The Interaction Between Race/Ethnicity and Traumatic Brain Injury on Alzheimer's Disease Risk in Late Life

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Abstract

Traumatic Brain Injury (TBI) has been identified as a risk factor for Alzheimer's Disease (AD) in late life. Research has shown that older adults with a history of TBI display more severe AD biomarkers and neurodegeneration patterns relative to those without a history of TBI. Non-Hispanic Black (NHB) and Hispanic/Latino (H/L) older adults are at increased risk of developing AD and are also more likely to experience worse health outcomes after experiencing TBI. However, research exploring whether TBI history is a fundamental factor underlying this increased risk for AD among racially/ethnically diverse older adults has not yet been completed. It has been well established that NHB and H/L community members face many challenges and disadvantages in their access to healthcare and treatment, and these ethnoracial groups are more likely to be exposed to poorly resourced environments and stressors that negatively impact long-term health outcomes. This study utilized data from the Health and Aging Brain Study — Health Disparities (HABS-HD) to investigate whether the association between TBI history and AD risk (assessed via AD plasma biomarker levels and cognitive z-score composites) differ across race/ethnicity. Results revealed that NHB older adults with a TBI history exhibited significantly higher AD risk (worse plasma amyloid-β 42/40 levels) than their NHW and H/L counterparts. No differential associations between TBI history and AD risk between NHW and HL adults were observed. These findings indicated that NHB older adults who have experienced a TBI experience elevated AD risk and may benefit from targeted interventions centered on reducing amyloid levels in an effort to prevent disease progression.

Introduction

Alzheimer's disease (AD) is the most common cause of dementia in adults aged 65 and older, and is associated with cognitive impairments (i.e., the ability to think, remember, or make decisions) that negatively impact everyday functioning. AD presents a significant global-health problem, as international and domestic estimates indicate that a greater proportion of the population will be above the age of 65 in coming decades (see He et al., 2016 for an international review; Vespa et al., 2018). As a result of the evolving age demographics of the population, the burden of AD in the United States is expected to double by 2060. These changes will negatively affect both domestic (American) and international economies (see Xu et al., 2017 for an international and regional review). The Alzheimer's Association reports that nearly $340 billion worth of care is provided by unpaid caregivers and that costs of managing and treating AD in the U.S. will exceed $345 billion in 2023. The broader impacts of AD include negative effects on family units and caregivers (a relative caring for someone with AD), which may understandably lead to elevated risk of depression, anxiety, and financial stress associated with managing their caregiving duties (Alzheimer's Disease Facts and Figures, n.d.).

The clinical symptoms Alzheimer's Disease (AD) are caused by the accumulation of amyloid plaques and tau tangles (amyloid and tau) in the brain and treatments for AD are currently severely limited (Joe & Ringman, 2019). Significant efforts have been placed on identifying factors that may ultimately prevent AD. There is growing recognition that a wide variety of genetic (e.g., carrying the APOE4 gene), environmental (e.g., chronic pollutant exposure), and lifestyle factors (e.g., chronic smoking) contribute to the development of AD. In recent years, several studies have identified that traumatic brain injury (TBI) is an important environmental risk factor for AD (see Zhang et al., 2021 for a review)**.** A TBI may occur within

the context of physical or blunt-force trauma to a person's head and can result in an alteration of consciousness (AOC), loss of consciousness (LOC), or post traumatic amnesia (PTA) (Galgano et al., 2017). The injury may also cause post-concussive symptoms including dizziness, confusion, blurred vision, or tinnitus. There are three identified levels of TBI severity: mild, moderate, and severe – the distinction between the three is made based on the LOC, AOC, and PTA duration. Moderate and severe TBI have been supported as well-established AD risk factors, with a dose-response effect between injury severity and AD risk (Masel & DeWitt, 2010). The link between mild TBI and AD remains more debatable, and current AD research is more focused on determining whether repeated mild TBI (rmTBI) and/or singular mild TBI (mTBI) should also be considered AD risk factors.

Further complicating matters, current research has not identified whether the negative effects of TBI on AD risk differ across racial/ethnic groups. Racially/ethnically diverse populations experience elevated rates of health-harming factors (i.e., chronic stress/allostatic load, inadequate access to healthcare, poverty, etc.) (Burris & Hacker, 2017). These groups are also more likely to experience worse TBI health outcomes, they are less often discharged to rehabilitation, and the quality of such rehabilitation is often worse (see Dismuke et al., 2015 for a review; Meagher et al., 2015). Considering these factors, this study sought to explore whether TBI would differentially impact racially/ethnically diverse populations such that they would experience elevated AD risk compared to their Non-Hispanic White counterparts.

Mechanisms linking TBI to AD

As stated previously, AD is identified as a unique type of dementia due to the biomarkers that are associated with it – amyloid plaques and tau tangles. RmTBI has been shown to increase amyloid and tau accumulation similar to AD pathology in animals, and many studies show that

acute TBI events (which commonly occur in sports and the military) can increase amyloid, though identifying rmTBI as an AD risk factor is still a complex issue (see Edwards et al., 2017 for a review). TBI has been associated with increased levels of amyloid, tau, and glial fibrillary acidic protein (GFAP) – another potential biomarker of AD risk – in blood plasma levels (Bogoslovsky et al., 2017; Chatterjee et al., 2021). TBI-induced neurovascular injuries accelerate amyloid β (Aβ) production, tau hyperphosphorylation and tau/Aβ-induced blood brain barrier damage (see Ramos-Cejudo et al., 2018 for a review). The complex connections between TBI and AD biomarkers qualified those biomarkers as adequate indicators of TBI induced AD risk for this study.

TBI has also been independently linked to cognitive impairment. Cognition, or cognitive function, is generally defined as an individual's ability to complete mental operations (e.g. perceiving, learning, remembering, understanding, etc.). Studies show that mild, moderate, and severe TBI is frequently associated with long-term cognitive impairments and that the number of TBIs sustained during one's lifetime can increase the likelihood of chronic impairments (Dikmen et al., 2017; see McInnes et al., 2017 for a review). A recent study by Li et al. (2016) also indicated that TBI accelerates the age at onset (AAO) of cognitive impairment by two or more years in late life. Research has shown that experiencing TBI is associated with an earlier onset of mild cognitive impairment, a prodromal stage of AD (LoBue et al., 2018). This connection between TBI and mild cognitive impairment has also been established in aging professional American football players, providing more support for a connection between rmTBI and AD risk, although other research investigations have not consistently observed these associations (Vos et al., 2018).

Some questions remain about TBI as an Alzheimer's Disease (AD) risk factor. Some research suggests that TBI contributes only to general dementia risk and is not disease-specific. In a review by Kokiko-Cochran and Godbout (2018), they explain that TBI causes inflammatory responses in the brain which are not always linked to abnormal AD pathology (the accumulation of tau and amyloid proteins), but that still contribute to changes in behavior and neuronal loss. In a review by Weiner et al. (2017), TBI was viewed as more closely related to the development of Lewy Body Disease and Parkinson's Disease (PD) instead of AD. Yet TBI has been shown to be associated with earlier development of AD and reduced cortical thickness in individuals who are genetically at risk for AD (Hayes et al., 2017; LoBue et al., 2017). Indeed, Dams-O'Connor et al. (2016) reviewed several studies from 2005 to 2015 which indicated that only TBI combined with genetic risk or older age and TBI in specific sub-groups (APOE e4 carriers, individuals who experienced chronic deficit or dysfunction, individuals with multiple or severe TBIs) could increase AD risk.

Though some doubts exist regarding TBI as a specific risk factor for AD, there is sufficient compelling evidence to suggest that it has links to AD given the outcomes of previously discussed studies. The doubts also make TBI an important point of further investigation of AD in well-characterized samples of older adults. However, disparities that affect racially/ethnically diverse older adults should also be taken into account when researching the connections between TBI and AD. Acknowledging such disparities and seeking to improve equality and equity is a current goal of AD research; achieving this goal is vital to improving quality of life for millions of individuals and families.

Racial/Ethnic Disparities in TBI and AD

Health disparities are generally understood as preventable and inequitable differences in health outcomes (how healthy people are as they age), treatment, healthcare access, and disease prevalence as experienced by different groups in society which are mainly experienced by racially/ethnically diverse populations. Current research provides convincing evidence for the existence of racial/ethnic health disparities in TBI and AD (Carter et al., 2016; Graham, 2015; Zavala et al., 2021).

Racially/ethnically diverse populations face social and structural disparities; this is why self-reported race/ethnicity can be used as a proxy for higher allostatic load (the physical burden of chronic stress experienced by an individual over their lifetime), lower socioeconomic status (SES), experienced discrimination, educational segregation, and many other factors that are known to cause worse health outcomes (Burris & Hacker, 2017). These factors must be taken into account when conducting AD research since they are also connected to many well-established AD risk factors (see Povova et al., 2012 for a review). Several years ago, the National Institute of Aging published its Health Disparities Research Framework which is actively guiding research into how social, structural, and health disparities disproportionately increase AD risk (see Carl V. Hill et al., 2015 for a review).

Racially/ethnically diverse populations in the U.S. experience health disparities, but research into how this experience impacts AD risk is still limited. Specific to this study, research investigating whether racially/ethnically diverse populations experience worse AD risk following a TBI is severely limited. There is some evidence that racially/ethnically diverse populations are at increased risk for TBI (Brenner et al., 2020; Bruns Jr. & Hauser, 2003). The cost and economic impacts of post-TBI care often disproportionately affect these groups (see Dismuke et

al., 2015 for a review), and they are more likely to experience worse mental health outcomes after experiencing TBI which are associated with increased AD risk (Burke et al., 2018; Kumar et al., 2020; Perrin et al., 2014). Racially/ethnically diverse populations also experience more barriers during every step of the TBI treatment and recovery process, in large part due to poorer access to adequate health insurance (Gao et al., 2018; Schiraldi et al., 2015). This lack of insurance is often identified as the cause of racially/ethnically diverse populations experiencing worse health outcomes after TBI (McQuistion et al., 2016). Oftentimes, racially/ethnically diverse populations receive fewer referrals for further care (Budnick et al., 2017; Kane et al., 2014) and experience a higher economic burden for post-TBI due to lower resources. Additionally, their lower access to quality insurance affects the quality of care provided to them. These disparities are linked to larger social and structural disparities that are real, complex, and largely avoidable. This makes TBI an important point of study in AD research; validating the existence of these disparities as well as their tangible and detrimental effects on racially/ethnically diverse populations' health is necessary.

Disparities faced by racially/ethnically diverse populations also exist within AD prevalence, incidence, treatment, and outcomes. Non-Hispanic Black individuals who are diagnosed with dementia tend to have greater cognitive impairment and more severe neuropsychiatric symptoms than Non-Hispanic White individuals (Lennon et al., 2022). Other research affirms that Black and Hispanic/Latino (H/L) dementia patients experience poorer cognitive function and more functional limitations than Non-Hispanic White patients at the time of diagnosis (Lin et al., 2021). In contrast, Lennon and colleagues (2022) found that Black individuals had lower dementia prevalence than White individuals, despite Black individuals having more risk factors. A study by Kornblith et al. (2020) found that dementia diagnosis was

higher in White veterans than in veterans from racially/ethnically diverse populations. Lin and colleagues (2021) identified a potential explanation: that Black and H/L seem to have more missed and delayed dementia diagnoses in many of these research studies. Delayed or missed diagnoses are potential reasons why Black and H/L dementia patients often have worse symptoms at time of diagnosis as well (Lin et al., 2021).

Other health disparities within AD exist and as highlighted in a recent review by Babulal et al. (2019) may be partially attributable to: 1) cognitive tests used to diagnose AD are often less accurate when used to examine racially/ethnically diverse populations, 2) research into how race/ethnicity impact AD biomarkers is lacking, and 3) most AD research does not take place in representative samples. This is especially problematic since racially/ethnically diverse populations are disproportionately affected by AD (Rajan et al., 2021). This means that the groups who are most affected by AD are often not the ones being included in AD research; homogeneous samples in AD research (samples which are predominantly or entirely made up of racial/ethnic majority/White individuals) do not help improve the health of racially/ethnically diverse patients since such studies are of unclear applicability to these groups. Issues such as these indicate that research needs to be more focused on/inclusive of racially/ethnically diverse populations.

To sum, racially/ethnically diverse populations are disproportionately affected by both TBI and AD. There are clear disparities in received treatment and health outcomes in both conditions as well. However, research exploring the link between race, TBI, and AD outcomes is very limited. The lack of racial/ethnic diversity in AD research is a moral issue we currently face, and researchers have an obligation to address and improve this situation.

Conclusions

AD and TBI both present significant threats to older adults, their loved ones, and their financial wellbeing. Experiencing either can be harshly detrimental to one's life and the lives of those around them. Both affect society at large as well, creating economic burdens and impoverished citizens who are forced to pay, or at least attempt to pay, impossible medical bills.

Recent AD research has turned to exploring the causes and consequences of health disparities, specifically those that affect racially/ethnically diverse populations the most. These groups experience many multifaceted health disparities that impact their AD and TBI risk and outcomes in several significant ways. The disparities faced by these populations within AD research is yet another injustice we must seek to address then fix once we have the ability to do so.

Most AD research has been conducted with racially/ethnically homogenous samples which causes a lack of generalizability. Racially/ethnically diverse populations experience higher risk of AD and TBI, though they are greatly underrepresented in AD research. Their experienced health outcomes for both conditions are worse than those experienced by the general population. The lack of research into how AD risk factors uniquely, disproportionately, and/or especially affect racially/ethnically diverse populations is a moral and scientific mistake.

The purpose of the present study was to examine whether race/ethnicity moderated the relationship between TBI and AD risk. The aims and hypotheses of this study were as follows:

Aim 1: To determine whether TBI differently affected AD biomarker levels (plasma Aβ42/40 ratio composites and t-tau composites) across racial/ethnic groups.

Hypothesis 1: Racially/ethnically diverse older adults with a history of TBI would exhibit significantly worse AD biomarker levels than their White counterparts; this

means that those groups would exhibit significantly lower Aβ42/40 ratio composites and higher t-tau composites on average.

Aim 2: To determine whether TBI differently affected cognitive test scores across racial/ethnic groups.

Hypothesis 2: Racially/ethnically diverse older adults with a history of TBI would exhibit significantly worse cognitive test scores (Memory composite and Executive Functioning (EF) composite) than their White counterparts.

The goals of this study were to 1) inform treatment options and/or preventative measures for racially/ethnically diverse older adults who are at risk of AD; 2) support the assertion that post-TBI health outcomes in racially/ethnically diverse populations are worse than those experienced by their White counterparts; and 3) encourage further research into the negative effects of societal inequities experienced by racially/ethnically diverse older adults in America.

Materials and Methods

Study Design Overview

Data from participants enrolled in the Health and Aging Brain Study — Health Disparities (HABS-HD) were analyzed in this study. Self-reported race/ethnicity and evaluated history of traumatic brain injury (TBI) were the two independent variables in this study. AD biomarkers (plasma Aβ42/40 ratio and t-tau) and cognitive test scores were measured by HABS-HD researchers. These variables acted as proxies for AD risk (low Aβ42/40 ratio and high t-tau are both separately indicative of increased AD risk). AD biomarker data was analyzed from blood plasma samples taken from each participant during their baseline study visit; these raw data were converted into z-scores prior to analyses. Cognitive test z-scores from memory or

executive functioning examinations in the cognitive battery were consolidated into cognitive z-score composites. All data were screened for outliers (scores greater than 3 standard deviations from the mean) and to ensure basic assumptions were met.

ANOVAs & chi-square tests examined racial group differences on sociodemographic, TBI injury, cognitive outcomes, and AD markers (cognitive and plasma biomarkers). ANCOVAs investigated TBI x Race interactions on AD cognitive and biomarker outcomes controlling for the effects of age, sex, income, TBI, and education. Follow-up regression analyses explored TBI injury severity x race and TBI quantity x race interactions on AD outcomes as well.

Participants

This study was conducted using previously collected data sourced from HABS-HD. HABS-HD operates within a community-based participatory research approach. This approach enables non-researchers, often community members or representatives of racially/ethnically diverse populations, to participate in every step of the research process; this community-based research approach (visiting public events, senior centers, churches, etc.) and virtual advertising were used to recruit participants. HABS-HD has enrolled over 1,000 H/L and 1,000 White participants; enrollment for 1,000 Black participants. HABS-HD began in February 2021 and is conducted at the University of North Texas in the Dallas/Fort Worth, TX metropolitan area (O'Bryant et al., 2021).

HABS-HD inclusion criteria included individuals who 1) identified as Mexican American, Black, or White, 2) were over the age of 50 years, 3) could fluently speak English and/or Spanish, and 4) were willing/able to provide blood samples and go through neuroimaging procedures. The HABS-HD researchers excluded participants who had any of the following medical conditions: 1) type 1 diabetes, 2) active infection, 3) presence of non-skin cancer or TBI

within the past 12 months of participation, 4) any mental illness except depression, 5) a recent history of any substance or alcohol abuse, 6) any current severe medical condition capable of affecting cognitive test scores, and 7) previous diagnosis of dementia or AD (O'Bryant et al., 2021). All necessary Institutional Review Board approval and informed consent were obtained by the original researchers. Additional details HABS-HD study overview, methods, and design have been described in detail elsewhere (O'Bryant et al., 2021).

The inclusion criteria for the current study were: 1) either conclusively did or did not have a history of TBI; and 2) had the following data available: self-reported race (Hispanic/Latino - H/L, Non-Hispanic White, Non-Hispanic Black), age, sex, and income, cognitive test scores. Note sample sizes for cognitive and plasma biomarker outcomes slightly differ. Biomarker data for the full sample was not available for all participants at the time of this study as some samples are still waiting to be processed (see Table 1 in Results for more details). For the present study, 1,649 HABS-HD participants met inclusion criteria.

TBI Assessment and Diagnostic Procedures

To obtain and measure TBI history, interviewers conducted TBI clinical interviews with study participants using the Ohio State University (OSU) Traumatic Brain Injury (TBI) Identification Method (OSU TBI-ID) (Bogner & Corrigan, 2009) (see Figure 1 in Appendix). The OSU TBI ID is a standardized method for uncovering a participant's lifetime TBI history. In a semi-structured interview, the HBAS-HD interviewer prompted each participant to recall if they experienced a head/neck injury in five different contexts (i.e., "In your lifetime, have you ever been hospitalized or treated in an emergency room following an injury to your head or neck? Think about any childhood injuries you remember or were told about."). Loss of consciousness (LOC) duration was self-reported for each injury event. LOC duration is

commonly used to determine TBI severity (<30 minutes = mild, >30 minutes and <24 hours = moderate, >24 hours = severe). Data about experienced alteration of consciousness (AOC)/post-traumatic amnesia (PTA) were documented, though no distinction between the two was made and no account for their duration was recorded. Additionally, the cause, location/setting, and age of occurrence was also collected for each reported injury. The reliability and predictive validity of the OSU TBI-ID as an accurate and detailed measure of lifetime TBI history has been well supported (Bogner & Corrigan, 2009; Corrigan & Bogner, 2007; McGinley, 2017).

The current study used data from participants who met one of the two following criteria: 1) answered that no injury took place in any of the five contexts (they were excluded if they failed to confirm or deny history of injury in any of the contexts) or 2) reported that any injury with a LOC had taken place in at least one of the five contexts. This strict inclusion criteria was chosen since it was impossible to conclusively assume the absence of TBI in participants who did not explicitly confirm or deny injury history in any of the contexts. Participants who met this criteria composed the non-TBI group (TBI-) in this study. The presence of injury and accompanying LOC is a common formal criteria for TBI diagnosis (Menon et al., 2010). Participants who met this criteria composed the TBI-positive (TBI+) group.

The quantity of TBIs experienced by each participant were also calculated (i.e., if a participant responded that an injury + LOC occurred in both contexts 2 and 3, then their TBI quantity was calculated as 2). Participants were sorted into TBI quantity groups (0 TBI, 1 TBI, 2+ TBIs). Each TBI+ participant's worst TBI severity was also calculated.

AD Biomarkers

AD biomarkers were measured to indicate AD risk and pathology. Fasting blood samples were collected and processed per the international guidelines (O'Bryant et al., 2015). Baseline levels of plasma $A\beta_{40}/A\beta_{42}$ and total tau (t-tau) were assessed using the ultra-sensitive Quanterix Simoa HD-1 (single molecule array) technology platform. The HABS-HD Biomarker Core has performed >5,000 assays and reported a coefficient of variation of ≤5% for the Quanterix platform (O'Bryant et al., 2021, 2022). These reports indicate that the measurement devices used were effective and reliable in measuring plasma Aβ42/40 and t-tau levels. APOE genetic data was gathered using commercial TaqMan Genotyping Kits using TaqMan GTXpress Master Mix from Thermo Fisher Scientific. Target amplification and detection were performed using the 7500 Real-Time PCR System from Applied Biosystems which has been proven reliable for DNA analyses (Spas & Zbieć-Piekarska, 2014). APOE genotype frequencies were confirmed to be in the Hardy–Weinberg equilibrium; this means that this sample's genetic variation was not vastly different from the variation in previous generations (O'Bryant et al., 2022).

Neuropsychological/Cognitive Battery

Participants completed a cognitive battery detailed in Figure 2 (see below). For this study, cognitive ability was assessed using z-score composites for Executive Functioning (EF) and Memory. First, the EF z-score composites were calculated using z-scores from the Wechsler Memory Scale: 3rd edition (WMS‑III) Digit Span task, the Trail Making Test Parts A and B, and the Digit Symbol Substitution Test (DSST) (Wechsler, 1997; Strauss et al., 2006; Lezak, 2004). The WMS-III Digit Span Task measures short-term attention and working memory (participants must repeat a string of digits forward or in reverse); the Trail Making Test measures the ability to plan, process visual information, and pay attention (participants must connect dots in certain

orders); and the DSST measures processing speed (participants must quickly translate numbers into corresponding shapes/symbols (i.e., 1 = ⌣, 2 = ◇, 3 = ⊦, etc.)). Second, the Memory z-score composites were calculated using z-scores from the Spanish-English Verbal Learning (SEVL) Test and WMS-III Logical Memory I and II (González et al., 2002; Wechsler, 1997). The SEVL Test measures unstructured verbal learning and recall ability (participants are read a list of words which they try to remember); the WMS-III Logical Memory tests measure structured verbal episodic memory (participants are read two short stories, then are later asked to recall the stories as best they can).

Figure 2: Neuropsychological test battery

Cognitive Domain	Tests
Attention/executive functioning	WMS-III Digit Span task (Wechsler, 1997), Trail Making Test (Strauss et al., 2006), Digit Symbol Substitution (Lezak, 2004)
Memory	Spanish-English Verbal Learning Test (González et al., 2002), Wechsler Memory Scale-III Logical Memory I and II (Wechler, 1997)

Note. This figure was adapted from O'Bryant et al. (2021).

Statistical Analysis

The latest version of R Markdown/RStudio and the Statistical Package for the Social Sciences were used for the data analysis (*https://www.r-project.org/*; IBM SPSS Statistics for Windows, Version 28.0). ANOVAs compared groups separated by race/ethnicity to show differences in sociodemographic information (i.e., income, education, etc.), TBI history (frequency and severity), and AD outcomes (biomarkers and cognitive diagnostic status). ANCOVAs measured race/ethnicity x TBI interactions on Aβ42/40 ratio, t-tau, EF z-score composites, and Memory z-score composites; covariates included race/ethnicity, age, education, income, presence of TBI, and sex. EF z-score composites were inverted to increase ease of

comprehension. Income was log transformed due to its distribution being abnormal and the transformed values were used in all statistical analyses. The level of significance was maintained at $p < .05$ for all analyses. Please note that analytic samples slightly differ across cognitive and biomarker analyses due to missing data. Missing data included Aβ42/40 (N = 333) and t-tau (N = 318) variables, and APOE ε4 data for all but one Non-Hispanic Black participants; due to this missingness, group differences on APOE genotype were not analyzed.

Results

Sample Characteristics

ANOVA and chi-square test results indicated significant differences between the three racial/ethnic cohorts in age, income, education, sex, TBI history, TBI quantity, and EF composite scores (ps < .001). The White cohort had significantly higher age, income, male representation, TBI history, and TBI quantity. The H/L cohort had significantly lower average education (see Table 1 below for more detail). In the White cohort, 174 participants (27.6%) were TBI+ (TBI + LOC) and 457 were TBI- (no injuries reported). In the H/L cohort, 117 participants (17.2%) were TBI+ and 564 participants were TBI-. Finally, in the Black cohort, 72 participants (21.4%) were TBI+ while 265 were TBI-.

Table 1: Descriptive Statistics of Sample

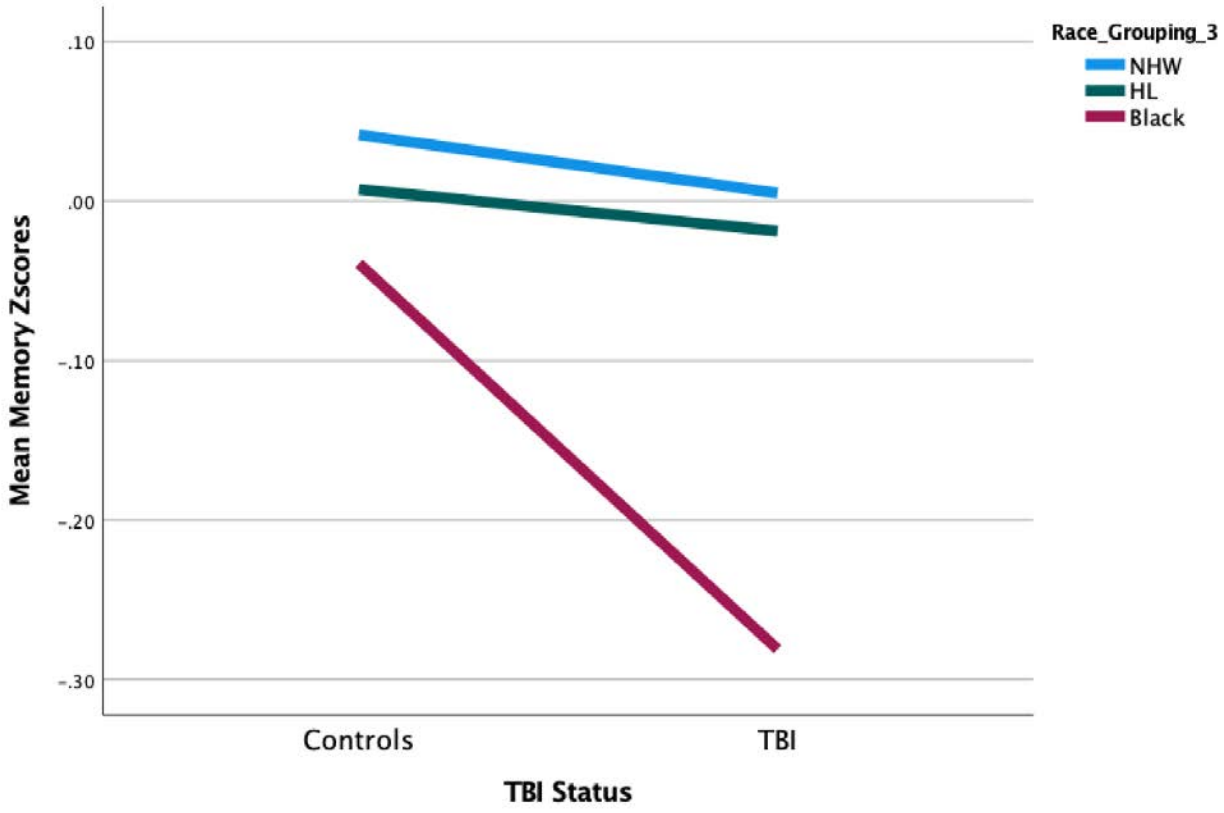
Variable	Total Sample	Non-Hispanic Whites	Hispanic/Latinos	African American/Black	Omnibus Test Result (by Race/Ethnicity)		
	n = 1649	*n* = 631	*n* = 681	*n* = 337	Test Statistic	p-value	*Effect Size (V or eta^2)*
Age, M(SD)	65.01 (8.50)	68.19 (8.50)	63.28 (8.06)	62.52 (7.51)	F = 79.839	p = <.001	.088
Income, M(SD)	66,082 (84,476)	93,363 (94,791)	37,759 (58,028)	72,237 (91,099)	F = 5.144E+11	p = <.001	.087
Education, M(SD)	12.93 (4.61)	15.64 (2.70)	9.48 (4.54)	14.81 (2.73)	F = 541.968	p = <.001	.397
APOE4					--	--	--
positive, *n* (%)	225 (13.6)	125 (19.8)	99 (14.5)	**			
negative, *n* (%)	776 (47.1)	335 (53.1)	441 (64.8)	**			
missing, *n* (%)	648 (39.3)	171 (27.1)	141 (20.7)	**			
Female, *n* (%)	1044 (63.3)	360 (57.1)	454 (66.7)	230 (68.2)	x2 = 17.480	p = <.001	.103
TBI Positive, *n* (%)	363 (22.0)	174 (27.6)	117 (17.2)	72 (21.4)	x2 = 20.717	p = <.001	.112
TBI Quantity					x2 = 29.942	p = <.001	.095
0 TBI, *n* (%)	1286 (78.0)	457 (72.4)	564 (82.8)	265 (78.6)			
1 TBI, *n* (%)	237 (14.4)	108 (17.1)	79 (11.6)	50 (14.8)			
≥ 2 TBIs, *n* (%)	126 (34.7)	66 (37.9)	38 (32.5)	22 (30.6)			
TBI Severity					x2 = 12.352	p = .015	.130
mild, *n* (%)	254 (70.0)	124 (71.3)	79 (67.5)	51 (70.8)			
moderate, *n* (%)	76 (20.9)	31 (17.8)	34 (29.1)	11 (15.3)			
severe, *n* (%)	33 (9.1)	19 (10.9)	4 (3.4)	10 (13.9)			
Cognitive Outcomes							
EF composite, M(SD)	.134 (.87)	-.01 (.81)	.25 (.92)	.15 (.84)	F = 15.193	p = <.001	.018
Memory composite, M(SD)	-.01 (.84)	.03 (.85)	.003 (.81)	-.09 (.86)	F = 2.416	p = .090	.003
AD Biomarker Outcomes							
Amyloid (Aβ40/42), M(SD)	-.03 (.81)	-.03 (.78)	-.05 (.78)	.04 (.96)	F = .737	p = .497	.001
Total Tau (t-tau), M(SD)	-.06 (.85)	-.11 (.88)	-.01 (.81)	-.08 (.88)	F = 2.035	p = .131	.003

Note. M = Mean; SD = Standard Deviation; TBI = Traumatic Brain Injury; EF = Executive Function; ** = APOE data was batched so AA data was not available; 1331 participants had t-tau data, 1316 participants had AB42/40 data.

TBI x Race Interactions on Cognition

ANCOVAs investigated TBI x Race interactions on AD cognitive and biomarker outcomes controlling for the effects of age, sex, income, TBI history, and education. No significant TBI x race/ethnicity interaction on memory (F = 1.79, df = 1639, p = 0.16) or the EF (F = .046, df = 1639, p = .955) composite were observed. Please see Figure 3 (below) for a depiction of memory outcomes across the TBI and non-TBI groups for each racial/ethnic group. While non-significant, it is important to note that the Black TBI cohort appeared to experience visually worse memory composite scores relative to the NHW and H/L TBI cohorts.

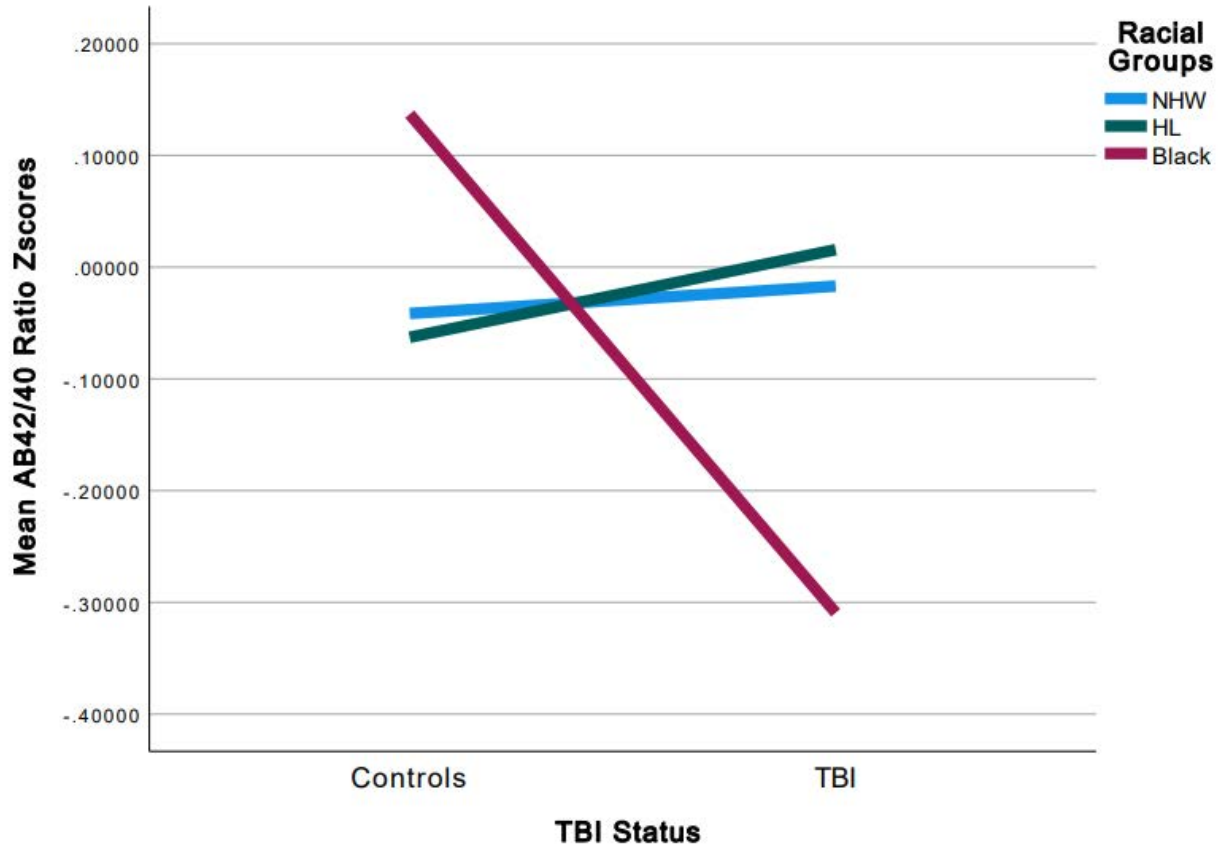
Figure 3: TBI x Race Interaction on Memory Functioning



TBI x Race Interactions on Plasma AD Biomarkers

ANCOVAs revealed there was a significant TBI x race interaction on the plasma Aβ42/40 ratio ($F = 5.214$, $df = 1306$, $p = .006$). See Figure 4 below. Black older adults with a TBI had significantly lower plasma Aβ42/40 levels (indicative of increased AD risk) relative to H/L ($p = .06$) and White ($p = .19$) with a TBI history. No significant TBI x race interaction on plasma t-tau level was found ($F = .159$, $df = 1321$, $p = .853$).

Figure 4: TBI x Race Interaction on Aβ 42/40 Ratio



Exploratory Analyses

Follow-up exploratory regression analyzes investigated TBI injury severity x race/ethnicity and TBI quantity x race/ethnicity interactions on AD outcomes. Results revealed there was a significant TBI x race interaction on memory; NHW older adults with multiple injuries (2+) had poorer memory performance relative to Black ($p = .002$) and Hispanic ($p = .07$) adults with multiple injuries. No other interactions on outcomes were observed ($ps > .05$). ANCOVAs revealed there was no significant TBI severity x race interaction on any cognitive or biomarker outcomes ($ps > .071$). However, these exploratory results may not have been statistically powered due to a small number of individuals with moderate TBIs in each racial/ethnic group.

Discussion

The present study investigated how TBI might differently affect cognition (EF and memory) and AD pathology (Aβ42/40 ratio and t-tau) in three racial/ethnic populations; in doing so, it sought to uncover drivers of increased AD risk in minoritized populations. Analyses evidenced that Black participants with a history of TBI displayed a significant increase in amyloid levels (a lower Aβ42/40 ratio) relative to Non-Hispanic White and H/L participants. While no significant group differences were observed in TBI's impact on t-tau, EF, or memory, there was a visual decrease in Black participants' memory functioning. Worst TBI severity was not found to differently relate to any cognitive or biomarker outcomes across any racial/ethnic groups. Additionally, White participants with a history of two or more TBIs exhibited poorer memory performance relative to their Black and H/L counterparts. These findings indicate that TBI may disproportionately increase AD risk in Black individuals, providing evidence of TBI as an AD-specific risk factor in Black populations.

Amyloid-β

Surprisingly, only Black participants experienced worse amyloid-β accumulation compared to White and H/L groups post-TBI. The H/L group did not display the same unbalanced increase in amyloid-β compared to the White group. This finding aligns with the vast majority of previous research indicating that TBI can contribute to the accumulation of amyloid-β (Johnson et al., 2010; Washington et al., 2014; Bogoslovsky et al., 2017; Chatterjee et al., 2021). Accumulation of amyloid-β can cause mitochondrial dysfunction, impairment of microglia (which remove damaged neurons and neurotoxic compounds/peptides such as Amyloid-β), direct phagocytosis of neurons, the loss of neuronal synapses, and several other

harmful effects that lead to neurodegeneration (Chen et al., 2017). However, why it was only the Black cohort and not the H/L group remains unclear. One potential explanation is due to differences in cardiovascular health between the groups. AD is highly connected to the brain's cerebrovasculature and cardiovascular disease. However, the relationship of causation between AD and cardiovascular health within racially/ethnically diverse populations is not fully understood. Evidence indicates either a reciprocal relationship between the two – amyloid-β deposition negatively affects vascular/cerebrovascular functioning and vice versa – exists, or that cardiovascular disease increases AD risk/pathology (Iadecola, 2010; Kalaria et al., 2012; Santos et al., 2017). Nonetheless, this relationship can explain why Black participants experienced worse amyloid-β accumulation compared to their counterparts. Due to structural determinants of health and social inequalities, Black individuals have higher risk of cardiovascular issues compared to other racial/ethnic groups in the U.S. (higher prevalence of high blood pressure, cardiovascular disease, stroke, heart failure, and mortality from cardiovascular conditions) (see Virani et al., 2021 for a review). Several other studies indicate worse cardiovascular health in Black Americans than in White Americans or H/L populations (see Carnethon et al., 2017 for a review; Yang et al., 2015). Relevant to this, the HABS-HD cardiovascular-related exclusion criteria (type 1 diabetes and chronic heart failure) indicates that cardiovascular health could certainly be a confounding variable in this study (O'Bryant et al., 2021).

Another potential explanation for the lack of elevated amyloid-β accumulation in this study's H/L group is what researchers have come to call an "epidemiological paradox" – the possibility that greater social/familial support in H/L populations may contribute to better health outcomes despite facing societal inequities (Katiria Perez & Cruess, 2014). A review and meta-analysis by Cahill et al. (2021) examined seventy-three different studies and found that

higher familism – a H/L cultural concept that emphasizes family, loyalty, honor, and attachment – was associated with better educational outcomes, greater family warmth/support, and less family conflict/negativity. Several other studies have documented familism's mental and physical health benefits (Corona et al., 2017; Gallegos & Segrin, 2022; Martin et al., 2019).

Total Tau

Given the relationship between TBI and amyloid-β accumulation, it was surprising that this study did not find the same relationship between TBI and total tau (t-tau). TBI has been shown to increase t-tau in veterans, hockey players, and boxers (Fossati et al., 2017; Olivera et al., 2015; Zetterberg & Blennow, 2016). However, a single mild or moderate TBI might only temporarily increase t-tau levels, while experiencing multiple TBIs (which is common for veterans, hockey players, and boxers) can lead to chronically high t-tau (Fossati et al., 2017). There is evidence that chronic mild TBIs can cause chronic traumatic encephalopathy (CTE). CTE is a type of tauopathy (neurodegenerative disease characterized by abnormal tau accumulation) primarily caused by repeated TBIs and is often diagnosed based on elevated and varied tau formations throughout the brain (not in AD specific areas such as the medial temporal lobe, middle frontal gyrus, and deeper parts of the brain – CTE tau accumulation is often in superficial areas) (Turner et al., 2016). Increased t-tau might not have been observed in this sample due to the small number of participants with multiple TBIs; it is possible that elevated t-tau indicative of CTE or AD was not found due to the small sample size. In simpler terms, since the majority of our sample only reported one TBI, it is understandable that no disproportionate increases in t-tau were observed since such elevation is primarily caused by multiple TBIs. A second reason for our null finding could be that measuring blood plasma t-tau is not optimal for indicating AD-specific risk. T-tau is a general marker of neurodegeneration and

axonal injury indicative of several dementia types (i.e., CTE), but phosphorylated tau (p-tau) is AD-specific since it correlates with the development of tau tangles which are found primarily in the brains of patients with AD (Karikari et al., 2022; Zetterberg, 2017; Andreasen et al., 2003). If this study had measured p-tau, then a direct and disproportionate link between TBI and AD risk in racially/ethnically diverse older adults might have been found. It is also important to note that while CTE and AD can occur together and share several risk factors, CTE may not be a driver of AD pathology since the type and placement of each disease's biomarkers are distinct (McKee et al., 2009; Turner et al., 2016).

Cognition

This study found no significant group differences in TBI's effect on cognition. This could be due to the fact that this study's sample was relatively young; both the Black and H/L groups were, on average, under the age of sixty-five years old. This is relevant since the vast majority of people who develop AD do so after turning sixty-five (Guerreiro & Bras, 2015). Additionally, HABS-HD excluded participants with a previous diagnosis of AD or dementia and participants with any medical condition that could affect cognition. It is likely that the relatively young age and exclusion criteria led this sample to exhibit low rates of cognitive impairment. The visually lower memory performance in the Black group post-TBI might indicate that Black individuals with a history of TBI are at increased risk for earlier age at onset (AAO) of AD. Most often, episodic memory is impaired in mild cognitive impairment (MCI) patients who develop AD (Albert et al., 2011). Other research indicates that EF is likely to decrease early on in AD progression too (Cohen et al,. 2022); however, it is possible that the visual decrease in memory function displayed by the Black cohort could be an early sign of cognitive impairment potentially leading to eventual AD.

Exploratory Findings

Exploratory regression analyses were conducted to investigate whether TBI severity and quantity differently affected AD risk across the three racial/ethnic groups. The only statistically significant finding was that White participants with a history of two or more TBIs exhibited significantly worse memory performance relative to their Black and H/L peers. This finding parallels previous research into the detrimental effects of multiple TBIs on cognitive impairment (Dikmen et al., 2017; see McInnes et al., 2017 for a review; Vos et al., 2018). This finding might also correlate with the visual decrease in memory function displayed by the Black cohort in this study. The basic assumption of this study would be that the Black cohort experienced worse memory outcomes due to societal inequities, but the White cohort's decrease might have been caused by uneven distribution of participants with multiple TBIs (the White cohort had more multiple TBI participants). It is important to note that the small sample size (small number of participants with multiple TBIs) likely means these results are not statistically powerful or generalizable. In terms of severity's effect on AD risk in different racial/ethnic groups, this study's null findings were slightly surprising. The results did not align with previous research in demonstrating that worse TBI severity is associated with increased AD risk (see Dams-O'Connor et al., 2016 for a review; Zhang et al., 2021). As it was with high TBI quantity, these results are likely not statistically powerful or generalizable due to the limited sample size (small number of participants with moderate or severe TBI).

Strengths

This study had a few important strengths. First, thanks to HABS-HD researchers, we were able to work with a racially/ethnically diverse sample; this allowed us to research how TBI increases AD risk in under-researched and underrepresented populations. Second, the use of the

OSU-TBI-ID enabled us to take undiagnosed TBIs into consideration; given society inequities such as inadequate access to quality healthcare, accounting for TBIs that were not followed up by a doctor's visit was essential for this study. Third, our strict TBI inclusion criteria allowed us to have confidence in our findings; we did not include 'grey-area' participants whose OSU-TBI-ID was inconclusive or missing relevant data (presence of injury + LOC). Fourth, this study utilized robust cognitive characterization outcomes and reliable plasma biomarker data; the cognitive composite scores encapsulated participant performance on several reliable cognitive tests.

Limitations

However, this study also possessed a few important limitations. First, our sample was not equally representative of all three racial/ethnic groups; the Black cohort only made up twenty percent of our sample. Second, we were not able to include p-tau as an outcome variable; this would have made our findings more helpful to future AD research. Third, the OSU-TBI-ID did not account for alteration of consciousness (AOC) or post-traumatic amnesia (PTA); the presence of either in conjunction with a reported head and/or neck injury can be used to clinically diagnose an injury as a TBI (Menon et al., 2010). This limited our TBI+ group to participants with a reported injury and experienced LOC. Finally, APOE e4 was not used as a covariate in this study since the data for the Black cohort was not available. There is a chance that genetic risk could have been a confounding factor that influenced our results.

Future Research

Future research should focus on recruiting a diverse group of participants with a wider range of TBI severity and quantity; normally such samples are gathered from veteran or athlete populations. However, limiting research to these populations, though important, likely minimizes

the generalizability of research investigating TBI, AD, and racial/ethnic health disparities. Moreover, we encourage future researchers to also examine the effects of TBI on AD risk in prison and former foster youth populations, if possible, since these populations also experience elevated rates of TBI (Cusimano et al., 2020 & 2021; O'Rourke et al., 2016). Next, future research should focus on measuring AD biomarkers using neuroimaging/PET technology; this will allow for more direct and representative measurement of t-tau, p-tau, and amyloid-β in the brain. Additionally, such research should also measure other markers of neurodegeneration such as cortical thickness (CT), grey matter volume, hippocampal shape, and others. Finally, more research is needed to examine the commonalities between CTE and AD; one step that can be taken is to develop better interviews to examine TBI history. Although the OSU-TBI-ID adequately suited this study's AD-specific interest, creating a more detailed TBI interview might allow future researchers to uncover subtleties in how TBI might increase CTE or AD risk instead of both simultaneously.

References

Albert, M. S., DeKosky, S. T., Dickson, D., Dubois, B., Feldman, H. H., Fox, N. C., ... & Phelps, C. H. (2011). The diagnosis of mild cognitive impairment due to Alzheimer's disease: recommendations from the National Institute on Aging‐Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimer's & dementia*, *7*(3), 270-279.

Alzheimer's Disease Facts and Figures. (n.d.). Alzheimer's Disease and dementia. Retrieved April 4, 2023, from https://www.alz.org/alzheimers-dementia/facts-figures

Andreasen, N., Sjögren, M., & Blennow, K. (2003). CSF markers for Alzheimer's disease: total tau, phospho-tau and Aβ42. *The world journal of biological psychiatry*, 4(4), 147-155.

Babulal, G. M., Quiroz, Y. T., Albensi, B. C., Arenaza-Urquijo, E., Astell, A. J., Babiloni, C., Bahar-Fuchs, A., Bell, J., Bowman, G. L., Brickman, A. M., Chételat, G., Ciro, C., Cohen, A. D., Dilworth-Anderson, P., Dodge, H. H., Dreux, S., Edland, S., Esbensen, A., Evered, L., … O'Bryant, S. E. (2019). Perspectives on ethnic and racial disparities in Alzheimer's disease and related dementias: Update and areas of immediate need. *Alzheimer's & dementia*, *15*(2), 292–312. https://doi.org/10.1016/j.jalz.2018.09.009

Bogner, J., & Corrigan, J. D. (2009). Reliability and Predictive Validity of the Ohio State University TBI Identification Method With Prisoners. *The Journal of Head Trauma Rehabilitation*, *24*(4), 279. https://doi.org/10.1097/HTR.0b013e3181a66356

Bogoslovsky, T., Wilson, D., Chen, Y., Hanlon, D., Gill, J., Jeromin, A., Song, L., Moore, C., Gong, Y., Kenney, K., & Diaz-Arrastia, R. (2017). Increases of Plasma Levels of Glial Fibrillary Acidic Protein, Tau, and Amyloid β up to 90 Days after Traumatic Brain Injury. *Journal of Neurotrauma*, *34*(1), 66–73. https://doi.org/10.1089/neu.2015.4333

Brenner, E. K., Grossner, E. C., Johnson, B. N., Bernier, R. A., Soto, J., & Hillary, F. G. (2020). Race and ethnicity considerations in traumatic brain injury research: Incidence, reporting, and outcome. *Brain Injury*, *34*(6), 801–810. https://doi.org/10.1080/02699052.2020.1741033

Bruns Jr., J., & Hauser, W. A. (2003). The Epidemiology of Traumatic Brain Injury: A Review. *Epilepsia*, *44*(s10), 2–10. https://doi.org/10.1046/j.1528-1157.44.s10.3.x

Budnick, H. C., Tyroch, A. H., & Milan, S. A. (2017). Ethnic disparities in traumatic brain injury care referral in a Hispanic-majority population. *Journal of Surgical Research*, *215*, 231–238. https://doi.org/10.1016/j.jss.2017.03.062

Burke, S. L., Cadet, T., Alcide, A., O'Driscoll, J., & Maramaldi, P. (2018). Psychosocial risk factors and Alzheimer's disease: The associative effect of depression, sleep disturbance, and anxiety. *Aging & Mental Health*, *22*(12), 1577–1584. https://doi.org/10.1080/13607863.2017.1387760

Burris, H. H., & Hacker, M. R. (2017). Birth outcome racial disparities: A result of intersecting social and environmental factors. *Seminars in Perinatology*, *41*(6), 360–366. https://doi.org/10.1053/j.semperi.2017.07.002

Cahill, K. M., Updegraff, K. A., Causadias, J. M., & Korous, K. M. (2021). Familism values and adjustment among Hispanic/Latino individuals: A systematic review and meta-analysis. *Psychological Bulletin*, *147*(9), 947–985. https://doi.org/10.1037/bul0000336.supp

Carl V. Hill, P., Eliseo J. Pérez-Stable, M. D., Norman B. Anderson, P., & Marie A. Bernard, M. D. (2015). The National Institute on Aging Health Disparities Research Framework. *Ethnicity & Disease*, *25*(3), Article 3. https://doi.org/10.18865/ed.25.3.245

Carnethon, M. R., Pu, J., Howard, G., Albert, M. A., Anderson, C. A. M., Bertoni, A. G.,

Mujahid, M. S., Palaniappan, L., Taylor, H. A., Willis, M., & Yancy, C. W. (2017). Cardiovascular Health in African Americans: A Scientific Statement From the American Heart Association. *Circulation*, *136*(21), e393–e423. https://doi.org/10.1161/CIR.0000000000000534

Carter, E. E., Barr, S. G., & Clarke, A. E. (2016). The global burden of SLE: Prevalence, health disparities and socioeconomic impact. *Nature Reviews Rheumatology*, *12*(10), Article 10. https://doi.org/10.1038/nrrheum.2016.137

Chatterjee, P., Pedrini, S., Stoops, E., Goozee, K., Villemagne, V. L., Asih, P. R., Verberk, I. M. W., Dave, P., Taddei, K., Sohrabi, H. R., Zetterberg, H., Blennow, K., Teunissen, C. E., Vanderstichele, H. M., & Martins, R. N. (2021). Plasma glial fibrillary acidic protein is elevated in cognitively normal older adults at risk of Alzheimer's disease. *Translational Psychiatry*, *11*(1), Article 1. https://doi.org/10.1038/s41398-020-01137-1

Chen, G., Xu, T., Yan, Y., Zhou, Y., Jiang, Y., Melcher, K., & Xu, H. E. (2017). Amyloid beta: Structure, biology and structure-based therapeutic development. *Acta Pharmacologica Sinica*, *38*(9), Article 9. https://doi.org/10.1038/aps.2017.28

Cohen, S., Cummings, J., Knox, S., Potashman, M., & Harrison, J. (2022). Clinical trial endpoints and their clinical meaningfulness in early stages of Alzheimer's disease. *The journal of prevention of Alzheimer's disease*, *9*(3), 507-522.

Corona, K., Campos, B., & Chen, C. (2017). Familism Is Associated With Psychological Well-Being and Physical Health: Main Effects and Stress-Buffering Effects. *Hispanic Journal of Behavioral Sciences*, *39*(1), 46–65. https://doi.org/10.1177/0739986316671297

Corrigan, J. D., & Bogner, J. (2007). Initial Reliability and Validity of the Ohio State University

TBI Identification Method. *The Journal of Head Trauma Rehabilitation*, *22*(6), 318. https://doi.org/10.1097/01.HTR.0000300227.67748.77

Cusimano, M. D., Zhang, S., Huang, G., Wolfe, D., & Carpino, M. (2020). Associations between Traumatic Brain Injury, Drug Abuse, Alcohol Use, Adverse Childhood Events, and Aggression Levels in Individuals with Foster Care History. *Neurotrauma Reports*, *1*(1), 241–252. https://doi.org/10.1089/neur.2020.0032

Cusimano, M. D., Zhang, S., Mei, X. Y., Kennedy, D., Saha, A., Carpino, M., Wolfe, D., Hoshizaki, B., Mann, R., Schweizer, T., Asbridge, M., Bhalerao, S., Clarke, D., Comper, P., Cukier, W., Cullen, J., Delay, D., Donnelly, P., Graham, S., … Voaklander, D. (2021). Traumatic Brain Injury, Abuse, and Poor Sustained Attention in Youth and Young Adults Who Previously Experienced Foster Care. *Neurotrauma Reports*, *2*(1), 94–102. https://doi.org/10.1089/neur.2020.0030

Dams-O'Connor, K., Guetta, G., Hahn-Ketter, A. E., & Fedor, A. (2016). Traumatic brain injury as a risk factor for Alzheimer's disease: Current knowledge and future directions. *Neurodegenerative Disease Management*, *6*(5), 417–429. https://doi.org/10.2217/nmt-2016-0017

Dikmen, S., Machamer, J., & Temkin, N. (2017). Mild Traumatic Brain Injury: Longitudinal Study of Cognition, Functional Status, and Post-Traumatic Symptoms. *Journal of Neurotrauma*, *34*(8), 1524–1530. https://doi.org/10.1089/neu.2016.4618

Dismuke, C. E., Walker, R. J., & Egede, L. E. (2015). Utilization and Cost of Health Services in Individuals With Traumatic Brain Injury. *Global Journal of Health Science*, *7*(6), 156–169. https://doi.org/10.5539/gjhs.v7n6p156

Edwards, G., Moreno-Gonzalez, I., & Soto, C. (2017). Amyloid-beta and tau pathology

following repetitive mild traumatic brain injury. *Biochemical and Biophysical Research Communications*, *483*(4), 1137–1142. https://doi.org/10.1016/j.bbrc.2016.07.123

Fossati, S., Cejudo, J. R., Debure, L., Pirraglia, E., Glodzik, L., Osorio, R. S., Chen, J., Provost, A., Jeromin, A., Haas, M., Marmar, C., & deLeon, M. (2017). [p4–133]: Differential value of plasma tau as a biomarker for alzheimer's disease and chronic traumatic brain injury. *Alzheimer's & Dementia*, *13*(7S_Part_27), P1307–P1307. https://doi.org/10.1016/j.jalz.2017.06.1999

Galgano, M., Toshkezi, G., Qiu, X., Russell, T., Chin, L., & Zhao, L.-R. (2017). Traumatic brain injury: Current treatment strategies and future endeavors. *Cell Transplantation*, *26*(7), 1118–1130.

Gallegos, M. L., & Segrin, C. (2022). Family Connections and the Latino Health Paradox: Exploring the Mediating Role of Loneliness in the Relationships Between the Latina/o Cultural Value of Familism and Health. *Health Communication*, *37*(9), 1204–1214. https://doi.org/10.1080/10410236.2021.1909244

Gao, S., Kumar, R. G., Wisniewski, S., & Fabio, A. (2018). Disparities in health care utilization of adults with traumatic brain injuries are related to insurance, race and ethnicity: A systematic review. *The Journal of Head Trauma Rehabilitation*, *33*(3), E40–E50. https://doi.org/10.1097/HTR.0000000000000338

González, H. M., Mungas, D., & Haan, M. N. (2002). A verbal learning and memory test for English- and Spanish-speaking older Mexican-American adults. *The Clinical Neuropsychologist*, *16*(4), 439–451. https://doi.org/10.1076/clin.16.4.439.13908

Graham, G. (2015). Disparities in Cardiovascular Disease Risk in the United States. *Current Cardiology Reviews*, *11*(3), 238–245.

Guerreiro, R., & Bras, J. (2015). The age factor in Alzheimer's disease. *Genome medicine*, *7*(1), 1-3.

Hall, J. R., Balldin, V. H., Gamboa, A., Edwards, M. L., Johnson, L. A., & O'Bryant, S. E. (2018). Texas Mexican American adult normative studies: Normative data for the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS). *Developmental Neuropsychology*, *43*(1), 27–35. https://doi.org/10.1080/87565641.2017.1401629

Hayes, J. P., Logue, M. W., Sadeh, N., Spielberg, J. M., Verfaellie, M., Hayes, S. M., Reagan, A., Salat, D. H., Wolf, E. J., McGlinchey, R. E., Milberg, W. P., Stone, A., Schichman, S. A., & Miller, M. W. (2017). Mild traumatic brain injury is associated with reduced cortical thickness in those at risk for Alzheimer's disease. *Brain*, aww344. https://doi.org/10.1093/brain/aww344

He, W., Goodkind, D., & Kowal, P. (2016). *An Aging World: 2015.* https://doi.org/10.13140/RG.2.1.1088.9362

Iadecola, C. (2010). The overlap between neurodegenerative and vascular factors in the pathogenesis of dementia. *Acta Neuropathologica*, *120*(3), 287–296. https://doi.org/10.1007/s00401-010-0718-6

IBM Corp. Released 2021. IBM SPSS Statistics for Windows, Version 28.0. Armonk, NY: IBM Corp

Joe, E., & Ringman, J. M. (2019). Cognitive symptoms of Alzheimer's disease: Clinical management and prevention. *BMJ*, *367*, l6217. https://doi.org/10.1136/bmj.l6217

Johnson, V. E., Stewart, W., & Smith, D. H. (2010). Traumatic brain injury and amyloid-β pathology: A link to Alzheimer's disease? *Nature Reviews Neuroscience*, *11*(5), Article 5.

https://doi.org/10.1038/nrn2808

Kalaria, R. N., Akinyemi, R., & Ihara, M. (2012). Does vascular pathology contribute to Alzheimer changes? *Journal of the Neurological Sciences*, *322*(1), 141–147. https://doi.org/10.1016/j.jns.2012.07.032

Kane, W. G., Wright, D. A., Fu, R., & Carlson, K. F. (2014). Racial/Ethnic and Insurance Status Disparities in Discharge to Posthospitalization Care for Patients With Traumatic Brain Injury. *The Journal of Head Trauma Rehabilitation*, *29*(6), E10. https://doi.org/10.1097/HTR.0000000000000028

Karikari, T. K., Ashton, N. J., Brinkmalm, G., Brum, W. S., Benedet, A. L., Montoliu-Gaya, L., ... & Zetterberg, H. (2022). Blood phospho-tau in Alzheimer disease: analysis, interpretation, and clinical utility. *Nature Reviews Neurology*, 18(7), 400-418.

Katiria Perez, G., & Cruess, D. (2014). The impact of familism on physical and mental health among Hispanics in the United States. *Health Psychology Review*, *8*(1), 95–127. https://doi.org/10.1080/17437199.2011.569936

Kokiko-Cochran, O. N., & Godbout, J. P. (2018). The Inflammatory Continuum of Traumatic Brain Injury and Alzheimer's Disease. *Frontiers in Immunology*, *9*. https://www.frontiersin.org/articles/10.3389/fimmu.2018.00672

Kornblith, E., Peltz, C. B., Xia, F., Plassman, B., Novakovic-Apopain, T., & Yaffe, K. (2020). Sex, race, and risk of dementia diagnosis after traumatic brain injury among older veterans. *Neurology*, *95*(13), e1768–e1775. https://doi.org/10.1212/WNL.0000000000010617

Kumar, R. G., Ornstein, K. A., Bollens-Lund, E., Watson, E. M., Ankuda, C. K., Kelley, A. S., & Dams-O'Connor, K. (2020). Lifetime history of traumatic brain injury is associated with

increased loneliness in adults: A US nationally representative study. *International Journal of Geriatric Psychiatry*, *35*(5), 553–563. https://doi.org/10.1002/gps.5271

Lennon, J. C., Aita, S. L., Bene, V. A. D., Rhoads, T., Resch, Z. J., Eloi, J. M., & Walker, K. A. (2022). Black and White individuals differ in dementia prevalence, risk factors, and symptomatic presentation. *Alzheimer's & dementia: The Journal of the Alzheimer's Association*, *18*(8), 1461–1471. https://doi.org/10.1002/alz.12509

Lezak, M. D. (2004). *Neuropsychological Assessment*. Oxford University Press.

Li, W., Risacher, S. L., McAllister, T. W., & Saykin, A. J. (2016). Traumatic brain injury and age at onset of cognitive impairment in older adults. *Journal of Neurology*, *263*(7), 1280–1285. https://doi.org/10.1007/s00415-016-8093-4

Lin, P.-J., Daly, A. T., Olchanski, N., Cohen, J. T., Neumann, P. J., Faul, J. D., Fillit, H. M., & Freund, K. M. (2021). dementia Diagnosis Disparities by Race and Ethnicity. *Medical Care*, *59*(8), 679–686. https://doi.org/10.1097/MLR.0000000000001577

LoBue, C., Wadsworth, H., Wilmoth, K., Clem, M., Hart, J., Womack, K. B., Didehbani, N., Lacritz, L. H., Rossetti, H. C., & Cullum, C. M. (2017). Traumatic brain injury history is associated with earlier age of onset of Alzheimer disease. *The Clinical Neuropsychologist*, *31*(1), 85–98. https://doi.org/10.1080/13854046.2016.1257069

LoBue, C., Woon, F. L., Rossetti, H. C., Hynan, L. S., Hart Jr., J., & Cullum, C. M. (2018). Traumatic brain injury history and progression from mild cognitive impairment to Alzheimer disease. *Neuropsychology*, *32*, 401–409. https://doi.org/10.1037/neu0000431

Martin, M. J., Conger, R. D., & Robins, R. W. (2019). Family stress processes and drug and alcohol use by Mexican American adolescents. *Developmental Psychology*, *55*(1), 170–183. https://doi.org/10.1037/dev0000629

Masel, B. E., & DeWitt, D. S. (2010). Traumatic Brain Injury: A Disease Process, Not an Event. *Journal of Neurotrauma*, *27*(8), 1529–1540. https://doi.org/10.1089/neu.2010.1358

McGinley, A. (2017). *Validating the Brain Injury Screening Index (BISI) and the Ohio State University Traumatic Brain Injury Identification Method (OSU TBI-ID) as screening tools for head injury in a Scottish prison setting: And clinical research portfolio* [DClinPsy, University of Glasgow]. https://eleanor.lib.gla.ac.uk/record=b3295222

McInnes, K., Friesen, C. L., MacKenzie, D. E., Westwood, D. A., & Boe, S. G. (2017). Mild Traumatic Brain Injury (mTBI) and chronic cognitive impairment: A scoping review. *PLOS ONE*, *12*(4), e0174847. https://doi.org/10.1371/journal.pone.0174847

McKee, A. C., Cantu, R. C., Nowinski, C. J., Hedley-Whyte, E. T., Gavett, B. E., Budson, A. E., ... & Stern, R. A. (2009). Chronic traumatic encephalopathy in athletes: progressive tauopathy after repetitive head injury. *Journal of Neuropathology & Experimental Neurology*, *68*(7), 709-735.

McQuistion, K., Zens, T., Jung, H. S., Beems, M., Leverson, G., Liepert, A., Scarborough, J., & Agarwal, S. (2016). Insurance status and race affect treatment and outcome of traumatic brain injury. *Journal of Surgical Research*, *205*(2), 261–271. https://doi.org/10.1016/j.jss.2016.06.087

Meagher, A. D., Beadles, C. A., Doorey, J., & Charles, A. G. (2015). Racial and ethnic disparities in discharge to rehabilitation following traumatic brain injury. *Journal of Neurosurgery*, 122(3), 595–601. https://doi.org/10.3171/2014.10.JNS14187

Menon, D. K., Schwab, K., Wright, D. W., & Maas, A. I. (2010). Position statement: definition of traumatic brain injury. *Archives of physical medicine and rehabilitation*, 91(11), 1637-1640.

O'Bryant, S. E., Gupta, V., Henriksen, K., Edwards, M., Jeromin, A., Lista, S., Bazenet, C., Soares, H., Lovestone, S., Hampel, H., Montine, T., Blennow, K., Foroud, T., Carrillo, M., Graff-Radford, N., Laske, C., Breteler, M., Shaw, L., Trojanowski, J. Q., … STAR-B and BBBIG working groups. (2015). Guidelines for the standardization of preanalytic variables for blood-based biomarker studies in Alzheimer's disease research. *Alzheimer's & Dementia: The Journal of the Alzheimer's Association*, *11*(5), 549–560. https://doi.org/10.1016/j.jalz.2014.08.099

O'Bryant, S. E., Johnson, L. A., Barber, R. C., Braskie, M. N., Christian, B., Hall, J. R., Hazra, N., King, K., Kothapalli, D., Large, S., Mason, D., Matsiyevskiy, E., McColl, R., Nandy, R., Palmer, R., Petersen, M., Philips, N., Rissman, R. A., Shi, Y., … Yaffe, K. (2021). The Health & Aging Brain among Latino Elders (HABLE) study methods and participant characteristics. *Alzheimer's & dementia : Diagnosis, Assessment & Disease Monitoring*, *13*(1), e12202. https://doi.org/10.1002/dad2.12202

O'Bryant, S. E., Petersen, M., Hall, J., Johnson, L., & Team, for the H.-H. S. (2022). Metabolic Factors Are Related to Brain Amyloid Among Mexican Americans: A HABS-HD Study. *Journal of Alzheimer's Disease*, *86*(4), 1745–1750. https://doi.org/10.3233/JAD-215620

O'Bryant, S. E., Zhang, F., Petersen, M., Hall, J. R., Johnson, L. A., Yaffe, K., Mason, D., Braskie, M., Barber, R. A., Rissman, R. A., Mapstone, M., Mielke, M. M., Toga, A. W., & HABLE Study Team. (2022). A blood screening tool for detecting mild cognitive impairment and Alzheimer's disease among community-dwelling Mexican Americans and non-Hispanic Whites: A method for increasing representation of diverse populations in clinical research. *Alzheimer's & Dementia: The Journal of the Alzheimer's Association*, *18*(1), 77–87. https://doi.org/10.1002/alz.12382

Olivera, A., Lejbman, N., Jeromin, A., French, L. M., Kim, H.-S., Cashion, A., Mysliwiec, V., Diaz-Arrastia, R., & Gill, J. (2015). Peripheral Total Tau in Military Personnel Who Sustain Traumatic Brain Injuries During Deployment. *JAMA Neurology*, *72*(10), 1109–1116. https://doi.org/10.1001/jamaneurol.2015.1383

O'Rourke, C., Linden, M. A., Lohan, M., & Bates-Gaston, J. (2016). Traumatic brain injury and co-occurring problems in prison populations: A systematic review. *Brain Injury*, *30*(7), 839–854. https://doi.org/10.3109/02699052.2016.1146967

OSU TBD ID I Ohio State Brain Injury Prevention & Rehabilitation. (n.d.). Retrieved March 29, 2023, from https://wexnermedical.osu.edu/neurological-institute/neuroscience-research-institute/research-centers/ohio-valley-center-for-brain-injury-prevention-and-rehabilitation/osu-tbi-id

Perrin, P. B., Krch, D., Sutter, M., Snipes, D. J., Arango-Lasprilla, J. C., Kolakowsky-Hayner, S. A., Wright, J., & Lequerica, A. (2014). Racial/Ethnic Disparities in Mental Health Over the First 2 Years After Traumatic Brain Injury: A Model Systems Study. *Archives of Physical Medicine and Rehabilitation*, *95*(12), 2288–2295. https://doi.org/10.1016/j.apmr.2014.07.409

Povova, J., Ambroz, P., Bar, M., Pavukova, V., Sery, O., Tomaskova, H., & Janout, V. (2012). Epidemiological of and risk factors for Alzheimer's disease: A review. *Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub*, *156*(2), 108–114.

Rajan, K. B., Weuve, J., Barnes, L. L., McAninch, E. A., Wilson, R. S., & Evans, D. A. (2021). Population estimate of people with clinical Alzheimer's disease and mild cognitive impairment in the United States (2020–2060). *Alzheimer's & dementia*, *17*(12), 1966–1975. https://doi.org/10.1002/alz.12362

Ramos-Cejudo, J., Wisniewski, T., Marmar, C., Zetterberg, H., Blennow, K., de Leon, M. J., & Fossati, S. (2018). Traumatic Brain Injury and Alzheimer's Disease: The Cerebrovascular Link. *EBioMedicine*, *28*, 21–30. https://doi.org/10.1016/j.ebiom.2018.01.021

Safieh, M., Korczyn, A.D. & Michaelson, D.M. ApoE4: an emerging therapeutic target for Alzheimer's disease. BMC Med 17, 64 (2019). https://doi.org/10.1186/s12916-019-1299-4

Santos, C. Y., Snyder, P. J., Wu, W.-C., Zhang, M., Echeverria, A., & Alber, J. (2017). Pathophysiologic relationship between Alzheimer's disease, cerebrovascular disease, and cardiovascular risk: A review and synthesis. *Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring*, *7*, 69–87. https://doi.org/10.1016/j.dadm.2017.01.005

Schiraldi, M., Patil, C. G., Mukherjee, D., Ugiliweneza, B., Nuño, M., Lad, S. P., & Boakye, M. (2015). Effect of Insurance and Racial Disparities on Outcomes in Traumatic Brain Injury. *Journal of Neurological Surgery Part A: Central European Neurosurgery*, *76*(3), 224–232. https://doi.org/10.1055/s-0034-1543958

Spas, A., & Zbieć-Piekarska, R. (2014). Internal validation of a DNA quantification method using the quantifiler® human DNA quantification kit and the 7500 real-time PCR system with the hid real-time PCR analysis software V 1.1 at the biology department of the central forensic laboratory of the police. Forensic practice. *Problemy Kryminalistyki*, 284(2), 1–8.

Strauss, E., Sherman, E. M. S., & Spreen, O. (2006). A compendium of neuropsychological tests: Administration, norms, and commentary, 3rd ed (pp. xvii, 1216). *Oxford University Press*.

Turner, R. C., Lucke-Wold, B. P., Robson, M. J., Lee, J. M., & Bailes, J. E. (2016). Alzheimer's

disease and chronic traumatic encephalopathy: Distinct but possibly overlapping disease entities. *Brain injury*, 30(11), 1279-1292.

Vespa, J., Armstrong, D. M., & Medina, L. (2018). *Demographic turning points for the United States: Population projections for 2020 to 2060* (pp. 25-1144). Washington, DC: US Department of Commerce, Economics and Statistics Administration, US Census Bureau.

Virani, S. S., Alonso, A., Aparicio, H. J., Benjamin, E. J., Bittencourt, M. S., Callaway, C. W., Carson, A. P., Chamberlain, A. M., Cheng, S., Delling, F. N., Elkind, M. S. V., Evenson, K. R., Ferguson, J. F., Gupta, D. K., Khan, S. S., Kissela, B. M., Knutson, K. L., Lee, C. D., Lewis, T. T., … American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics Subcommittee. (2021). Heart Disease and Stroke Statistics-2021 Update: A Report From the American Heart Association. *Circulation*, *143*(8), e254–e743. https://doi.org/10.1161/CIR.0000000000000950

Vos, B. C., Nieuwenhuijsen, K., & Sluiter, J. K. (2018). Consequences of Traumatic Brain Injury in Professional American Football Players: A Systematic Review of the Literature. *Clinical Journal of Sport Medicine*, *28*(2), 91. https://doi.org/10.1097/JSM.0000000000000432

Wang, L., Benzinger, T. L., Su, Y., Christensen, J., Friedrichsen, K., Aldea, P., McConathy, J., Cairns, N. J., Fagan, A. M., Morris, J. C., & Ances, B. M. (2016). Evaluation of Tau Imaging in Staging Alzheimer Disease and Revealing Interactions Between β-Amyloid and Tauopathy. *JAMA Neurology*, *73*(9), 1070–1077. https://doi.org/10.1001/jamaneurol.2016.2078

Washington, P. M., Morffy, N., Parsadanian, M., Zapple, D. N., & Burns, M. P. (2014).

Experimental Traumatic Brain Injury Induces Rapid Aggregation and Oligomerization of Amyloid-Beta in an Alzheimer's Disease Mouse Model. *Journal of Neurotrauma*, *31*(1), 125–134. https://doi.org/10.1089/neu.2013.3017

Wechsler, D. (1997). Wechsler Adult Intelligence Scale—Third Edition. https://doi.org/10.1037/t49755-000

Weiner, M. W., Crane, P. K., Montine, T. J., Bennett, D. A., & Veitch, D. P. (2017). Traumatic brain injury may not increase the risk of Alzheimer disease. *Neurology*, *89*(18), 1923–1925. https://doi.org/10.1212/WNL.0000000000004608

Xu, J., Zhang, Y., Qiu, C., & Cheng, F. (2017). Global and regional economic costs of dementia: A systematic review. *The Lancet*, *390*, S47. https://doi.org/10.1016/S0140-6736(17)33185-9

Yang, Q., Zhong, Y., Ritchey, M., Cobain, M., Gillespie, C., Merritt, R., Hong, Y., George, M. G., & Bowman, B. A. (2015). Vital Signs: Predicted Heart Age and Racial Disparities in Heart Age Among U.S. Adults at the State Level. *MMWR. Morbidity and Mortality Weekly Report*, *64*(34), 950–958. https://doi.org/10.15585/mmwr.mm6434a6

Zavala, V. A., Bracci, P. M., Carethers, J. M., Carvajal-Carmona, L., Coggins, N. B., Cruz-Correa, M. R., Davis, M., de Smith, A. J., Dutil, J., Figueiredo, J. C., Fox, R., Graves, K. D., Gomez, S. L., Llera, A., Neuhausen, S. L., Newman, L., Nguyen, T., Palmer, J. R., Palmer, N. R., … Fejerman, L. (2021). Cancer health disparities in racial/ethnic minorities in the United States. *British Journal of Cancer*, *124*(2), Article 2. https://doi.org/10.1038/s41416-020-01038-6

Zetterberg, H., & Blennow, K. (2016). Fluid biomarkers for mild traumatic brain injury and related conditions. *Nature Reviews Neurology*, *12*(10), Article 10.

https://doi.org/10.1038/nrneurol.2016.127

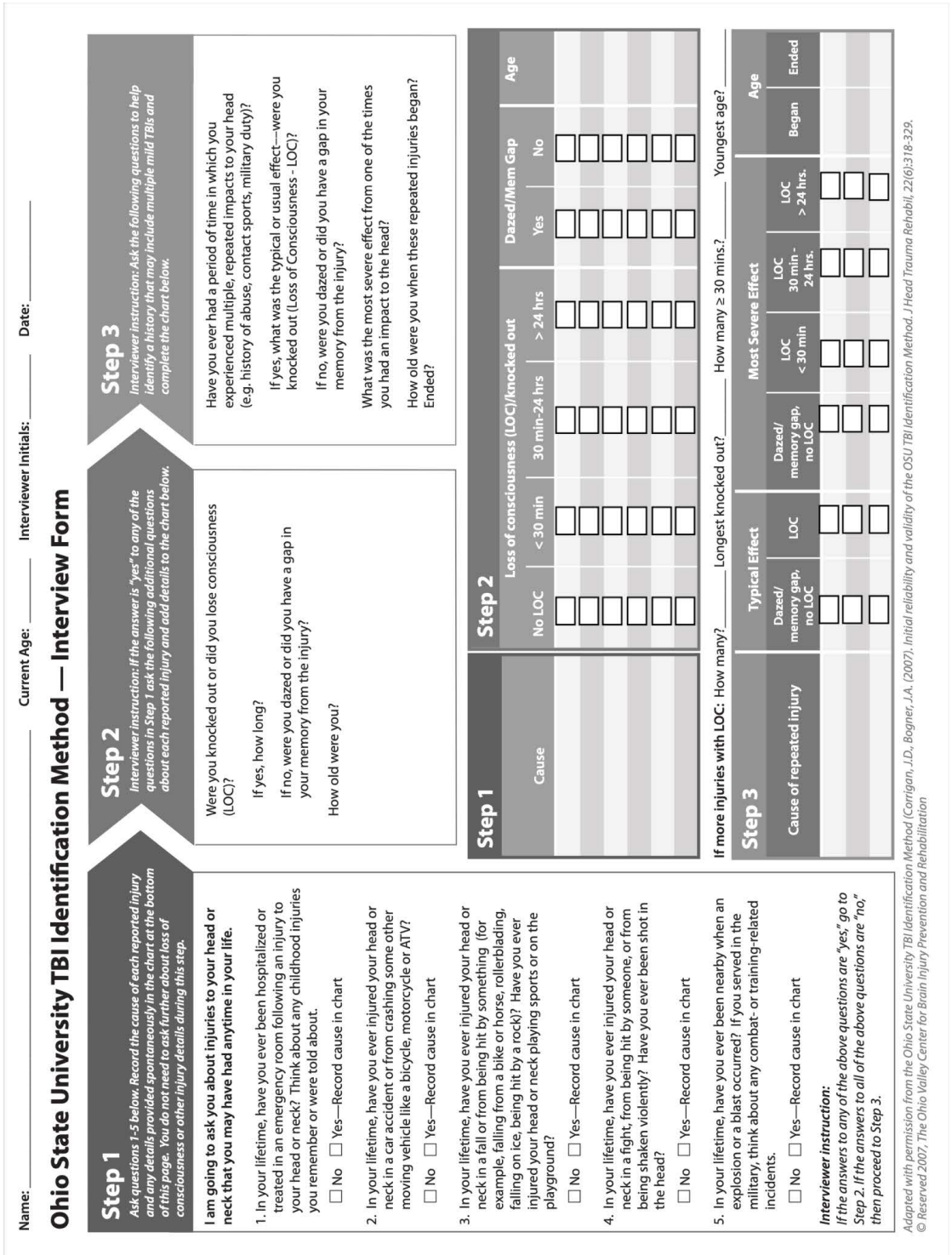
Zetterberg, H. (2017). Tau in biofluids–relation to pathology, imaging and clinical features. *Neuropathology and applied neurobiology*, 43(3), 194-199.

Zhang, J., Zhang, Y., Zou, J., & Cao, F. (2021). A meta-analysis of cohort studies: Traumatic brain injury and risk of Alzheimer's Disease. *PloS one*, *16*(6), e0253206.

Zhang, X.-X., Tian, Y., Wang, Z.-T., Ma, Y.-H., Tan, L., & Yu, J.-T. (2021). The Epidemiology of Alzheimer's Disease Modifiable Risk Factors and Prevention. *The Journal of Prevention of Alzheimer's Disease*, *8*(3), 313–321. https://doi.org/10.14283/jpad.2021.15

Appendix

Figure 1: Ohio State University (OSU) Traumatic Brain Injury (TBI) Identification Method (OSU TBI ID).



Name:_____ Current Age:_____ Interviewer Initials:_____ Date:_____

Ohio State University TBI Identification Method — Interview Form

Step 1

Ask questions 1-5 below. Record the cause of each reported injury and any details provided spontaneously in the chart at the bottom of this page. You do not need to ask further about loss of consciousness or other injury details during this step.

I am going to ask you about injuries to your head or neck that you may have had anytime in your life.

1. In your lifetime, have you ever been hospitalized or treated in an emergency room following an injury to your head or neck? Think about any childhood injuries you remember or were told about.
   ☐ No ☐ Yes—Record cause in chart
2. In your lifetime, have you ever injured your head or neck in a car accident or from crashing some other moving vehicle like a bicycle, motorcycle or ATV?
   ☐ No ☐ Yes—Record cause in chart
3. In your lifetime, have you ever injured your head or neck in a fall or from being hit by something (for example, falling from a bike or horse, rollerblading, falling on ice, being hit by a rock)? Have you ever injured your head or neck playing sports or on the playground?
   ☐ No ☐ Yes—Record cause in chart
4. In your lifetime, have you ever injured your head or neck in a fight, from being hit by someone, or from being shaken violently? Have you ever been shot in the head?
   ☐ No ☐ Yes—Record cause in chart
5. In your lifetime, have you ever been nearby when an explosion or a blast occurred? If you served in the military, think about any combat- or training-related incidents.
   ☐ No ☐ Yes—Record cause in chart

Interviewer instruction:
If the answers to any of the above questions are "yes," go to Step 2. If the answers to all of the above questions are "no," then proceed to Step 3.

Step 2

Interviewer instruction: If the answer is "yes" to any of the questions in Step 1 ask the following additional questions about each reported injury and add details to the chart below.

Were you knocked out or did you lose consciousness (LOC)?

If yes, how long?

If no, were you dazed or did you have a gap in your memory from the injury?

How old were you?

Step 3

Interviewer instruction: Ask the following questions to help identify a history that may include multiple mild TBIs and complete the chart below.

Have you ever had a period of time in which you experienced multiple, repeated impacts to your head (e.g. history of abuse, contact sports, military duty)?

If yes, what was the typical or usual effect—were you knocked out (Loss of Consciousness - LOC)?

If no, were you dazed or did you have a gap in your memory from the injury?

What was the most severe effect from one of the times you had an impact to the head?

How old were you when these repeated injuries began? Ended?

Step 1

Cause	Loss of consciousness (LOC)/knocked out				Dazed/Mem Gap		Age
	No LOC	< 30 min	30 min-24 hrs	> 24 hrs	Yes	No	
	☐	☐	☐	☐	☐	☐	
	☐	☐	☐	☐	☐	☐	
	☐	☐	☐	☐	☐	☐	
	☐	☐	☐	☐	☐	☐	
	☐	☐	☐	☐	☐	☐	

If more injuries with LOC: How many?_____ Longest knocked out?_____ How many ≥ 30 mins.?_____ Youngest age?_____

Step 3

Cause of repeated injury	Typical Effect		Most Severe Effect				Age	
	Dazed/ memory gap, no LOC	LOC	Dazed/ memory gap, no LOC	LOC < 30 min	LOC 30 min - 24 hrs.	LOC > 24 hrs.	Began	Ended
	☐	☐	☐	☐	☐	☐		
	☐	☐	☐	☐	☐	☐		
	☐	☐	☐	☐	☐	☐		

Adapted with permission from the Ohio State University TBI Identification Method (Corrigan, J.D., Bogner, J.A. (2007). Initial reliability and validity of the OSU TBI Identification Method. J Head Trauma Rehabil, 22(6):318-329.

(Continuation from reverse side, if needed)

Name: ______________ **Current Age:** ________ **Interviewer Initials:** ________ **Date:** ____________

Step 1	Step 2						
	Loss of consciousness (LOC)/knocked out				Dazed/Mem Gap		Age
Cause	No LOC	< 30 min	30 min-24 hrs	> 24 hrs	Yes	No	
	☐	☐	☐	☐	☐	☐	
	☐	☐	☐	☐	☐	☐	
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	☐	☐	☐	☐	☐	☐	

If more injuries with LOC: How many?________ Longest knocked out?________ How many ≥ 30 mins.?________ Youngest age? ________

Step 3	Typical Effect		Most Severe Effect				Age	
Cause of repeated injury	Dazed/ memory gap, no LOC	LOC	Dazed/ memory gap, no LOC	LOC < 30 min	LOC 30 min - 24 hrs.	LOC > 24 hrs.	Began	Ended
	☐	☐	☐	☐	☐	☐		
	☐	☐	☐	☐	☐	☐		
	☐	☐	☐	☐	☐	☐		
	☐	☐	☐	☐	☐	☐		
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	☐	☐	☐	☐	☐	☐		
	☐	☐	☐	☐	☐	☐		

Interpreting Findings

A person may be more likely to have ongoing problems if they have any of the following:

- **WORST**
  Individual reports one moderate to severe TBI. Moderate and severe TBI indicated by report of loss of consciousness (LOC) greater than 30 minutes.
- **FIRST**
  Individual reports TBI with LOC before age 15
- **MULTIPLE**
  Individual reports a period where 3 or more blows to the head caused altered consciousness
  -OR-
  2 or more TBIs with LOC within a three month period

For more information about TBI or the OSU TBI Identification Method visit:

- Ohio Valley Center at OSU
  www.ohiovalley.org/informationeducation
- BrainLine.org
  www.brainline.org

(Updated July 2013)