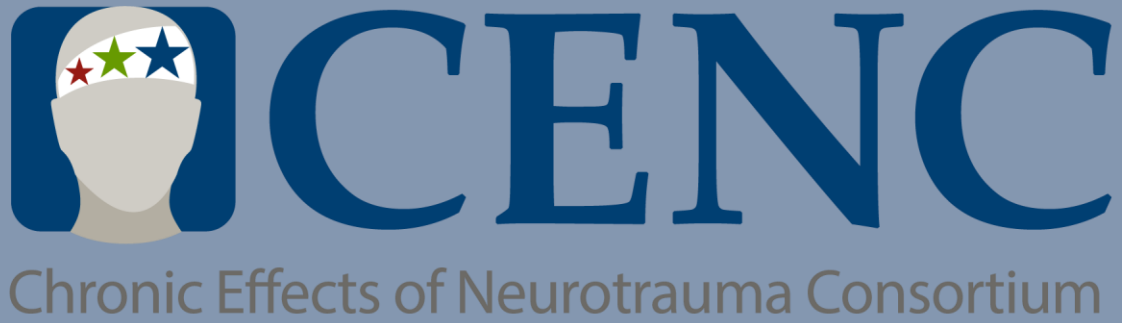
Balance Dysfunction after mild TBI: Findings form the Chronic Effects of NeuroTrauma Consortium Longitudinal Study

Presenters:

William C. Walker MD, David X. Cifu MD



Conflict of Interest

- **Grant funding from:**
  - Dept of Defense, Chronic Effects of Neurotrauma Consortium (CENC) Award W81XWH-13-2-0095
  - Dept of Veterans Affairs CENC Award I01 CX001135.
- **Drs. Walker and Cifu have no conflicts of interest to disclose**
- **Acknowledgements:**
  - CENC Observational Study Site PIs, co-PIs, and Leadership Working Group.
- **Disclaimer:**
  - The views, opinions, and/or findings contained in this article are those of the authors and should not be construed as an official Veterans Affairs or Department of Defense position, policy, or decision unless so designated by other official documentation.

Learning Objectives

- Become familiar with the CENC research portfolio including its multicenter observational study of combat-exposed Veterans and Service members
- Understand the importance of balance dysfunction after Traumatic Brain Injury (TBI) and describe methods of measuring it
- Describe components of vestibular rehabilitation
- Describe the relationship between historical mild TBI and balance performance found in the CENC multi-center study
- Describe other predictors of balance performance found in this study and the implications for clinical assessment and treatment

Poll Question #1

What is your primary role in VA? (Pick one answer)

- Student, trainee, or fellow
- Clinician
- Researcher
- Administrator, manager or policy-maker
- Other

Chronic Effects of Neurotrauma Consortium

- Departments of Defense and Veterans Affairs funded nationwide research consortium to study the short- and long-term effects of repeated concussions in combat injured servicemembers and Veterans.
- Five year, $62.2 million award begun October 2013, with 5-year renewal underway.
- 30+ Universities, 15 VA's and 12 MTFs working together
- Collaborations with NIH, NINDS, NIDILRR, NCAA, InTBIR and NFL research groups to jointly study civilian, sports and combat concussions.
- More than 114,000 unique data elements loaded into federal registry (FITBIR) to date.

CENC.RTI.ORG

CENC Findings 2018

- 2,000 OEF/OIF participants with $\geq$ 1 mTBI enrolled across all studies :
  - 2/3rds with persistent symptoms and related issues are still high functioning, employed and managing well in the community more than 9 years after injury
  - 1/3rd of the cohort with persistent symptoms are demonstrating ongoing and increasing difficulties that are requiring significant health care utilization.

- None of the participants are exhibiting signs of dementia on average 9 years (range 3-18 years) from last mTBI.

- Female subjects have greater symptoms than male.

- Servicemembers and Veterans with combat-related concussions and associated conditions (PTSD, pain, depression, substance use, elevated suicide risk) represent a unique and high-risk population.

CENC Findings 2018

- Linkages have been identified between elevated lifetime risks for neuro-degeneration, including Alzheimer's dementia (2.3x) and Parkinson's disease (1.5x), chronic pain, opioid misuse, suicide and PTSD and combat-related concussion
- Multi-modal, high technology research assessment techniques have been developed, but from a clinical standpoint using a standard set of questionnaires (NSI, CAPS, BDI, VAS, PSQI) and basic physical exam is still appropriate
- Longitudinal Observational Study (current n = 1,500) continues with annual re-assessment and monitoring for recovery and/or neurodegeneration patterns.
- Epidemiologic Study (1.6 million unique subjects) is exploring associations between mTBI/co-morbidities and persistence of symptoms (pain, opioid usage, behavioral), recovery patterns, health care utilization, and neurodegeneration.
- Interventional trials are being implemented using the Longitudinal Cohort.

CENC multicenter longitudinal study of the late neurologic effects of OEF/OIF/etc. deployment

- Inclusion criteria: Veterans and SMs with post-911 military deployments and combat exposure
- Exclusion criteria: Moderate or Severe TBI, Major neurologic or psychiatric disorder
- Comprehensive baseline and longitudinal assessments
- Eight sites now enrolling, > 1,500 enrolled
- Interim analysis: 1st 492 participants, original 4 sites, cross-sectional

CENC multicentre study interim analysis:

Differences between participants with pos. versus neg. mild TBI histories.

Walker WC, et al. *Brain Inj*. 2018;32(9):1079-1089.

<u>Overall findings, unadjusted comparisons:</u>

- Worse widespread symptoms if mTBI positive
- Poorer life functioning if mTBI positive

BUT

- Differences in many other attributes
- Fairly equal performance measures with the following exceptions:
  - processing speed (WAIS IV coding)
  - visual-motor integration and executive function (Trails B)
  - postural control (select CDP SOT conditions)

Brain Inj 2018;32(10) CENC Special Edition CENC multicenter study articles focusing on Pain

- Current Pain relation to mTBI history (positive, negative)
  - Structural Equation modeling
  - Association found but only indirect effect significant
  - Pain Intensity
    - Mediator: Sleep
    - Covariates: Arthritis, Extracranial Injury
  - Pain Interference
    - Mediators: Sleep, PTSD, Depression, Anxiety
    - Covariates: Arthritis, Extracranial Injury, Age, Self Efficacy

- Relation of Pain Interference to MRI functional connectivity & cortical thickness
  - Unadjusted preliminary analyses
  - Higher pain interference associated with:
    - Less FC between mesial prefrontal cortex and posterior regions of the default mode network
    - Greater cortical thickness of specific regions

Brain Inj 2018;32(10) CENC Special Edition Other CENC multicenter study articles

- Relationship of Lifetime mTBI history to SC disability ratings
  - Covariate adjusted regression analysis
  - mTBI associated with increased SCD (3.6% per mTBI)
  - Among subgroups, blast-related mTBI showed largest effect
- Blood-based Brain-derived proteins (Tau & Beta Amyloid) and mTBI history
  - Unadjusted preliminary analysis of subset
  - Exosomal phosphorylated tau, exosomal tau, and a trend of plasma tau in group with repetitive mTBI ($\geq$3)
  - No relationship of mTBI history to Beta Amyloid
- Description of Recruitment, Lessons Learned, Best Practices

Poll Question #2

The CENC Multicenter Longitudinal Study enrolls Veterans & SMs with prior:

(select all that apply)

A. Post-911 deployment
B. Combat exposure
C. Absence of any traumatic brain injury
D. Mild traumatic brain injury
E. Severe traumatic brain injury

Brain Inj 2018;32(10) CENC Special Edition **Postural stability and mTBI history**

Background, Rationale

- Postural instability is a known acute sequela of mTBI
- After deployment, persisting dizziness and imbalance symptoms are common but:
  - objective post-acute data are lacking
  - the relatedness to the mTBI(s) is unclear

Objective:

- Determine if historical mild traumatic brain injury (mTBI) has an influence on balance performance.

Prior Research; Balance & Military mTBI

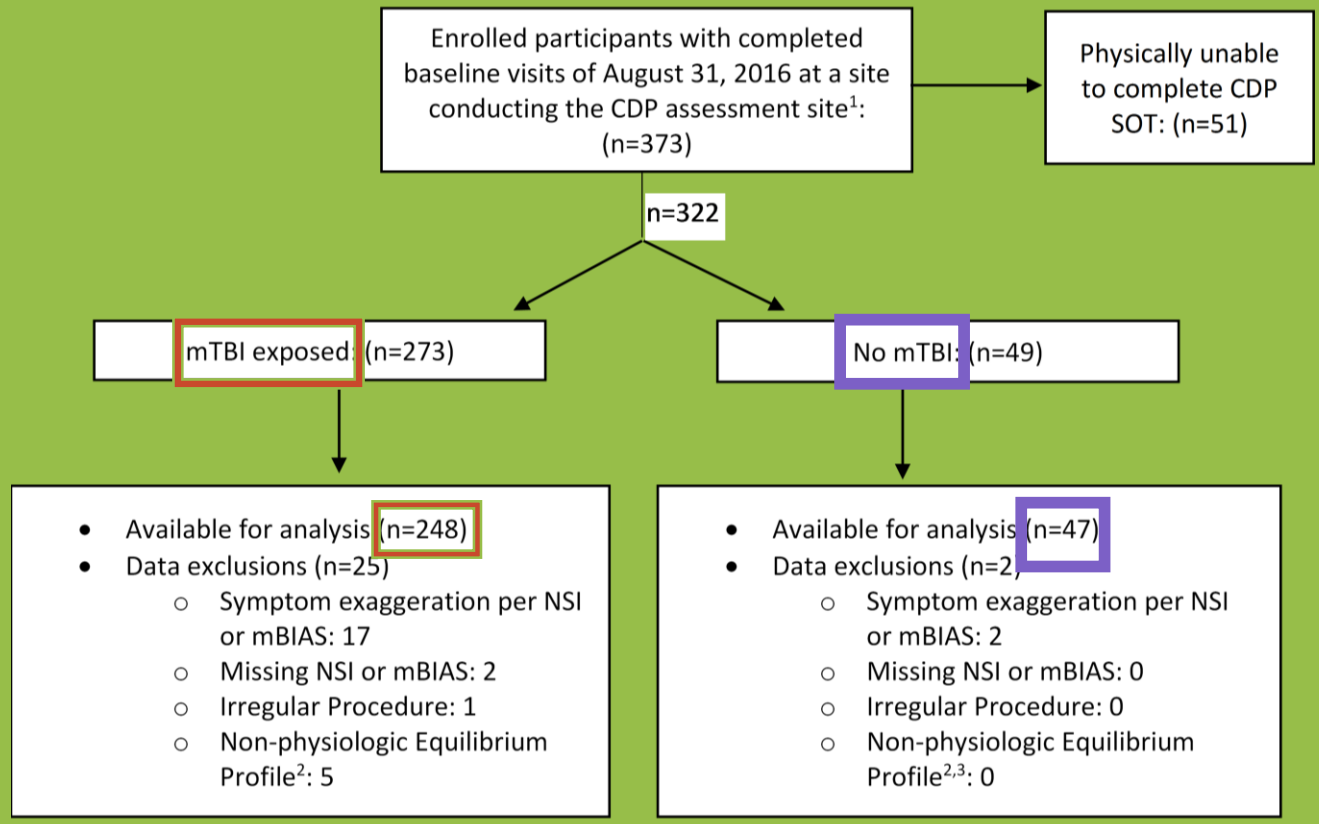
Wares JR, Hoke K, Walker WC, et al. J Rehabil Res Devel 2015;52(5):591-604.

- CDMRP funded observational study of individuals blast exposed during OEF/OIF/OND deployment

- Using mTBI and PTSD group analyses with CDP SOT testing on average one year after military blast exposure, we found poorer balance after blast mTBI with PTA compared to blast exposure without mTBI.

- Limitations:
  - Did not adjust for other variables of potential influence
  - Dichotomized into mTBI groups (mTBI with PTA vs No TBI or mTBI without PTA)

CDP Balance Analysis PARTICIPANT FLOW DIAGRAM



[1] The Houston site did not administer the CDP assessment, and instead used the BESS to assess posturography and balance. As such the CDP analyses exclude all subjects from the Houston site (N=119). An additional 51 individuals did not complete the CDP assessment due to nontolerance of CDP protocol or technical issues with the machine.

[2] Unreliable Effort was assigned if a subject performed poorly on conditions 1 and 2, but performed better on the later, more challenging conditions.

[3] One subject in the No mTBI group removed due to Invalid per NSI or mBIAS would have also been removed for Non-physiologic Effort.

SEM Candidate Variables

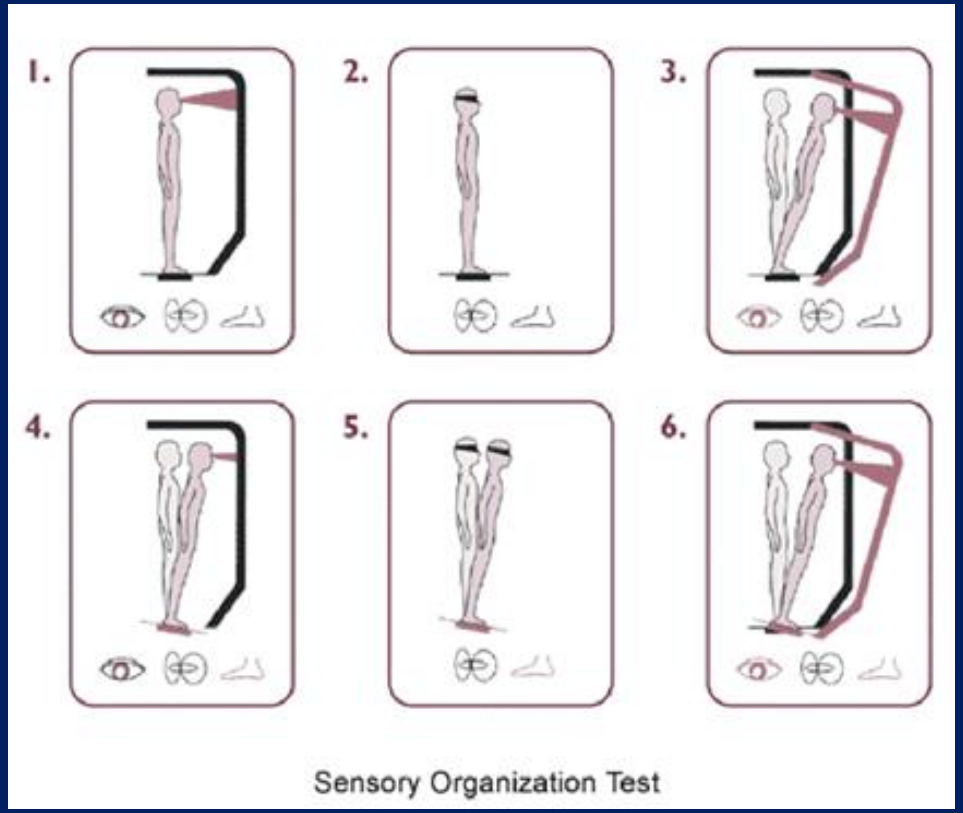
- Key I.V.: Comprehensive structured interviews were used to diagnose all lifetime mTBIs.
- Other studied variables were measured by structured interviews, record review, and questionnaires.
- Candidate Interaction Variables
  - Mediators: PTSD, Depression, Anxiety, Mental Health hx, Pain, Pain med use
  - Covariates: Time since index PCE, Age, EtOH, Learning disability hx, TOPF
  - Moderators: Gender, Arthritis hx
  - Confounders: site, Combat intensity, # months deployed

Outcome Measure: CDP SOT Equilibrium scores

1. Eyes open, fixed surface and visual surround.
2. Eyes closed, fixed surface.
3. Eyes open, fixed surface, sway referenced visual surround.
4. Eyes open, sway referenced surface, fixed visual surround.
5. Eyes closed, sway referenced surface.
6. Eyes open, sway referenced surface and visual surround.

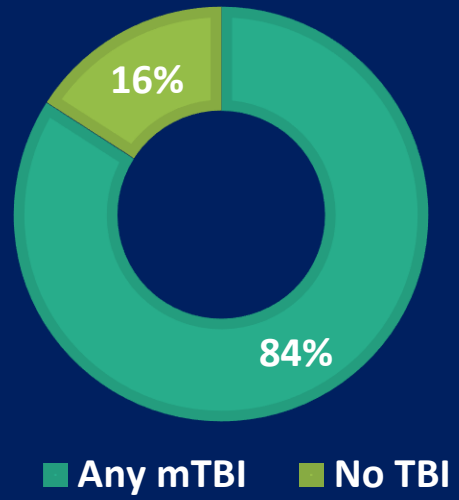
Composite Equilibrium: weighted average of these 6 scores (conditions 1 and 2 are weighted 1/3 as much as conditions 3 through 6)

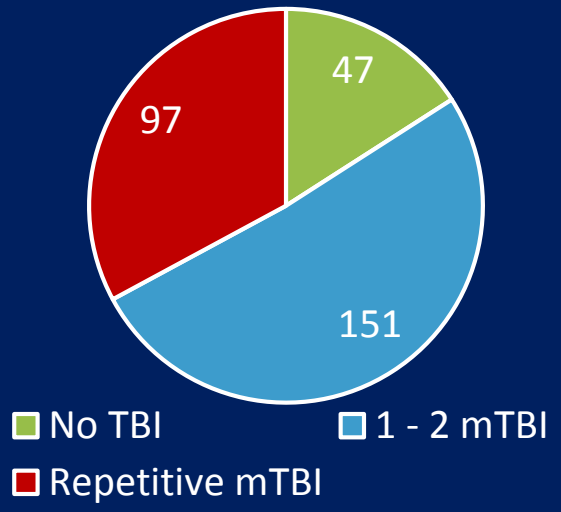
Sensory Organization Test (SOT)
6 sensory feedback conditions

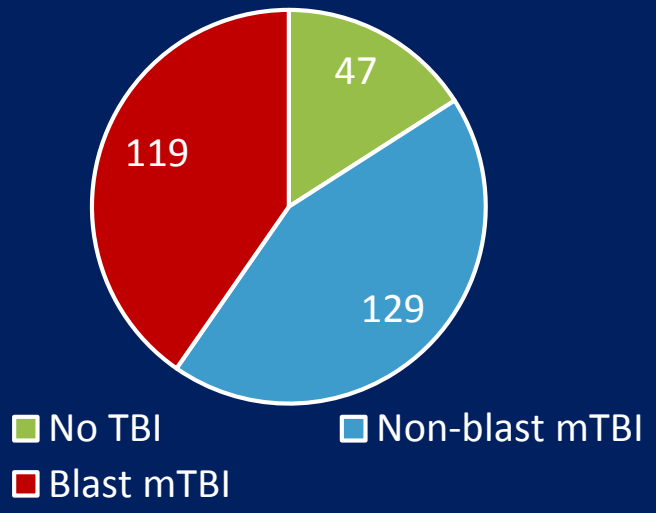


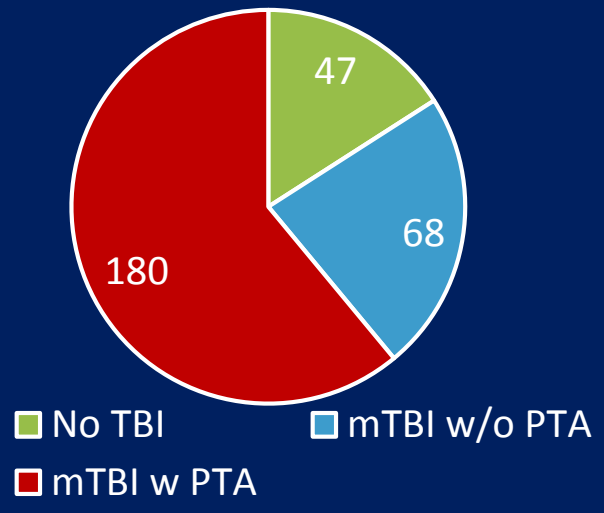
Lifetime mTBI History

- Positive (n=248) vs Entirely Negative (n=47) history of mTBI
- mTBI subgroups examined
  - Repetitive (≥ 3mTBIs)
  - Blast associated
  - With PTA/LOC









Statistical Methods

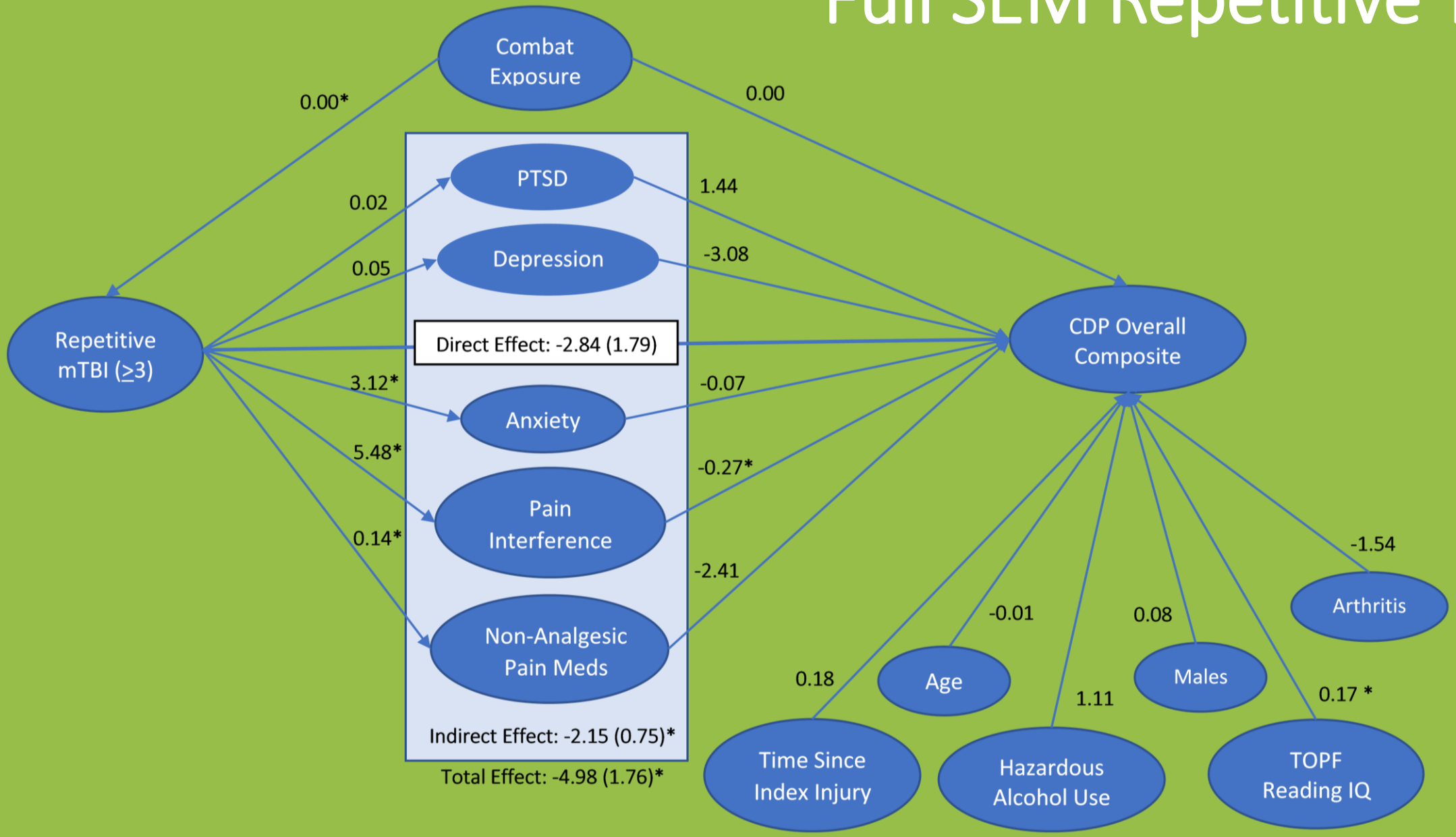
- Preliminary work
  - Bivariate analyses between each candidate IV and Equilibrium scores using linear regression methods appropriate for each variable's distribution.
    - Then fit to include interaction with mTBI status
    - Covariate or moderator interactions at $p \leq 0.1$ were promoted
  - Covariate adjusted regression (CAR) analyses
  - Preliminary SEM
  - If IV did not have significant interaction across CAR and SEM, it was removed

- Final SEMs built

Results; TBI effect in SEMs for Composite Equilibrium

	mTBI vs. No mTBI	mTBI with PTA	Repetitive mTBI	Blast mTBI
Total Effect				
Parameter Estimate	-1.7300	1.6194	-4.9842	-1.7477
P-value	0.4222	0.4015	0.0046*	0.3783
Direct Effect				
Parameter Estimate	0.5203	2.9190	-2.8352	-0.0596
P-value	0.8133	0.1234	0.1134	0.9761
Indirect Effect				
Parameter Estimate	-2.2504	-1.2996	-2.1490	-1.6881
P-value	0.0125*	0.0722	0.0044*	0.0212*

Full SEM Repetitive TBI



TBI effect in SEMs for all Equilibrium scores; Repetitive vs Nonrepetitive mTBI

Sensory Conditions	Total Effect	Direct Effect	Indirect Effect
1	NS	--	--
2	-3.3, p=0.003	-2.3, p=0.038	-1.0, p=0.032
3	-3.4, p=0.002	-2.3, p=0.036	-1.1, p=0.027
4	-5.9, p=0.016	-4.4, p=0.080	NS
5	-7.7, p=0.002	-4.8, p=0.061	-2.9, p=0.006
6	-4.9, p=0.098	NS	-4.1, p=0.001

Results Summary; Did mTBI history influence balance performance (SOT equilibrium score)?

- Overall +/- mTBI classification did NOT
  - Model did show significant effects for other variables including:
    - Mediator: Pain Interference
    - Covariate: Test of Premorbid Function (TOPF)
- However repetitive mTBI sub-classification did have influence
  - ≥ 3 mTBIs lowered Composite score by 5.0 (1.8) points
  - Only Indirect portion of effect significant on Composite score
    - Mediator: Pain Interference
    - Covariate: TOPF
  - But several sensory condition scores did show significant (2, 3) or nearly significant (4, 5) direct effects

Discussion

- **Veterans and SMs with repetitive mTBI are at heightened risk for later life balance disturbances**

- Potential mechanisms for mediating effect of pain interference on balance performance:
  - Peripheral: Splinting, guarding, altered neuromuscular firing patterns
  - Central: Attentional resources, fear/avoidance

- Covariate effect of TOPF
  - Consistent with evidence in other populations: Intellectually impaired, Dyslexia, Elderly with low cognition
  - Potential mechanisms: Inefficient sensory feedback, lower attentional resources

- Lack of influence by PTSD, anxiety, or combat exposure intensity

Poll Question #3

Our CENC study found what relationship to balance scores (composite equilibrium on CDP-SOT)?

(Select all that apply)

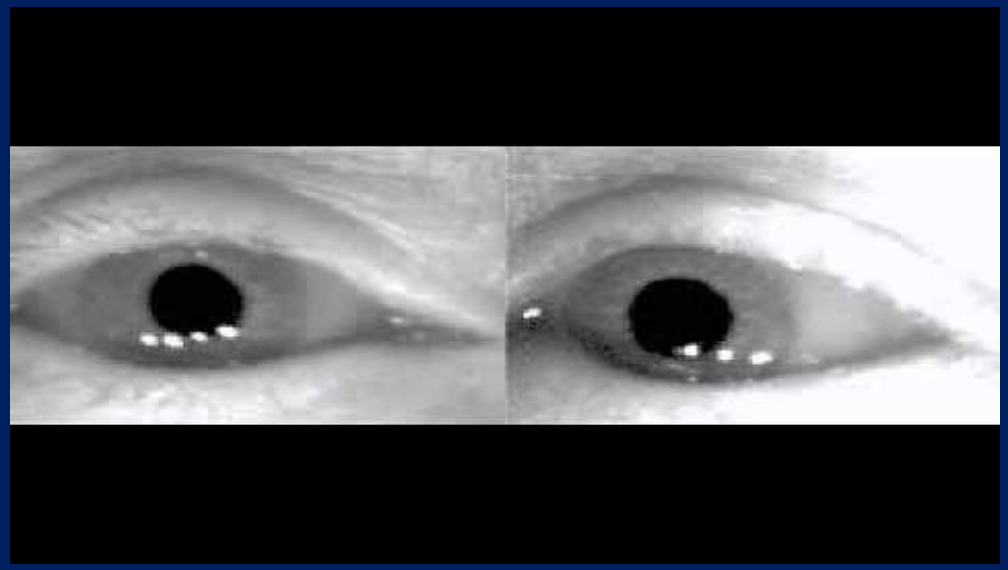
A. A single past mTBI reduced balance
B. ≥ 3 past mTBIs indirectly reduced balance via higher Pain
C. ≥ 3 mTBIs directly reduced balance
D. Lower innate intelligence reduced balance

Office Balance Assessment in mTBI

- History
  - TBI: Determine number*, severity and recency
  - Query for any other neurologic, vestibular, or ENT disorders
  - Dizziness: COŁDER; vertigo vs other variants of dizziness
  - Hearing, tinnitus
  - Balance, falls, syncope, seizures
  - Standardized symptom measures (e.g. DHI, NSI)
- Focus of Neurologic Physical Exam
  - Eye and EOM
  - FNF, HTS, RAM, finger tapping
  - Romberg and variants
  - Single leg stance and variants
  - Gait and variants
  - Special tests: Dix-Hallpike, UPDRS

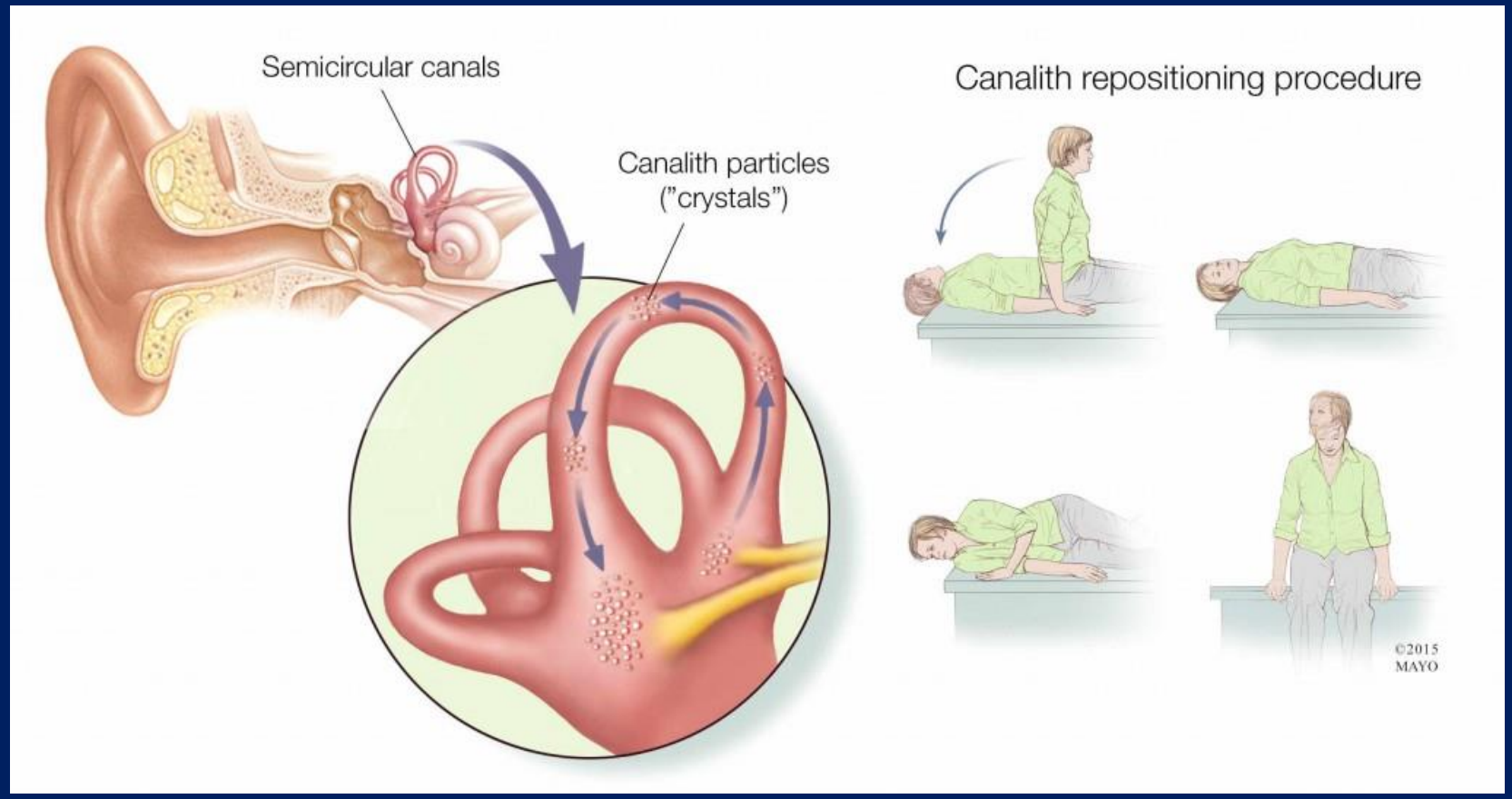
*CENC study shows chronic lower balance after 3 or > mTBIs

Dix Hallpike Maneuver for Benign Paroxysmal Positional Vertigo (BPPV)



Treatment of BPPV

- Canalith repositioning maneuver (Eppley)



Common Physical Therapy Balance Tests

- Berg Balance Scale (BBS)
- Dynamic Gait Index (DGI)
- Balance Error Scoring System (BESS)
- Computerized Posturography
  - Static: measures COG sway on force plate
  - Dynamic (CDP): Sensory Organization Test; formerly NeuroCom, now Natus

ENT consult

- When to refer
- Vestibular system tests
  - ELECTRO/VIDEO-NYSTAGMOGRAPHY (ENG OR VNG)
    - Target eye movements
    - Head movements
    - Caloric stimulation
  - Rotation tests including computerized chair
  - VIDEO HEAD IMPULSE TESTING (VHIT)
  - VESTIBULAR EVOKED MYOGENIC POTENTIAL (VEMP)

Poll Question #4

Which test is most sensitive for detecting balance deficit?
(select one answer)

A. Tandem Gait
B. Computerized posturography
C. Balance Error Scoring System (BESS)
D. Berg Balance Scale
E. Romberg

Vestibular rehabilitation therapy (VRT)

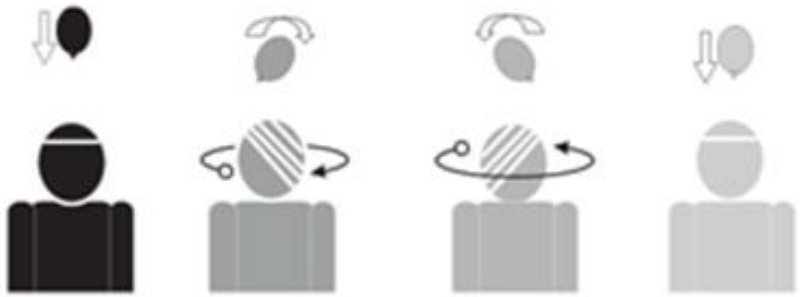
- Form of physical therapy using specialized exercises designed to reduce:
  1) vertigo and dizziness
  2) gaze instability, and/or
  3) imbalance and falls
- Most VRT exercises involve head movement, and head movements are essential in stimulating and retraining the vestibular system.
- Mechanism of action largely compensatory in nature
- three principal methods of exercise can be prescribed:
  1) Habituation
  2) Gaze Stabilization
  3) Balance Training

Habituation Exercises

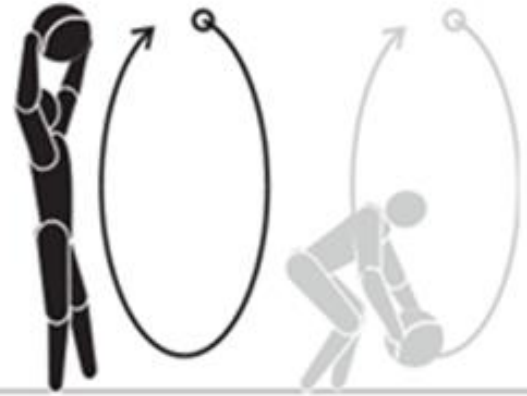
- Best for symptoms of dizziness produced by self-motion and/or visual stimuli
- Not suited for dizziness symptoms that are spontaneous in nature and do not worsen because of head motion or visual stimuli.
- Exercises: Repeated exposure to specific movements or visual stimuli that provoke patients' dizziness (mildly, or at the most moderately, and temporarily)
- Goal: Over time, the brain learns to ignore the abnormal signals

Habituation

Horizontal Head Movements

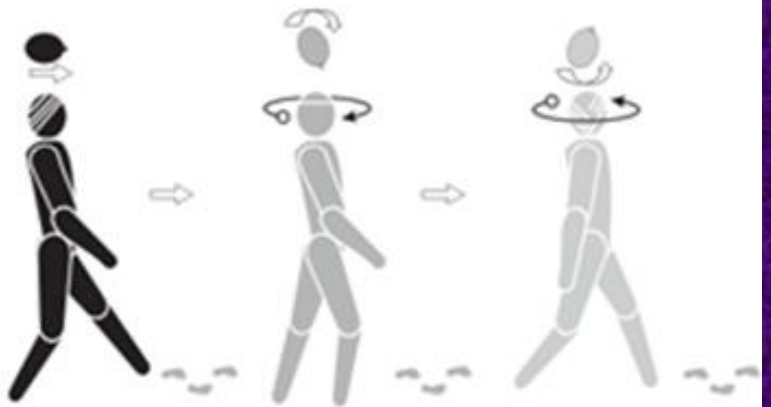


Ball Circles



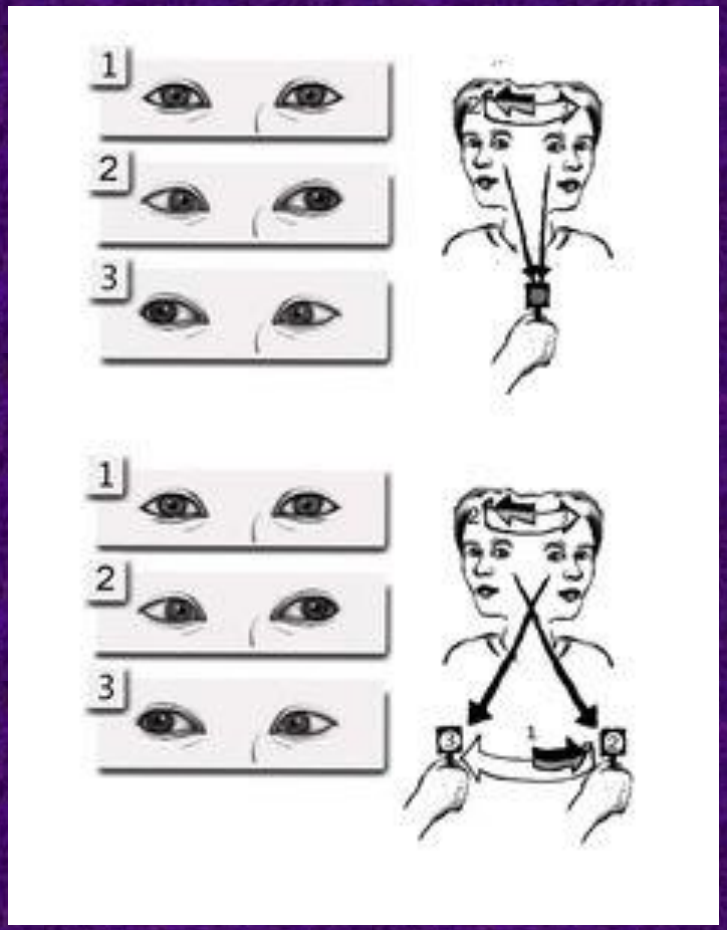
Head Circles

Gait with Head Turns



Gaze Stabilization Exercises

- Goal: improve control of eye movements so vision can be clear during head movement.
- Best for: problems seeing clearly because visual world appears to bounce or jump around
- Exercises types:
  - Fixation exercises: Fixating on an object while repeatedly moving head back and forth or up and down for up to a couple of minutes
  - Gaze shifting and remembered target exercises: designed to use vision and somatosensation (body sense) as substitutes for the damaged vestibular system. Especially useful with poor to no vestibular function


1
2
3
1
2
3


UP
UPPER LEFT
UPPER RIGHT
LATERAL LEFT
CENTRAL FOCUS
LATERAL RIGHT
Forced motion of eye exercises
LOWER LEFT
LOWER RIGHT
DOWN

Balance Training exercises

- Goal: improve steadiness during functional tasks
- Method: Gradually titrate up challenges to balance but safe enough to avoid fall.
- Exercise components:
  - Visual and/or somatosensory cues
  - Stationary positions and dynamic movements
  - Coordinated movement strategies (movements from ankles, hips, or a combination of both)
  - Dual tasks (performing a task while balancing)
  - Functional task specific training

Vestibular rehabilitation for BPPV

- After BPPV has been successfully treated and spinning symptoms resolved, some patients will continue to report non-specific dizziness (symptoms other than spinning) and/or imbalance.

- In these cases, treatment using habituation exercise and/or balance training may be indicated.

Maximizing success from VRT after TBI

- Identify and if found treat BPPV first
- Results of CENC study highlight the importance of:
  - Identify and treat pain generators first
  - Set individualized goals; e.g. higher intellect = higher baseline postural stability
- Potential Barriers:
  - Fluctuating conditions causing spontaneous attacks of dizziness or vertigo
  - Sedentary Lifestyle
  - Medications:
    - Antivert (or similar meds) may suppress brain function and interfere with compensation
    - Psychotropics and antiepileptics may contribute to dizzy symptoms
  - Other medical conditions
  - Emotional disorder
  - Adherence

VRT Adherence

- VRT exercises are not difficult to learn, but to achieve maximum success patients must be committed to doing them.

- Since the exercises can sometimes be tedious, setting up a regular schedule so that the exercises can be incorporated into daily life is very important.

- Exercises may, at first, make symptoms seem worse. But with time and consistent work, symptoms should steadily decrease, making participation in activities of daily life easier.

Poll Question #5

Which is not a component of vestibular rehabilitation therapy?
(select one answer)

A. Habituation exercises
B. Gaze stabilization exercises
C. Antivert
D. Individualized goals
E. Treatment of pain

The End

Questions?