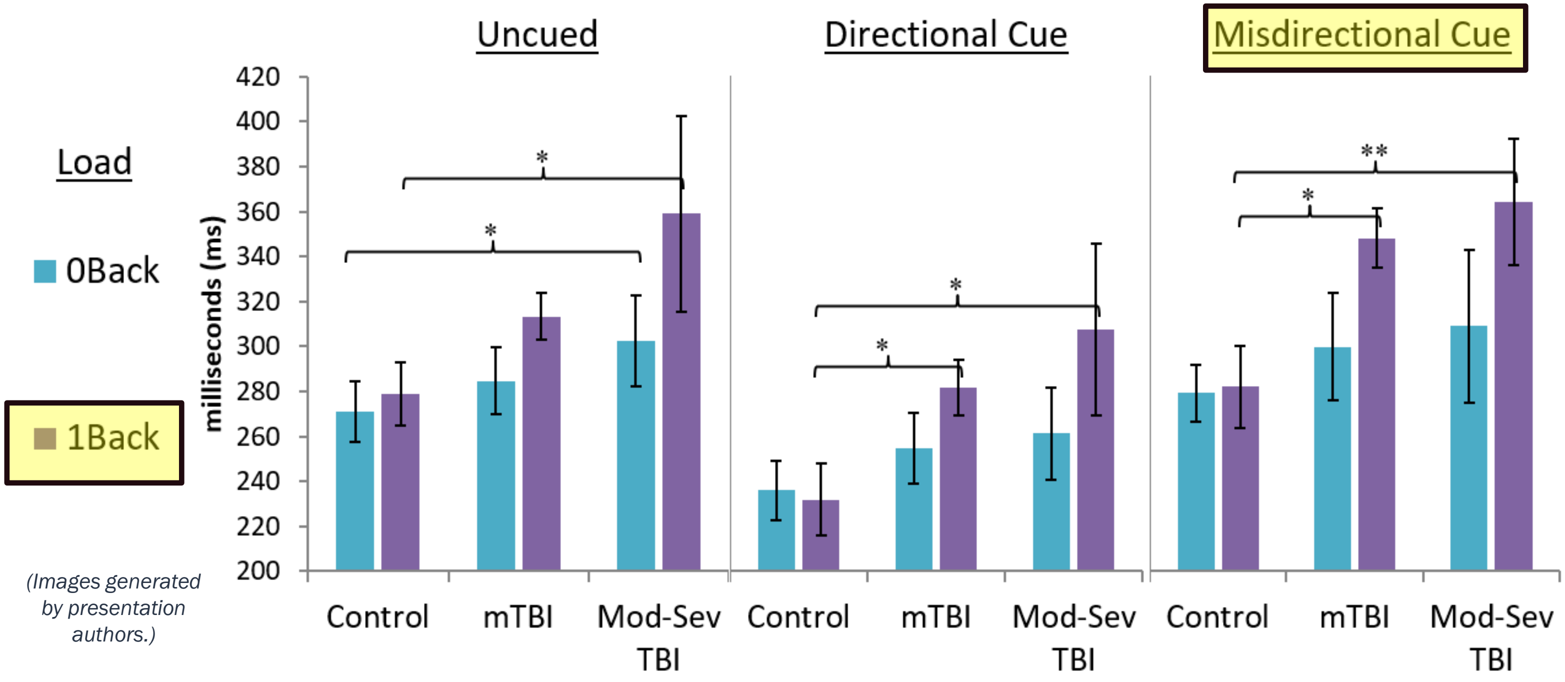
(Source: Ettenhofer et al. [5])

Active Duty/n-Back



(Source: Ettenhofer, Gimbel, and Cordero [9])

Higher Cognitive Load ⟶ Poorer Oculomotor Function After TBI

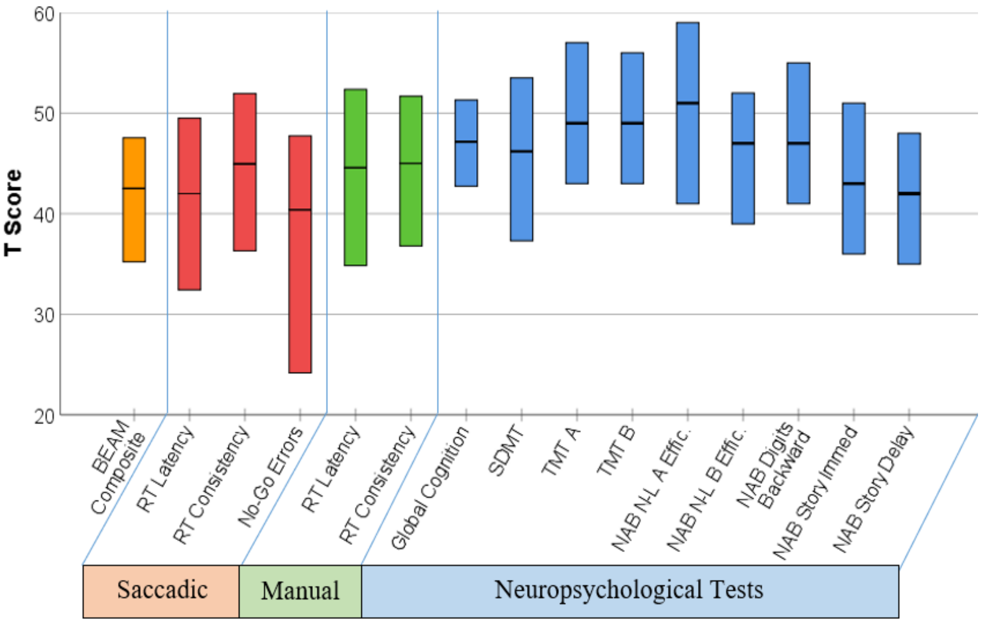


- N = 26 uninjured controls
- N = 20 mTBI (chronic stage)
- N = 15 Mod-Sev TBI (chronic stage)

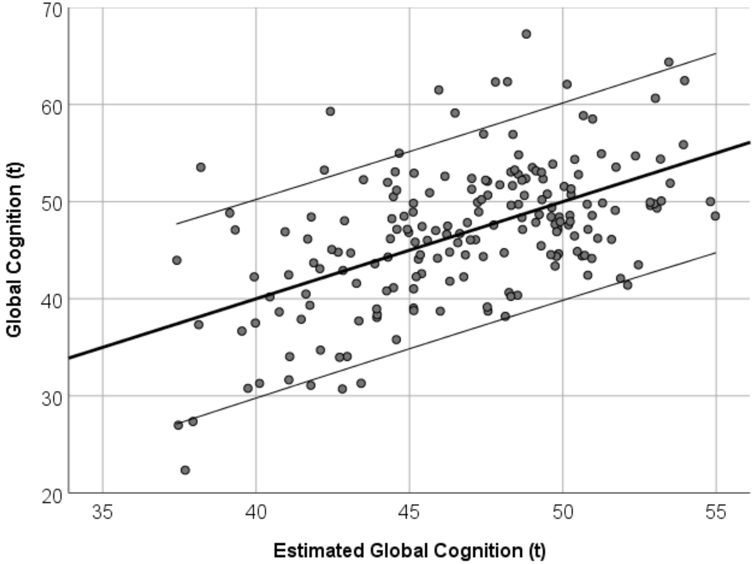
(Images generated by presentation authors.)

(Source: Ettenhofer et al. [5])

BEAM vs. Conventional Cognitive Screening in the NMCSD TBI Clinic



Note: SDMT = symbol digit modalities test, TMT = trail making test, NAB = neuropsychological assessment battery, N-L = number-letter, Effic = efficiency



Note: Regression predictors include BEAM saccadic RT consistency, saccadic no-go errors, and manual RT latency. Total model $R^2 = .30$. N = 191.

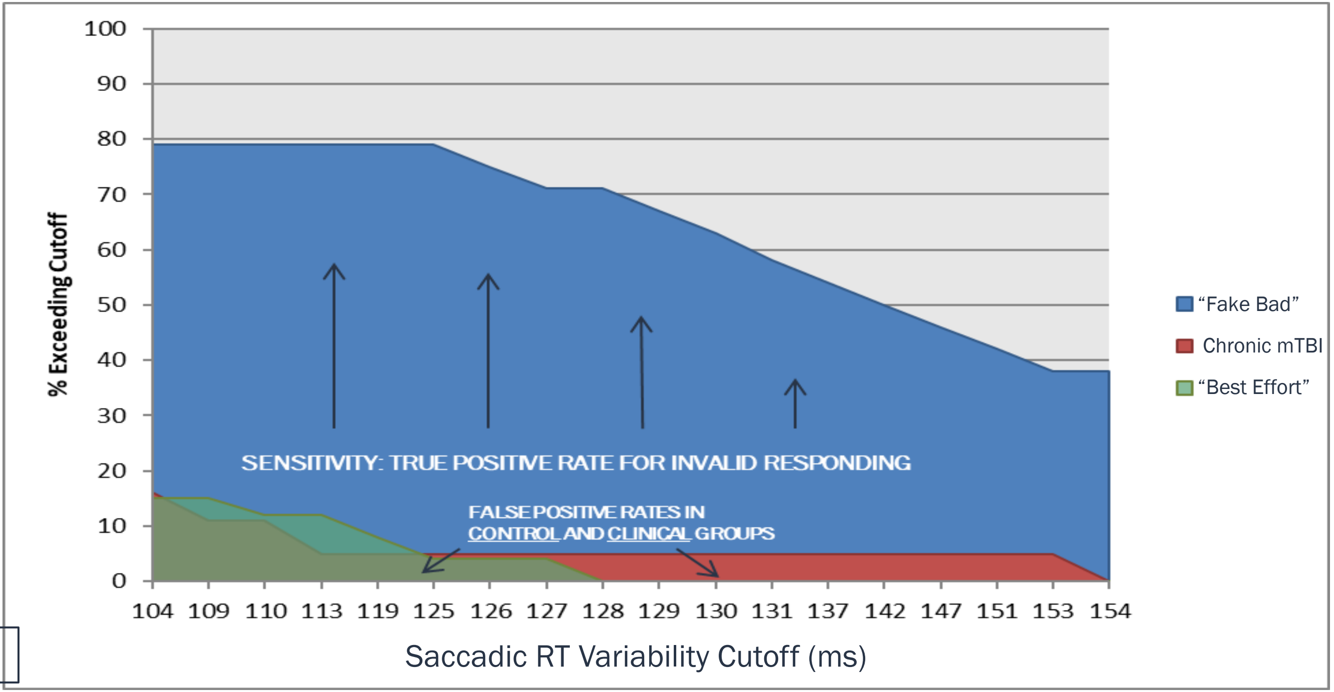
(Source: Ettenhofer, Hungerford, and Agtarap [10])

Embedded Validity Indicators

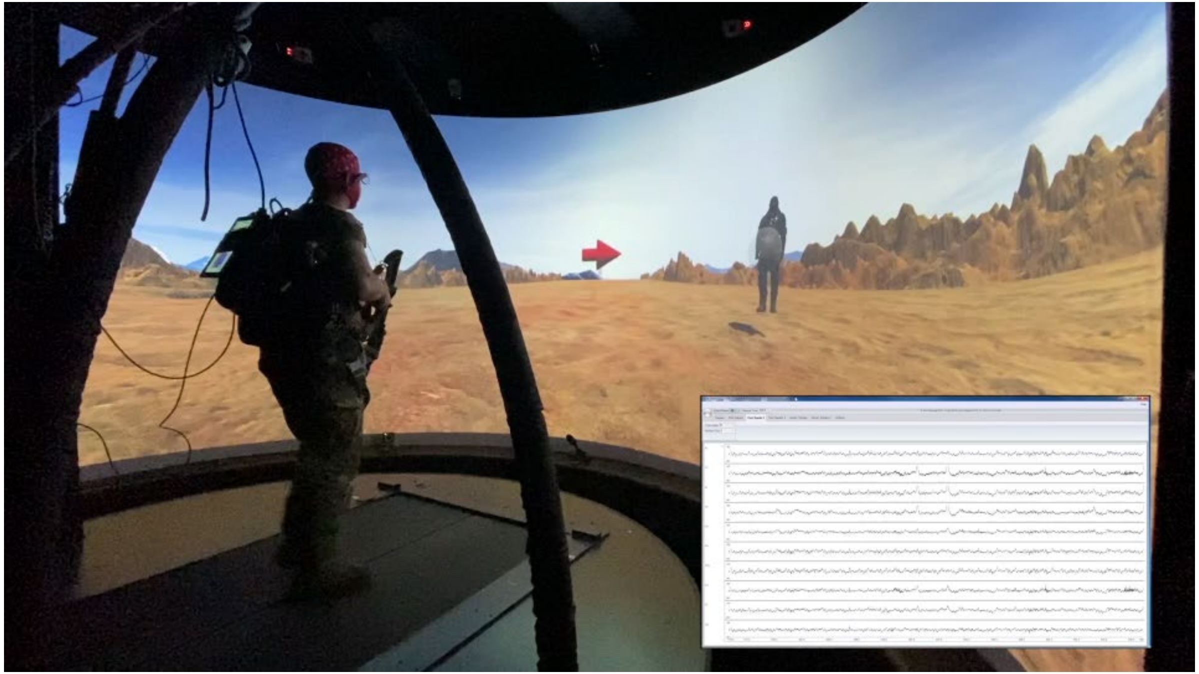
- BEAM distinguished “fake bad” from “best effort” and mTBI samples on par with gold standard tests of validity

- BEAM results accurately classified “fake bad” vs. mTBI with >90% accuracy

(Source: Barry and Ettenhofer [11])



Neurocognitive Eye Tracking as a Predictor of Military Performance (Fusion-VR)



(Video by Hedaya Rizeq, Naval Health Research Center.)

Sensor Modalities:

- *Eye tracking*
- *Electroencephalography shot speed/accuracy*
- *Gait (motion capture)*
- *Electromyography galvanic skin response*
- *Respiration*
- *Heart rate*
- *Heart rate variability*

Correlation b/w Clinical and VR Eye Tracking:

$r_{avg} = .64^{**}$

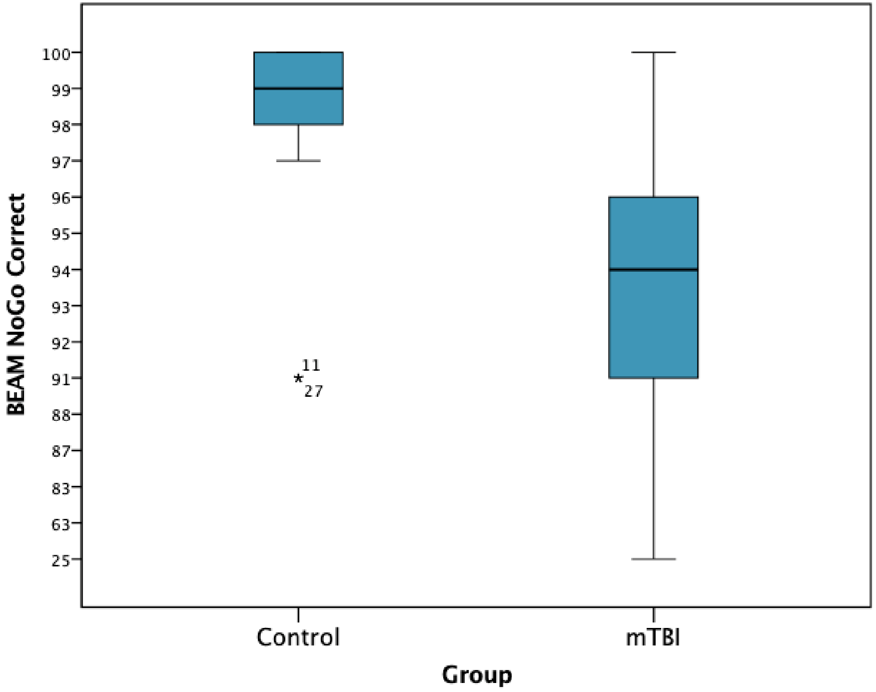
Fusion-VR Shooting Task: Saccadic Inhibition in mTBI vs. Control

	Control	mTBI
n	12	25

BEAM-VR Task: No-Go Errors

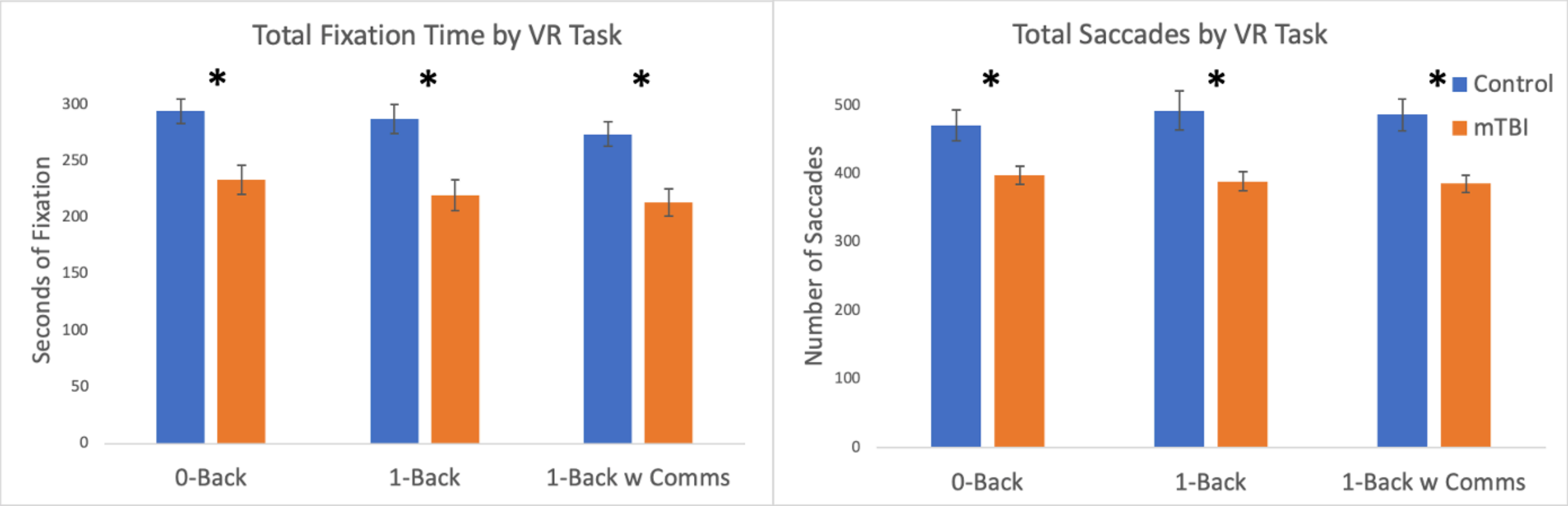
Instructions: When you see a red arrow, do not look at or fire at the target.

Elevated no-go error rate on fusion-VR suggests significant impairment (disinhibition) on military tasks in chronic mTBI.



(Image generated by presentation authors.)

Fusion-VR: Reduced Fixations and Saccades in Chronic mTBI



Note: Probability value (p) <.05

(Image generated by presentation authors.)

Neurocognitive Eye Tracking: Ongoing Research

Fusion-VR+ Study

- Examine eye movements for subacute mTBI, chronic mTBI, and control on simulated military patrol (target acquisition and engagement)
- Measure trajectory of recovery of eye movements and operational performance during mTBI recovery

Fusion Military Normative Study (NMCSD + Fort Liberty)

- Establish control norms, evaluate test-retest reliability
- Examine effects of post-traumatic stress disorder, insomnia, orthopedic injury
- Examine trajectory of recovery in subacute mTBI

Fusion-MRI Study

- Evaluate neurocognitive eye tracking as a biomarker for white matter injury after TBI

(Photo by Sarah I. Gimbel. Used with Permission)

(Photo by Jenna K. Trotta, TBICoE.)

Summary and Discussion

- Multiple studies have shown that neurocognitive eye tracking can provide enhanced sensitivity to TBI-related cognitive and oculomotor impairments
- These TBI-related impairments are most notable when an individual is under a high level of cognitive load
- Oculomotor impairments present in similar ways on clinical tasks and during military/operational activities
- Additional work is ongoing to extend this work and expand neurocognitive eye-tracking capabilities within DoD clinical and operational environments

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