



Summer 202

E-Newsletter

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The Mary S. Easton Center for Alzheimer's Disease Research at UCLA has very active teams working on basic research, drug discovery, biomarkers for early diagnosis and clinical activity including clinical trials, cognitive testing, and patient care.

Alzheimer's Association 2021 Facts and Figures Report

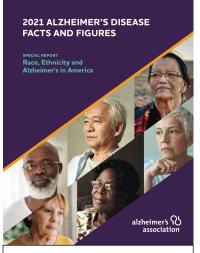


Image courtesy of Alzheimer's Association.

By: Monica Moore, MSG, Mirella Díaz-Santos, PhD, and Keith Vossel, MD, MSc

Earlier this year, the Alzheimer's Association released the <u>2021 Facts and</u> <u>Figures Report</u>. Each year this report highlights the significant impact Alzheimer's disease has on our society and health care system and includes a Special Report focusing on a population or issue of heightened concern. In previous years, the Special Report discussed topics such as caregiving, diagnosis, and the impact of Alzheimer's on the health care system. This year's Special Report was entitled "Race, Ethnicity and Alzheimer's in America".

COVID-19 upended all our lives last year and had a substantial impact on people with Alzheimer's disease and their care partners. In fact, deaths due to Alzheimer's were up 16% last year. Many people with Alzheimer's disease who contracted COVID-19 lived in care facilities where outbreaks were more common. The isolation that resulted from the COVID-19 restrictions caused increased stress on caregivers, who were already at heightened levels of stress, anxiety and depression prior the COVID-19 pandemic. Isolation secondary to

public health mandates of physical distancing also disrupted the social, communal and individual routines of people with Alzheimer's disease, which in turn, likely caused many to progress at a faster rate. The complete impact of COVID-19 on people with Alzheimer's disease is still unknown and the Alzheimer's Association will provide a more in-depth report in the 2022 Facts and Figures Report.

The COVID-19 pandemic exacerbated and shined a light to how structural racism (Khazanchi et al. 2020) is at the root of the longstanding health and health care disparities faced by communities of color. These communities experience lack of access, lack of culturally and linguistically congruent/responsible providers and cognitive tests, mistrust in the health care system driven by a systemic history of discrimination and oppression based on race, ethnicity, nationality, age, immigration status, sex, gender, sexual orientation, ability, and religion, including all the unique intersectionalities (Crenshaw, 1994). These injustices and inequities have led to increased Alzheimer's

and dementia risk and prevalence in underrepresented racial and ethnic groups. We have long recognized that older Black/Black Americans, Native/Indigenous Americans, and Hispanic/Latino/a/x Americans are disproportionately more likely to have Alzheimer's and other dementias compared to white Americans. Older Asian Americans and Pacific Islanders (AAPI) are also at high risk for dementia but are rarely included in research studies. Underrepresented racial and ethnic groups experience less timely-accurate diagnoses and patient-family centered treatments. Training in cultural humility for providers and education about dementia in communities of color as well as reciprocal partnerships with community stakeholders and community members are essential first steps to break down these barriers and improve health outcomes.

Not only do racial, ethnic and cultural differences exist in the care of Alzheimer's but they also exist in the perceptions and attitudes about individual experiences with Alzheimer's disease. At the end of 2020, the Alzheimer's Association conducted a cross cultural survey of US adults and dementia caregivers to explore perceptions and experiences of caregiving, trust of the health care system, participation in clinical trials and research, and access to care and support services. This survey included the following populations: Black, Hispanic, Native American, Asian American, and white. The results of this survey show that discrimination continues to be a large barrier to care in underserved and marginalized communities, that research is biased in favor of affluent, educated, white communities, and that understanding, concern, and stigma about Alzheimer's varies widely across groups. The survey illustrated the tremendous work that needs to be done to reduce disparities, build trust and improve health outcomes in communities of color.

The Facts and Figures 2021 Report also discusses the new area of research that focuses on the biological beginning of Alzheimer's disease and the changes that occur in the brain years before dementia symptoms present. For many years, it was believed that the first symptoms of dementia began at the same time as the biological changes in the brain, but now researchers know that these biological changes begin 20 years or more before symptoms present. This discovery allows researchers to find ways to intervene in the progression of the disease before significant cognitive and biological changes occur. In addition, research advances expand the field's understanding of which therapies may be most effective at which points in the Alzheimer's disease continuum, and in which individuals.

The report discusses new knowledge about modifiable risk factors for Alzheimer's disease. Modifiable risk factors have been the focus of many studies including World Wide FINGERS (Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability) and the US POINTER (Protect Brain Health Through Lifestyle Intervention to Reduce Risk), which is sponsored by the Alzheimer's Association. Factors highlighted include education, diet, exercise, social and cognitive engagement. Research has shown that people with more years of formal education are at lower risk for Alzheimer's and other dementias, supporting the idea that higher education can create a "cognitive reserve" in the brain. Diet and exercise have long been associated with heart healthy habits that are encouraged to maintain a healthy lifestyle. What is good for your heart is also good for your brain and may help reduce dementia risk in later years. But once again we see how social, economic and environmental factors, and disparities therein, come to the forefront in the area of risk reduction. These social determinants of health have a major role in Alzheimer's risk as well as other health conditions.

The report goes into great detail about the growing prevalence of Alzheimer's disease, which now exceeds six million in the US, estimated numbers of deaths due to Alzheimer's disease, as well as substantial effects of this disease on patients, caregivers, and families. To read the complete Alzheimer's Association 2021 Facts and Figures report please visit https://www.alz.org/media/Documents/alzheimer's disease, as well as substantial effects of this disease on patients, caregivers, and families. To read the complete Alzheimer's Association 2021 Facts and Figures report please visit https://www.alz.org/media/Documents/alzheimer's Association 2021 Facts and

In summary, this year's Alzheimer's Association report is a call to action for the Easton Center and colleagues around the globe. Not only is Alzheimer's prevalence growing, but it is disproportionately affecting communities of color. With prospects of meaningful treatments on the horizon, we must be proactive to engage everyone in the exciting new future of Alzheimer's research and care.

2021 ALZHEIMER'S DISEASE FACTS AND FIGURES

DISCRIMINATION

is a barrier to Alzheimer's and dementia care. These populations reported discrimination when seeking health care:







of Black of Native Americans Americans of Asian Americans

of Hispanic Americans



Figure. Summary statistics from the 2021 Facts and Figures Report. (Courtesy of Alzheimer's Association)

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Chronic Traumatic Encephalopathy: History, Challenges, and Updates



By: Kevin Bickart, MD

Chronic traumatic encephalopathy (CTE) is a hot button topic, skyrocketing in research and media coverage over the last 10 years. This is largely due to work from Boston University (BU), which popularized brain donations from ex-National Football League (NFL) players for post-mortem investigation. CTE however was first coined by Macdonald Critchley in 1949 and elaborated by John Corsellis and colleagues in 1973 to describe a progressive neurologic condition in ex-boxers marked by slowed movements, tremors, stupor, and behavioral changes with associated neurodegeneration, presumably due to repetitive head injuries. In 2005, CTE was adapted to describe similar degenerative brain

changes in an autopsy of an ex-NFL player, Mike Webster, by neuropathologist Bennet Omalu. He noted Webster's brain seemed normal in weight, size, and gross appearance, but beneath the surface, there was a similar accumulation of abnormal proteins to that of the ex-boxers. In parallel, Anne McKee, neuropathologist at BU, found similar pathology in the brain of another ex-NFLer, John Grimsley. BU's brain bank has since received hundreds of brain donations, mostly from ex-NFLers but also from ex-athletes in different contact or collision sports as well as veterans.

Dr. McKee and a large network of colleagues have formed a consensus that CTE is a unique neuropathology. It is similar to other neurodegenerative dementias like Alzheimer's disease in that abnormal proteins deposit in areas of the brain that correlate with the symptoms of the dementia, such as in the hippocampus relating to short-term memory difficulty in Alzheimer's. For CTE however, the proteins accumulate in brain areas that may be most vulnerable to traumatic forces, such as next to arteries, at the depths of the brain's folds, and in the frontal and temporal lobes. This is why it has been deemed a unique disease by many neuropathologists, though not all agree.

Several *retrospective* studies have since linked worsened CTE pathology on autopsy to estimates of head injury exposure in life, such as the number of years playing contact or collision sports or first age of experiencing head injuries. Nevertheless, there has been no *prospective* study to link estimates of head injury exposure to CTE or show a causal effect of repetitive head injury on CTE in humans. As such, much of the research today focuses on finding ways to diagnose CTE in life using both clinical symptom criteria and biomarkers, such as brain imaging or blood tests. This would enable clinicians and researchers to determine such things as a person's risk for CTE, the quantity or severity of head injury needed to cause CTE, or the most vulnerable ages for head injury exposure.

Unfortunately, it has been very difficult to find a sensitive and specific set of diagnostic criteria to identify those individuals with a history of repetitive head injury who will go on to develop CTE pathology on autopsy. In fact, investigations of the consensus criteria from 2014 for making a diagnosis of this condition in life (Mez et al., 2021), if applied to the general population, would lead to many false diagnoses of CTE, particularly for people who have

mood, anxiety, or pain disorders (Iverson and Gardner, 2021). Due to this and other weaknesses in the 2014 criteria, they have just been revised (Katz et al., 2021). The 2020 criteria show excellent sensitivity for picking up cases of CTE based solely on clinical symptoms blind to the pathology, missing very few true cases. The criteria however, still show poor specificity, in that many false positive diagnoses of CTE are made.

There is still much work to be done in this area. Prospective studies are needed to weigh the benefits of cardiorespiratory and social health benefits of playing sports, along with new measures to reduce exposure to head injury in collision sports, and risks of dementia. The media, public, and medical community should be wary of jumping to a diagnosis of CTE in someone because they played sports and show cognitive or behavioral changes. In clinical practice, it seems most reasonable to consider each individual person with a history of head injury who develops cognitive or behavioral changes on a case-by-case basis, first testing for the most common and better-known causes of these symptoms before suspecting a diagnosis of CTE.

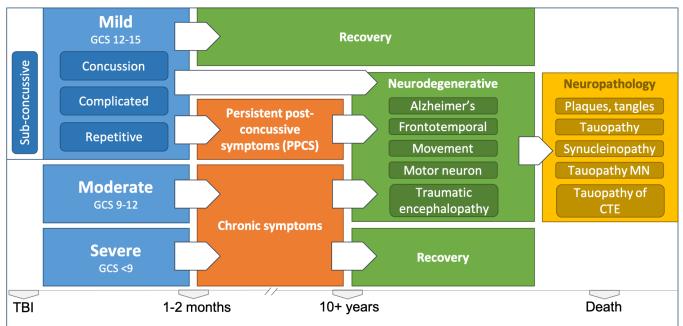


Figure 1. Inter-relation between forms of traumatic brain injury and symptom trajectories. People can recover from all forms of traumatic brain injury (TBI), but a minority of individuals have persistent or chronic symptoms (>1-2 months after injury), and an even smaller number of individuals theoretically develop a protracted, progressive neurologic condition. The arrows represent these possible recovery trajectories after TBI across the spectrum of severity. One possibility discussed in this newsletter is that repetitive sub-concussive head injuries can increase risk of developing CTE many years after head injury exposure, as represented by the longer arrow towards the top of the figure. Abbreviations: TBI traumatic brain injury; GCS Glasgow Coma Scale, MN motor neuron; CTE chronic traumatic encephalopathy.

References:

Iverson GL, & Gardner AJ. Symptoms of traumatic encephalopathy syndrome are common in the US general population. *Brain Communications* 2021;3(1):fcab001. https://doi.org/10.1093/braincomms/fcab001

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Mez J, Alosco ML, Daneshvar DH, Saltiel N, Baucom Z, Abdolmohammadi B, ... McKee AC. Validity of the 2014 traumatic encephalopathy syndrome criteria for CTE pathology. *Alzheimer's & Dementia: The Journal of the Alzheimer's Association* 2021 Apr 7. http://doi.org/10.1002/alz.12338. Online ahead of print.

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Los Angeles Neurological Society Leadership Panel



By: Aaron McMurtray, MD, PhD

The Los Angeles Neurological Society (LANS) meeting on February 17, 2021 showcased a variety of national leaders in the field of dementia care who all completed some portion of their training at UCLA. Panel members included: Dr. Bruce Miller, Director, Memory and Aging Center, University of California San Francisco, Weill Institute for Neurosciences and UCLA Neurology Residency alumnus; as well as several UCLA Neurobehavioral Fellowship alumni Dr. Edmond Teng – Lead Medical Director, Genentech, San Francisco, CA; Dr. Andrew Fras – Chair, Neurology Department, Martin Luther King Jr. Outpatient

Center, Los Angeles, CA; Dr. Liana Apostolova – Barbara and Peer Baekgaard Professor in Alzheimer's Disease Research, Professor in Neurology, Radiology. Medical and Molecular Genetics, Indiana University School of Medicine, Indiana Alzheimer's Disease Center; Dr. Gad Marshall – Associate Professor of Neurology, Harvard Medical School, Associate Medical Director of Clinical Trials, Center for Alzheimer Research & Treatment, Brigham and Women's Hospital, Massachusetts General Hospital.

Dr. Keith Vossel, director of the Mary S. Easton Center for Alzheimer's Disease Research at UCLA started off the meeting introducing Dr. Miller and speaking about his time as a fellow in Dr. Miller's neurobehavior fellowship program.

Dr. Michael Mahler was in attendance and provided an insightful perspective regarding the time when Dr. Miller, Dr. Mario Mendez, and himself were all residents in the various UCLA affiliated training programs at the same time.

Panel members highlighted the significant milestones in their career pathways, including what motivated them to join the field of behavioral neurology and how they had enjoyed their time at UCLA. The panel members also discussed the current state of the field and where they perceived opportunities for young physicians starting out in their careers who might be considering specializing in behavioral neurology. Dr. Fras also discussed the benefits of working in government service and providing care to underserved and underrepresented populations, and stressed the need for improved access to clinical trials in these populations as an area for improvement in the future.

Dr. Mendez was in attendance and happy to see so many of the graduates of his fellowship program successfully serving in prominent roles in academic medicine, neuroscience research, the pharmaceutical industry, and in advocacy. Dr. Mendez closed the meeting with a heartfelt message to his former graduates (Dr. Teng, Dr. Fras, Dr. Apostolova, Dr. Marshall) expressing his pride in them as graduates of his program and their career achievements.

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New Addition to the Easton Center

Please join us in welcoming a new staff member to the Easton Center.



Photo: Aisha Mohammed, BA

Aisha received her Bachelor of Arts degree in Psychology from the University of San Francisco with minors in Neuroscience, Health Studies, and Business Entrepreneurship & Innovation. During her undergraduate studies, she worked for Neuroscape at the University of California, San Francisco where she focused on projects surrounding cognitive training and assessments for adolescents. Before joining the Easton Center, she also interned at the University of Pennsylvania where she focused on topics of social interaction and neuroeconomics. Outside work, she enjoys going to the movies and spending time

outdoors. Aisha is excited to contribute to the mission of the UCLA Easton Center.

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Clinical Research Opportunities

If you would like to advance Alzheimer's disease research, please consider being a study participant. Below are the current recruiting trials. For a complete list of enrolling studies, visit our website at <u>www.eastonad.ucla.edu</u>.

EASTON CENTER KAGAN CLINICAL TRIALS PROGRAM

• <u>Alzheimer's Disease Neuroimaging Initiative 3 (ADNI3) Protocol</u>

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Caregiver Support Groups



In partnership with the <u>UCLA Alzheimer's and Dementia Care Program</u>, the <u>Easton Center</u> is excited to announce two upcoming new caregiver support groups!

Adult Children Caring for a Parent with Dementia

Caregivers of People with Frontotemporal Lobar Degeneration (additional group)

Date and times of these groups are still to be determined, but please email **Monica Moore** at <u>MRMoore@mednet.ucla.edu</u> for additional information and to be added to the distribution list! <u>Click here</u> for our current list of support groups.



For more information on our upcoming lectures and events, please visit the Easton Center <u>Community</u> <u>Calendar</u>.

Update on Alzheimer's Disease Research Date: Friday, July 9, 2021 Time: 11:00 A.M. – 12:30 P.M. (PST) Virtual Forum

This presentation is in partnership with Alzheimer's Los Angeles. Please call (844) 435-7250 to RSVP and to receive access information.

Update on Alzheimer's Disease Research Date: Thursday, July 15, 2021 Time: 11:30 A.M. – 12:30 P.M. (PST) Location: Watermark Westwood Village (in-person) 947 Tiverton Ave. Westwood, CA 90095

Please call (310) 208-4590 to RSVP and for more information.

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