

Supplementary Data

Medical History	2
Pathologic Diagnosis of Chronic Traumatic Encephalopathy	2
Pathologic Diagnosis of Alzheimer's disease	2
Neuropsychiatric Inventory Questionnaire	3
eTable 1: Neuropathological Syndromes Routinely Examined	3
eTable 2: Motor Symptoms and Unified Parkinson's Disease Rating Scale (UPDRS) Motor Exam Calculation for Subscores	3

Medical History

ADRC participants, including a study partner when available, were interviewed by ADRC clinicians to acquire a general medical history. The following medical co-morbidities were examined: traumatic brain injury (TBI) with loss of consciousness (LOC), substance use disorders (alcohol and drugs), vitamin B12 deficiency, seizures, myocardial infarction, atrial fibrillation, angioplasty, cardiac bypass, congestive heart failure, stroke, hypertension, hypercholesterolemia, and diabetes. Information about TBI without LOC or multiple injuries was unavailable for subjects in the dataset. TBI data were coded as absent, recent/active (occurring within 1 year of visit or currently requiring treatment), or remote/inactive (occurring >1 year of visit and not currently receiving treatment) and were compared between the groups.

Pathologic Diagnosis of Chronic Traumatic Encephalopathy

Neuropathological diagnosis of CTE was defined by the following criteria 1) perivascular foci of p-tau immunoreactive astrocytic tangles and neurofibrillary tangles, 2) irregular cortical distribution of p-tau immunoreactive neurofibrillary tangles and astrocytic tangles with a predilection for the depth of cerebral sulci, 3) clusters of subpial and periventricular astrocytic tangles in the cerebral cortex, diencephalon, basal ganglia and brainstem, and 4) neurofibrillary tangles in the cerebral cortex located preferentially in the superficial layers. Tissue sampling procedures followed the standard protocols used for identifying tau-related AD pathology for Alzheimer Disease Research Centers set forth by the NIA-AA in 2012 (Montine et al., 2012). This approach involves a sampling of sections considered to be the most valuable in detecting CTE as outlined by the NINDS/NIBIB consensus panel in 2016, which are the superior/middle frontal gyrus, superior/middle temporal gyrus, and inferior parietal gyrus.

Pathologic Diagnosis of Alzheimer's disease

NIA-AA criteria for a neuropathological diagnosis of AD uses Thal amyloid-beta immunopositivity stages, Braak neurofibrillary tangle stages, and CERAD neuritic plaque scores to determine the distribution pattern and extent of deposition of neurofibrillary tangles and neuritic plaques, the hallmarks of AD. Thal stages reflect the anatomical location of amyloid-beta immunopositivity, not density. Thal Phase 0 reflects an absence of amyloid-beta within the brain, one or more amyloid-beta plaques anywhere within the brain reflects Phase 1, accumulation additionally seen within the hippocampus reflects Phase 2, accumulation seen also within the basal forebrain reflects Phase 3, accumulation additionally within the midbrain reflects Phase 4, accumulation also found within the cerebellum reflects the highest stage, Phase 5. Braak stages I-II reflect deposition of neurofibrillary tangles in the transentorhinal region, III-IV in the limbic and hippocampal regions, and V-VI diffusely through the neocortex. The CERAD score reflects the density of neuritic plaques, which consist of argyrophilic dystrophic neurites with and without amyloid cores, in select neocortical regions including midfrontal, superior middle temporal, and inferior parietal areas. For example, diffuse plaques without

neuritic plaques would be given a score of *C0*. One to five neuritic plaques per 1mm² of tissue, reflecting *sparse neuritic plaques*, would have a score of *C1*. More than 5 but less than 20 neuritic plaques per 1mm² of tissue, reflecting *moderate neuritic plaques*, would have a score of *C2*. When there are 20 or more neuritic plaques per 1mm² of tissue, reflecting *frequent neuritic plaques*, a score of *C3* would be rated. The combination of Thal, Braak, and CERAD scores is used to infer whether AD-related pathology explains the presence of dementia symptoms, and NIA-AA 2012 criteria require Thal Phase ≥ 1 and Braak stages III-VI with *moderate/frequent* CERAD plaque scores (C2-C3) to be an intermediate to high likelihood that AD neuropathologic change is significant.

Neuropsychiatric Inventory Questionnaire

Content assessed by the Neuropsychiatric Inventory Questionnaire includes delusions, hallucinations, agitation, dysphoria, anxiety, euphoria, apathy, disinhibition, and irritability. Symptoms were rated by a study partner as being absent or present within the past month, and if present, 1 = mild, 2 = moderate, or 3 = severe.

eTable 1: Neuropathological Syndromes Routinely Examined

Alzheimer's disease	Demyelinating disease
Lewy body disease	Cerebral amyloid angiopathy
Multiple systems atrophy	Hippocampal sclerosis
Pick's disease	Neoplasms
Corticobasal degeneration	Brain injury contusion
Argyrophilic Grain Disease	Arteriosclerosis
Motor neuron disease	Leukodystrophy
Prion disease	

eTable 2: Motor Symptoms and Unified Parkinson's Disease Rating Scale (UPDRS) Motor Exam Calculation for Subscores

hypophonia/slurred speech: item 1 rated as being 1,2, or 3 on the UPDRS, indicating abnormal speech volume or production
Facial expression: item 2 rated at being ≥ 2 , indicating at least mild impairment in facial expression.
Tremor: at least one item from 3a, 3b, 3c, 3d, 3e, 4a, or 4b rated as ≥ 2 , indicating at least mild impairment from a tremor.
Rigidity: at least one item from 5a, 5b, 5c, 5d, or 5e rated as ≥ 2 , indicating at least mild impairment from rigidity.

Hand movement abnormality: at least one item from 6a, 6b, 7a, 7b, 8a, or 8b rated as ≥ 2 , indicating at least mild impairment in hand movements.

Leg agility abnormality: items 9a or 9b rated as ≥ 2 , indicating at least mild impairment in leg movements.

Arising abnormality: item 10 rated as being ≥ 2 , indicating at least mild impairment in arising from chair.

Postural abnormality: item 11 or 13 rated as being ≥ 2 , indicating at least mild impairment in posture (abnormally stooped posture or postural stability).

Bradykinesia = item 14 rates as being ≥ 2 , indicating at least mild impairment in slowness of movements.