STUDY MEASURES IN DETAIL

Study Measure Acronyms:

AUDIT-C:	Alcohol Use Disorders Test-Consumption
BESS:	Balance Error Scoring System
BETS	Blast Exposure Threshold Survey
BRFSS:	Behavioral Risk Factor Surveillance System
BSIT:	Brief Smell Identification Test
BTACT:	Brief Test of Adult Cognition by Telephone
BVMT-R:	Brief Visuospatial Memory Test-Revised
CAPS-5	Clinician-Administered PTSD Scale for DSM5
CDP:	Computerized Dynamic Posturography
CDR	Clinical Dementia Rating
CRIS:	Community Reintegration of Injured Service Members
CSHQ:	Contact Sports History Questionnaire
CVLT-II:	California Verbal Learning Test
DAST-10:	Drug Abuse Screening Test, 10 item version
D-KEFS VFT:	Delis-Kaplan Executive Function System Verbal Fluency Test
DHI-S:	Dizziness Handicap Inventory, Screening version
D-KEFS:	Delis-Kaplan Executive Function System
DRRI-2:	Deployment Risk and Resiliency Inventory, Version 2
EEG:	Electroencephalography
EQ-5D-5L:	EuroQol Group 5 dimension 5 level
ERP:	Event Related Potentials
EDF:	Epilepsy Documentation Form (medical records)
ESQ:	Epilepsy Screening Questionnaire
GSE:	General Self Efficacy Scale
GOS-E:	Glasgow Outcome Scale - Extended
HHIA-S:	Hearing Handicap Inventory for Adults, Screening version
HIT-6:	Headache Impact Test Short Form
mBIAS:	Mild Brain Injury Atypical Symptoms
MRI:	Magnetic Resonance Imaging
MSVT:	Medical Symptom Validity Test
MTHJEQ:	Military Head Jolt Exposure Questionnaire
TBIQOL:	Quality of Life in Traumatic Brain Injury
NSI:	Neurobehavioral Symptom Inventory
OSU TBI-ID	The Ohio State University Traumatic Brain Injury Identification Method
PCL-5:	PTSD Checklist for DSM-V
PHQ-8:	Patient Health Questionnaire Depression Scale; 8 item version
PHQ-9:	Patient Health Questionnaire Depression Scale; 9 item version
PSQI:	Pittsburg Sleep Quality Index
SCAN-3:	Tests for Auditory Processing Disorders

SWLS:	Satisfaction With Life Scale
TBIMS PIHQ:	TBI Model Systems Pre-Injury History Questionnaire
TFI:	Tinnitus Functional Index
TMT:	Trail Making Test
UPDRS:	Unified Parkinson's Disease Rating Scale
VCU RCDI-B	Virginia Commonwealth University Retrospective Concussion Diagnostic Interview- Blast
VCU RCDI-G	Virginia Commonwealth University Retrospective Concussion Diagnostic Interview - General
WAIS-IV	Wechsler Adult Intelligence Scale 4th Version

1) Independent (Predictor) Variables

mTBI(s), number and severity (see below for indexing) and cause (blast vs. other)

- Potential Concussive Events (PCEs) Mapping Process: modification of The Ohio State University Traumatic Brain Injury Identification Method (OSU TBI-ID)* which is a standardized procedure to elicit the lifetime history of TBI for an individual[29] based on CDC case definitions and recommendations for TBI surveillance (see Appendix A).
- Structured Interview for PCE's using VCU rCDI (see Appendix A for which PCEs)
- DoD injury report information (MACE, PDHA, PDHRA, ANAM): electronic records search.
- Vetting of Interview algorithm and record reviews for final determination on mTBI status of each PCE (see 5.5.2.2 for more detail)
- Date of all historical mTBIs. A detailed "mTBI history profile" for both deployment and non-deployment time periods will be created.

mTBI History Profile

mTBI without PTA or LOC	**mTBI with PTA but no LOC**	**mTBI with LOC (& PTA)**
None	None	None
Single	Single	Single
Multiple, total #	Multiple, total #	Multiple, total #

Personal Fixed Factors

- Demographics, age, highest level of completed education using The CDC Behavioral Risk Factor Surveillance System (BRFSS) [68] core battery, section 8.1-8.4, 8.6-8.8, 8.11-8.12, 8.24-8.25. 5 minutes to administer
- Past health using selected items from TBIMS Pre-injury History Questionnaire (TBIMS PIHQ). 3 minutes to administer. [Baseline only]
- Genotyping: at baseline only, blood will be collected to assay for multiple genetic variants that have been reproducibly associated with chronic effects of neurotrauma including: *APOE, DRD2, COMT, MAO-A, BDNF, DAT1*. Genotyping at other alleles will be carried out as more information becomes available regarding their association with neurodegenerative disorders after TBI, per Biomarkers Core.

Environmental Factors

- Military history and Rehabilitation treatments received using select items from the DVBIC 15 yr study General Assessment Form. 5 minutes to administer
- Combat exposure; Deployment Risk and Resiliency Inventory, Version 2, Section D;Combat Experiences* (DRRI-2-D) is a 17-item self-report measure that assesses wartime stressors experienced by combatants. Respondents are asked to respond based on their exposure to various combat situations. The DRRI was developed to update the CES[31] to include modern wartime experience[Repeated after Baseline only for participants who have been redeployed after baseline data collection.]
- Social support; DRRI-2-Section O, Post-deployment Social Support Scale (DRRI-2-O): this 10-item scale is part of the National Center for PTSD Deployment Risk and Resilience Inventory; Cronbach's alpha on these items was .82.[33] It assesses extent to which family, friends, coworkers, employers, and community provide emotional sustenance (understanding,

companionship, a sense of belonging, and positive self-regard) and instrumental assistance (tangible aid). 4 minutes to test. A shortened version with only relevant items will be used for longitudinal evaluations.

- Compensation and Pension qualified for: VA records
- Other Disability Income: self-report of Social Security, other
- Subconcussive brain insult exposures:
    - Contact Sports History Questionnaire (CSHQ): Self-report measure of organized sports participant history focusing on football, hockey, and boxing as a gauge of exposure to subconcussive athletic head impacts
    - Military Training Head Jolt Exposure Questionnaire (MTHJEQ): Brief self-report measure of military career exposure to activities associated with repetitive subconcussive forces to the head; also queries neurotoxin exposure and PTSD history. Developed by CENC investigators specifically for this study.
    - Blast Exposure Threshold Survey (BETS): brief self report questionnaire developed by the JPC-5 Exposures Standards Working Group to standardize the calculation of lifetime exposure of military personnel to blast overpressure
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Moderating Factors

- Effort & Exaggeration; Medical Symptom Validity Test* (MSVT): The MSVT is a computer-based test of the ability to learn and remember information presented on a computer screen. Result profiles are different for actual severe memory impairment vs. insufficient effort to produce valid test results (feigned impairment). It has very high specificity (close to 100%) in people with dementia, a finding that has been independently replicated in three separate countries.[34] 6 minutes to administer.
- Self-efficacy; The General Self Efficacy (GSE) Scale: This is a 10-item scale of perceived self-efficacy (Schwarzer, 1992).[35] This is the optimistic belief that one can perform novel or difficult tasks, or cope with adversity in various domains of human functioning. Each item refers to successful coping and implies an internal attribution of success. The scale is one-dimensional. 4 minutes to test.
- Resiliency; The TBI-QOL* resilience module: the development of this tool and supportive psychometric data should be completed by the time of project startup.[36] Takes 2 minutes to test.
- PTSD; PTSD Checklist for DSM V* (PCL-5): See below. Longitudinal measure of PTSD symptom severity.
- Alcohol use; Alcohol Use Disorders Test-Consumption* (AUDIT-C), is a brief (3-item) screening tool for heavy drinking or active alcohol abuse/dependency.[37] 1-2 minutes to administer.
- Illicit substances use/misuse; Drug Abuse Screening Test 10 item version (DAST-10): Excellent screening tool for the abuse of drugs other than alcohol. The original 28-item self-report scale has been abbreviated and all versions have satisfactory measures of reliability and validity. The 10-item version takes up to 3 minutes to test.[38]

Comorbidities

- Sleep disorders:

- The Pittsburg Sleep Quality Index (PSQI): The PSQI has 19 individual items which are used to generate scores in seven categories: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction. It takes 5-10 minutes to test. Good sensitivity for sleep disorders.[39]
- The STOP BANG instrument is comprised of eight dichotomous choice items designed to detect the presence of obstructive sleep apnea. Most of the content will be imported from other testing instruments such that the participant will be asked to complete only one unique questionnaire item (<1 minute)[40]

– Depression (PHQ-9); Patient Health Questionnaire Depression Scale* (PHQ-9) [47] the PHQ-9 is a 9-item self-administered tool that is half the length of many other depression measures, has comparable sensitivity and specificity, and consists of the actual nine criteria upon which the diagnosis of DSM-IV depressive disorders is based. This can help track a patient's overall depression severity and the specific symptoms that are improving or not. 5 minutes to test.
– PTSD:
  - PTSD Checklist for DSMV* (PCL-5): The DSM-IV version [41] was updated for DSM-V in 2013 and consists of a 20 item self-report rating of the DSM-V symptoms of PTSD (Weathers, Litz, Keane, Palmieri, Marx, & Schnurr -- National Center for PTSD). 3 min to test.
  - Clinician-Administered PTSD Scale for DSM5 (CAPS-5) is a gold-standard 30-item structured diagnostic interview that can be used to make a current (past month) diagnosis of PTSD, a lifetime diagnosis of PTSD, and assess PTSD symptoms over the past week. Administration time is 30 minutes. (Weathers, F. W., Keane, T. M., & Davidson, J. R. (2001). Clinician-Administered PTSD Scale: A review of the first ten years of research. (PDF) Depression and Anxiety, 13, 132-156. doi: 10.1002/da.1029)
  – Fatigue: TBIQoL module, short-form, 2-4 minutes to administer
  – Anger: TBIQoL module, short-form, 2 minutes to administer

  – Anxiety: TBIQoL module, short-form, 2 minutes to administer
  – General Co-Morbidities: The CDC Behavioral Risk Factor Surveillance System (BRFSS) [68] collects data via telephone interview on six individual-level behavioral health risk factors associated with the leading causes of premature mortality and morbidity among adults: 1) cigarette smoking, 2) alcohol use, 3) physical activity, 4) diet, 5) hypertension, and 6) safety belt use. .Core battery Core Sections 1-3, 5-7, 9,11,and 12. 20 minutes to administer.
  – Biometrics: BMI (height and weight), BP, HR, RR

Abbreviated Battery of Outcome Measures, remotely collected: *Purpose is to briefly assesses the key outcomes in an efficient manner while minimizing costs and subject burden.*

– Will be conducted annually by telephone
– Cognitive Function Performance Tests:
  - Brief Test of Adult Cognition by Telephone* (BTACT): The BTACT assesses dimensions central to adult cognitive functioning: episodic memory, working memory, reasoning, verbal fluency, and executive function without the need for an in-person assessment.[44] This is the first instrument which integrates measures of processing speed, complex reaction time, and task switching and inhibitory control for use over the telephone. The battery was administered to a large (N= 4,706) national sample, aged 32 to 84, from the study of Midlife in the United States (MIDUS) and provides normative data, reliability, and factor structure. The tests parallel the NIH tool-box (see below), alternate forms are available, and

individual tests can sum into combined measure. Administration time is 15-20 min. In addition to the annual telephone administration, the BTACT will also be given by phone within a 2 week time period POST comprehensive assessment.
    - Digit Span Forward from WAIS-IV*: a brief test of verbal-auditory working memory.[45]
  - Cognitive Symptom Scales:
    - TBIQOL* Applied Cognition modules: TBI-QOL is part of a multisite NINDS-funded project that developed a clinically relevant and psychometrically robust health-related quality of life (HRQL) assessment tool for adults and children.[46] Its use will facilitate comparisons of data across clinical trials in different diseases. TBI-QOL incorporates patient reported outcomes of functioning, such as social, psychological, and mental well-being.
    - Applied Cognition - General Concerns module, short form, 2-5 minutes.
    - Applied Cognition - Executive Function module, short form, 2-5 minutes.
  - Emotional-Behavioral Function Symptom Scales
    - Impulsive Control & Emotional Instability & Irritability & Aggression: TBI-QOL* Emotional-Behavioral Dyscontrol module, short form, 2-5 minutes to administer.[46]
    - Depression: eight-item Patient Health Questionnaire Depression Scale* (PHQ-8) (J Affect Disord. 2009 Apr;114(1-3):163-73. doi: 10.1016/j.jad.2008.06.026. Epub 2008 Aug 27. The PHQ-8 as a measure of current depression in the general population. Kroenke K1, Strine TW, Spitzer RL, Williams JB, Berry JT, Mokdad AH). the PHQ-8 is the PHQ-9 without the final item on suicidiality. It was devised to lessen the potential for triggering participant emotional stress when collected in non-face-to-face settings and has been validated in large population studies.
      .
  - Participation/Disability Scale
    - TBI-QOL Abilities to Participate in Social Roles and Activities, short form, 2 minutes.

Comprehensive In-person Outcome Measures Battery

- Collection Schedule – baseline, 1 yr post index mTBI, 3 yrs. post-index mTBI, 5 yrs. Post index mTBI, then every 5 yrs. [self-report questionnaires may be completed prior to visit, reviewed by study staff for completeness and reviewed with subject at visit; alternatively they may be collected remotely, such as over the telephone, if the participant is logisitically unable to come in person to a post-baseline comprehensive visit to achieve partial data collection instead of entirely missed visit].
- Repeat Abbreviated Battery: TBI-QOL Emotional-Behavioral, Applied Cognition, and Social Roles and Activities Short Form modules, and BTACT components not covered in below comprehensive battery.
- Biologic Measures
  - Neuroimaging (Structural & Physiological):
    - *Mock Scanner Training*. To mitigate fear, enhance comfort, and reduce motion artifact participants expressing apprehension or anxiety about scanning will be invited to undergo mock scanner training with guided imagery and relaxation techniques to become desensitized to scanning environment, if this may be helpful for the participant.
    - *Neuroimaging Data Acquisition*. Volumetrics, FLAIR white matter hyper intensity analysis, DTI/DKI, fcMRI, and ASL will be done at comprehensive evaluation time points

to measure changes in white matter integrity, total and regional brain volumes, functional connectivity changes, and alterations in perfusion. The Neuroimaging Core SOPs details the imaging protocol proposed for Project 1. The clinical sequences, volumetric, and fcMRI data are based on CDEs and thought to generally be robust to differences induced by use of magnets of different manufacture, model, and field strength; so data from these modalities will be used from across sites, with careful attention to systematic and site-specific differences. Given the difficulties that using different scanner manufacturers introduces in terms of compatibility of quantitative results for DTI and ASL,[49] DTI and ASL data collected will be used either via longitudinal analysis methods where the quantitative values have less impact, or when combined with data acquired at other sites, using only data that is acquired using very similar acquisition parameters and scanner manufacture/model.

- The imaging will be performed at the MEDVAMC, SAMMC, and Richmond (VCU) using comparable Siemens 3T scanners, and at Tampa VA using a GE 3T scanner. Sequence parameters will be adjusted for the GE scanner in Tampa and the Philips scanner at VCU, but T1-weighted, FLAIR, and fcMRI parameters will be adapted from existing ADNI parameters for this scanner. In addition, similar phantoms are used with each to assess data quality and equivalency (see Neuroimaging Core for details). The scanning parameters are detailed in the Neuroimaging Core SOPs. Briefly, sequences will include an axial resting state echo planar imaging (EPI) sequence for fcMRI analysis, a high-resolution sagittal T1-weighted for volumetric analysis, a 66-direction axial diffusion sequence for DTI and DKI, an axial ASL sequence for perfusion, an axial T2-weighted (fast field echo) for clinical reading and CDE coding (e.g., lesion analysis, detection of blood), and an axial FLAIR for detection of white matter hyperintensities, clinical reading, and CDE coding (e.g., lesion analysis, detection of gliosis). The specific protocol sequence that each participant will undergo is as follows:
  1) Localizer
  1a) Calibration/Reference Scan
  2) Sagittal 3D T1 MPRAGE/IR-SPGR
  3) Axial 3D T2* GRE/SWAN/SWI
  4) Axial DTI
  5) Axial Resting State fMRI - Subjects should have eyes OPEN.
  6) Axial 3D T2-FLAIR (CUBE/SPACE/VISTA)
  7) Sagittal 3D T2 (CUBE/SPACE/VISTA)
  8) Axial ASL
  9) HDFT protocol (SAMMC and MEDVAMC only)
  All scans are performed in straight orthogonal planes -- ***No manual adjustments should be made to this protocol***

- *Primary Imaging Variables.* Numerous variables are generated from acquisition and analysis and will be readily available for specific exploratory analysis at little additional effort. However, to reduce the number of variables and analyses for the primary aims of the grant, the following measures will be used
    - Volumetrics (volume in cubic millimeters): Total frontal gray matter and white matter (GM, WM), total temporal GM/WM, total parietal GM/WM, right and left cingulate GM/WM, right and left hippocampus and amygdala, right and left

caudate, right and left thalamus, right and left cerebellum GM/WM, total GM, total WM, ventricle-to-brain-ratio.

- DTI tractography (fractional anisotropy [FA] and mean diffusivity [MD]: right and left cingulum bundles, fornix, total corpus callosum, uncinate fasciculus, ventral striatum, anterior thalamic radiation.
- FLAIR white matter hyperintensity analysis: total lesion volume and count, anterior cerebral middle cerebral, posterior cerebral, and vertebral basilar system (feeding brainstem and cerebellum) vascular territories
- ASL cerebral blood flow (CBF) in the same vascular territories as detailed above as well as whole brain GM and WM CBF, and CBF of the thalamus and posterior cingulate
- fcMRI connectivity changes in seedpoints involving anterior cingulate cortex, lateral prefrontal cortex, default mode network, posterior cingulate cortex, and hippocampus.
- Common Data Elements: presence or absence of potentially clinically relevant pathology.

– Biologic Fluids: At comprehensive time points, biologic fluids will be collected for neuroendocrine screening, evaluation, and collected and processed for CENC BioRepository biomarker and genetic analyses. Biospecimens collected include whole blood, saliva, and at some sites, urine (for Pregnancy testing prior to MRI). In general, the following should be collected:

- Blood for Commercial Lab Neuroendocrine Panel (NO Biorepository specimen collction, shipping or storage):
    - Blood (serum (red top tube) for insulin-like growth factor 1 (IGF-1), thyroid stimulating hormone (TSH) and testosterone) collected for neuroendocrine assays will be sent separately to Quest after local processing and freezing.
- Blood and Saliva for the CENC BioRepository: serum, plasma, buffy coat (baseline visit only) and PAXgene™ RNA tubes, saliva for cortisol (processed and frozen locally and shipped in batch to the Biorepository for long-term storage and distribution for research)
    - The blood collected for the CENC BR will be processed into plasma, serum and buffy coat fractions, aliquotted, frozen at the study site and then shipped to the CENC BR.
    - Frozen samples are to be submitted at least quarterly. In general, the following volumes must be submitted to the CENC Repository for each sample type:
        - Plasma/Serum (purple/red top tubes): minimum 6 milliliters (ml) each
        - PAXgene™ tube (for RNA): minimum 2.5 ml
- *Some sites* - Urine: depending on local MRI policies procedures, sites may obtain specimen solely for pregnancy testing in premenapausal females to confirm nongravida status. Specimens are teststed locally and destroyed after testing. No urine specimens are collected, processed or stored in the CENC Biorepository.

– Physiological
    - Clinical Seizures:

- *EEG sites only:*: At baseline and at comprehensive follow-up points, participants will undergo wakeful EEG testing per the standard paradigm used in the VA Epilepsy Centers of Excellence (CoE) clinical protocol.
- *All Sites*: At baseline assessment and at all follow-up points, all participants will complete the "Epilepsy Screening Questionnaire" (ESQ). Those participants screening positive will be referred to their respective Epilepsy CoE for clinical evaluation.
- *All sites*: at baseline and comprehensive follow-up points study staff will use medical record review to complete an Epilepsy Documentation Form (EDM).

▪ *EEG sites only* –

- 10 minutes of resting EEG will be collected for Quantitative EEG (QEEG) analyses
- Electrophysiology of Cognition: Event Related Potentials (ERP): Computerized behavioral tasks will be performed during EEG recording to generate ERPs. Tasks will include both auditory and visual modalities of the "oddball task" and a semantic priming task.

• The oddball task will consist of detection of a target image or sound within a pseudo randomly ordered series of targets, nontarget distracters, and nontarget standards. This task will be used to generate sensory potentials (P50, N100) and the cognitive P300 (P3a and P3b).[50] Amplitudes and latencies of the P50, N100, and the P3a at the frontal midline electrode site and the P3b at the parietal midline site will be the outcome measures.

• To generate the semantic and episodic memory potentials N400 and P600, a semantic categorization task after Olichney[51] will be used. Subjects will hear a category name (e.g., furniture) and then read a word presented on a computer monitor and decide whether the word fits in the category (chair: congruent; eagle: incongruent). Subjects will press a button on the same button pad described above to indicate their choice. Amplitudes of the N400 (site Cz; central midline) and P600 (Pz; parietal midline) in response to target words and the attenuation of both potentials due to target repetition will be the outcome measures.

- Body Function Performance Measures
  - Emerging State-of-Art Neuropsychological Cognitive Performance Tests

    NIH Toolbox Cognition Battery*: The NIH Toolbox is a recently developed comprehensive assessment tool with an emphasis on measuring outcomes in longitudinal epidemiologic studies and prevention or intervention trials across the lifespan.[9] The cognition battery is a brief and efficient computer-based neuropsychological test of the seven key cognitive domains: Executive Function, Episodic Memory, Working Memory, Processing Speed, Language, Attention and Reading. The Oral Reading subtest will not be administered to reduce subject burden. The battery requires only 20-30 minutes to administer.
  - Historical Neuropsychological Cognitive Performance Tests

    Wechsler Adult Intelligence Scale 4th version* (WAIS-IV): working memory index (Digit Span, Letter-Number Sequencing), processing speed index (Symbol Search, Coding), and Visual Puzzles. The WAIS-IV is one of the most established and commonly used instruments for the assessment of IQ.[45] Administration time for these WAIS-IV subtests is about 20 minutes.

Trail Making Test* (TMT) Part A&B: the TMT is a test of visual attention and task switching.[52] The TMT requires visuomotor integration while engaging in concurrent mental manipulation of numbers and letters and thus provides a measure of executive control. It can provide information about visual search speed, scanning, speed of processing, mental flexibility, and executive functioning. It is also sensitive to detecting several cognitive impairments such as AD and dementia. The test requires 2-10 minutes, depending on degree of impairment.

California Verbal Learning Test* (CVLT-II). [53, 54] CVLT-II evaluates a wide diversity of cognitive functions: verbal learning and memory, including retroactive and proactive interference, retention, encoding versus retrieval, and subjective organization.[include citation here] Clients are given a list of 16 words repeated over 5 different trials and are asked to repeat. A distracter list of 16 words is given and the client must again repeat the original list of 16 words and then again after 20 minutes. Approximately 10 to 15 minutes is required (not including 20 min. interval).

Brief Visuospatial Memory Test-Revised* (BVMT-R). The BVMT-R is a measure of immediate and delayed visual memory.[55] The test requires 10 minutes to administer

Delis-Kaplan Executive Function System (D-KEFS) Verbal Fluency Test* (VFT). The VFT is composed of three conditions: Letter Fluency (aka the Controlled Oral Word Association Test), Category Fluency, and Category Switching. It measures an individual's ability to generate words fluently in an effortful, phonemic format, from overlearned concepts, while simultaneously shifting between these concepts. 6 minutes to administer.[56]

- Motor/Movement Performance Tests:
  - Fine motor; Grooved Pegboard*: The Grooved Pegboard assesses fine-motor speed and dexterity.[184] It requires approximately 5 minutes to administer.
  - Gait; NIH Toolbox 4-Meter Walk Gait Speed Test: This test is adapted from the 4-meter walk test in the Short Physical Performance Battery.[9] Participants are asked to walk 4 meters at their usual pace and the time in seconds is measured during each of two trials, with the better trial used for scoring. 3 minutes to administer (including instructions and practice).
  - Motor Examination Index from Unified Parkinson's Disease Rating Scale (UPDRS): UPDRS is a structured physical examination with Likert scale scoring of 14 possible Parkinson type motor impairments.[58] 10 minutes to complete.
  - Visual Motor system:
    - Anti-saccade test in Examiner Battery, Boxer, motor inhibition.[59] This is an eye movement task using three blocks of trials in which subjects look at a fixation point in the center of a computer screen and move their eyes upon presentation of a laterally presented stimulus. In the first block (pro-saccade), subjects are instructed to move their eyes in the direction of the presented stimulus. In the second and third blocks (anti-saccade), subjects are instructed to move their eyes in the opposite direction of the presented stimulus and so must suppress the reflexive urge to look at a visual target. 5 minutes to test. [Note: this test will be discontinued once programmed into the computerized oculomotor test; see below]
- Computerized oculomotor (eye tracking) test: Eye tracking allows objective measurement of eye position in response to specific visual target movement. This non-invasive test measures basic horizontal and vertical eye movement and pupillary and accommodative response dynamics.Types of eye movements measured include fixational, saccadic, and smooth pursuit movements. Administration time is 10 minutes.Sensory Systems Performance Tests:

- Smell: BRIEF Smell Identification Test (BSIT)-12 item smell test to detect smell loss quickly. Odors are well-known in most cultures. The test employs: banana, chocolate, cinnamon, gasoline, lemon, onion, paint thinner, pineapple, rose, soap, smoke and turpentine. Time: 5 minutes.[61] [Sensonics, Inc.Haddon Heights, NJ 08035];
- Hearing (note Portland site differs with specialized audiology protocol):
  - Audiometry (includes air and bone conduction) testing for hearing thresholds
  - SCAN-3. This test is comprised of a battery of tests to detect auditory processing disorders in adolescents and adults. Results can help identify the presence of a temporal processing problem, can test the ability to listen with background noise, and provides a dichotic listening task. Time: 10-15 minutes[62]
- ual Acuity a standard eye chart will be used to measure monocular aacuity.

- Postural Stability as Motor-Sensory (Vestibular, Visual, & Proprioception) Integration Performance Test:

  CDP sites only- Computerized Dynamic Posturography (CDP): Postural stability will be assessed using a dual-plate force platform, the NeuroCom Smart Balance Master(r) (NeuroCom; NeuroCom International, Inc., Clackamas, OR). The Sensory Organization Test (SOT) of the CDPT is a composite index that defines abnormalities across somatosensory, visual, and vestibular systems.[63] 30 min to test.

  Sites not doing CDP– Balance Error Scoring System (BESS): standardized measure of assessing static postural stability on a firm and foam surface. The BESS has moderate to good reliability to assess static balance and correlates with other measures of balance using testing devices.[64]

- Sensory Systems Symptom Measures including pain
  - Hearing; Hearing Handicap Inventory for Adults, Screening version (HHIA-S): The HHIA is well-studied and widely used self-report measure of the respondent's perceived hearing difficulty.[65] The 10-item screening version is composed of two subscales (emotional and situational). 3 minutes to test.
  - Tinnitus; TinnitusFunctional Index (TFI): The TFI is a validated self-reporting test instrument that is comprehensive, easy to administer and provides a standardized measure of the patient's perceived tinnitus severity.[66] The 25-item questionnaire consists of eight factor subscales of tinnitus severity and negative impact. 5 minutes to administer.
  - Dizziness; Dizziness Handicap Inventory, Screening version (DHI-S): The DHI is a validated measure of the respondent's perceived handicap as a result of dizziness.[67] The 10-item short version assesses physical, occupational, and emotional effects of the dizziness symptoms. 3 minutes to administer.
  - Headache; Headache Impact Test Short Form (HIT-6): The HIT-6 is a short-form questionnaire with six questions that cover pain severity, loss of work and recreational activities, tiredness, mood alterations and cognition. Each question is scored on a five-point scale, with a maximum total of 30 points. The HIT-6 is reliable and valid measure for headache (HA) severity and HA related disability across different diagnostic groups of HA.[43] 3 minutes to administer.
  - Body Pain; NIH Toolbox (PROMIS version) Pain Intensity Numerical 0-10 scale: the patient rates the overall intensity of pain on a numerical scale (0 to 10) for over the past 7 days.
  - Body Pain; TBIQol Pain Interference module, short form: 2-5 minutes to administer.

Participation, Activity, and Global Outcome Rating Scales

- Post-concussion Syndrome symptom severity; Neurobehavioral Symptom Inventory* (NSI): The NSI is a 21-item assessment of post-concussive symptoms with a 3-factor structure (somatic/sensory, affective, and cognitive).[69] To be compatible with merging the mBIAS into a single, the NSI Likert response item numeric values presented on the form will be shifted up one level such that 1=0,2=1,3=2,4=3,5=4.
- Global Outcome; Extended Glasgow Outcome Scale - Extended* (GOS-E): To improve responsiveness the GOS-E refines the original GOS from 5 to 8 categories. It also contains a structured interview mechanism to improve reliability within the rating system. It has been shown to have increased sensitivity with mild to moderate cases of traumatic brain injury.[70] 5 minutes to administer. It can be administered to either the participant or, if the participant assents, to an informant (significant other, family member, or close friend). Health Care Utilization and Costs:
  - Health Care Utilization Questionnaire developed from literature: Quantitative measures of self- and informant-reported usage of seven domains of medical (hospitalization, outpatient treatment and procedures, assistive devices, and medications) and nonmedical care (home health aides, respite care, and adult day care).[71, 72] Time to test 5-15 minutes.
- Documented utilization and costs: The VA Informatics and Computing Infrastructure (VINCI) resource center, which facilitates access to data from the Veterans Information System Technology Architecture (VistA), and additional relevant data sets will be used to acquire all data relevant to the health economics analyses. Given the longitudinal design of this study, updated data will be requested and acquired on an annual basis for reach subject.
- Economic Impact; EuroQol Group 5 dimension 5 level version quality of life questionnaire* (EQ-5D-5L) is a standardized measure of 5 dimensions of health status (mobility, self-care, usual activities, pain/discomfort, anxiety/depression).[73] Applicable to a wide range of health conditions and treatments, it provides a simple descriptive profile and a single index value for health status. 2-3 minutes to test.
- Participation; TBI-QOL module (annual; see above). Also, select items from The Community Reintegration of Injured Service Members (CRIS)[48] ; a validated instrument using OIF/OEF cohorts and consists of three scales measuring extent of, perceived limitations in and satisfaction with community reintegration. Select items from the extent of participation scales will be used (scale 1, item 1 & 13, scale 2, item 2 & 9; scale 3, item 7, 8, & 10; scale 4 items 14 & 16). Total time about 2 minutes.
- Employment; TBI-MS follow-up form Modified Abbreviated Employment Module. 1-5 minutes to administer.
- Life Satisfaction; Satisfaction With Life Scale* (SWLS): The SWLS is a validated 5 question self-report global measure of satisfaction with one's life.[74] Life satisfaction is one factor in the more general construct of subjective well-being. It is distinguished from affective appraisal in that it is more cognitively than emotionally driven. Administration time is 1-3 minutes.

Dementia Assessment

- Clinical Dementia Rating (CDR): this is a 'gold standard' research measure of clinical dementia, a critical study outcome (Morris JC. The Clinical Dementia Rating (CDR): current version and scoring rules. Neurology. 1993;43(11):2412–2414). It is a structured interview

administered to an informant (significant other, family member, or close friend) indentified by and with the consent of the participant. Administration time is 15-20 minutes.

2) Longitudinal Cohort Study Schedule of Evaluations

	2 Day Baseline Visit	Comprehensive Assessment Anniversary Year 1 (of Index Date)	Telephone Interview Year 2	Comprehensive Assessment Year 3	Telephone Interview Year 4	Comprehensive Assessment Year 5[1]	Telephone Interview Years 6-9	Comprehensive Assessment Year 10	Telephone Interview Years 11-14	Comprehensive Assessment Year 15
Informed Consent	X									
MRI	X	X		X		X		X		X
Blood Collection[8]	X	X		X		X		X		X
Saliva Collection	X	X		X		X		X		X
Urine Pregnancy[1]	X	X		X		X		X		X
Vital Signs										
BP	X	X		X		X		X		X
HR	X	X		X		X		X		X
RR	X	X		X		X		X		X
WT	X	X		X		X		X		X
HT	X									
PCE mapping	X	X		X		X		X		X
VCU rCDI[2]	X	PRN		PRN		PRN		PRN		PRN
Electronic Medical Records Search	X									
Establish Index Date	X									
TBIMS PIHQ[9]	X									
Military HX & Rehab treatments (MHMSDVBIC)[9]	X									
EEG[3] and ERP[3]	X	X		X		X		X		X
ESQ baseline	X									
ESQ follow-up		X	X	X	X	X	X	X	X	X
EDF	X	X		X		X		X		X
ERP[3]	X	X		X		X		X		X
AUDIT-C	X	X		X		X		X		X
BESS[4]	X	X		X		X		X		X
BETS	X	PRN		PRN		PRN		PRN		PRN
BRFSS	X	X		X		X		X		X
BSIT	X	X		X		X		X		X
BTACT	X[7]	X[7]	X	X[7]	X	X[7]	X	X[7]	X	X[7]
BVMT-R	X	X		X		X		X		X
CAPS-5	X	X		X		X		X		X

	2 Day Baseline Visit	Comprehensive Assessment Anniversary Year 1 (of Index Date)	Telephone Interview Year 2	Comprehensive Assessment Year 3	Telephone Interview Year 4	Comprehensive Assessment Year 5[1]	Telephone Interview Years 6-9	Comprehensive Assessment Year 10	Telephone Interview Years 11-14	Comprehensive Assessment Year 15
CDP[4]	X	X		X		X		X		X
CDR	X	X		X		X		X		X
DAST-10	X	X		X		X		X		X
CVLT-II	X	X		X		X		X		X
DHI-S	X	X		X		X		X		X
DRRI-2-D[6]	X	PRN		PRN		PRN		PRN		PRN
D-KEFS VFT	X	X		X		X		X		X
EQ-5D-5L	X	X		X		X		X		X
GSE	X	X		X		X		X		X
GOS-E	X	X		X		X		X		X
Grooved Pegboard	X	X		X		X		X		X
HHIA-S	X	X		X		X		X		X
HIT-6	X	X		X		X		X		X
Healthcare Utilization Questionnaire	X	X		X		X		X		X
mBIAS	X	X		X		X		X		X
MSVT	X	X		X		X		X		X
MTHJEQ[10]	X	PRN		PRN		PRN		PRN		
TBIQOL Applied Cognition, Cognition & Emo-Behav Dyscontrol & Social Roles and Activities	X	X	X	X	X	X	X	X	X	X
TBI QoL other modules Resilience, Anger, Fatigue, Pain & Anxiety	X	X		X		X		X		X
NIH Toolbox battery	X	X		X		X		X		X
NSI	X	X		X		X		X		X
PCL-5	X	X		X		X		X		X
DRRI-2-O	X	X		X		X		X		X
PHQ-88			X		X		X		X	
PHQ-9	X	X		X		X		X		X
PSQI + 1 STOP-BANG item	X	X		X		X		X		X

Audiometry	X	X		X		X		X		X
SCAN-3	X	X		X		X		X		X
SWLS	X	X		X		X		X		X
TBI-MS Abbreviated Employment Module	X	X		X		X		X		X
TFI	X	X		X		X		X		X
TMT A&B	X	X		X		X		X		X
UPDRS	X	X		X		X		X		X
Anti-Saccade	X	X		X		X		X		X
RightEye	X	X		X		X		X		X
VINCI accessable health-care utilization and cost data pull	X	X	X	X	X	X	X	X	X	X
WAIS-IV Digit Span Forward	X	X	X	X	X	X	X	X	X	X
WAIS-IV Letter-Number Sequencing, Symbol Search, Coding, Visual Puzzles	X	X		X		X		X		X
AEs/unanticipated problem collection	X	X	X	X	X	X	X	X	X	X
Medications	X	X		X		X		X		X
CPRS review for disabilities	X	X		X		X		X		X
CRIS	X	X		X		X		X		X
Demographics[9]	X	X		X		X		X		X
Deviation Report	PRN	PRN	PRN	PRN	PRN	PRN	PRN	PRN	PRN	PRN
Eligibility Assessment	X									
End of Study		PRN	PRN	PRN	PRN	PRN	PRN	PRN	PRN	PRN
Healthcare Utilization	X	X		X		X		X		X
Completion/Reliability Codes	X	X		X		X		X		X
Visual Acuity Test	X	X		X		X		X		X

Walk Test (separated from NIH Toolbox battery)	X	X		X		X		X		X
Contact Sports History Questionnaire (CSHQ) [9, 10]	X	PRN		PRN		PRN		PRN		PRN

[1]Females only at some sites; prior to MRI per local policies and procedures
[2]Repeated only if PCE mapping is positive
[3]EEG sites only
[4]CDP sites only
[5] Not all sites
[6]Administered after screening only for subjects who are redeployed
[7]BTACT: call cener will administer within 2 weeks AFTER the in-person comprehensive assessment (specifically, completion of CVLT and KEFS), but not on same day.
[8] Genotype is only collected at baseline. Other blood collections continue at all in-person comprehensive assessments
[9] A subset of questions will continue at all in-person comprehensive assessments
[10] Complete full questionnaire at baseline. If not completed at baseline it may be completed at a comprehensive in-person index assessment. For CSHQ: Full assessment will be repeated only if there is continued participation in organized sport.