Transforming Lives: How Your Donation to the Brain Bank is Reshaping Neurodegenerative Disorders!

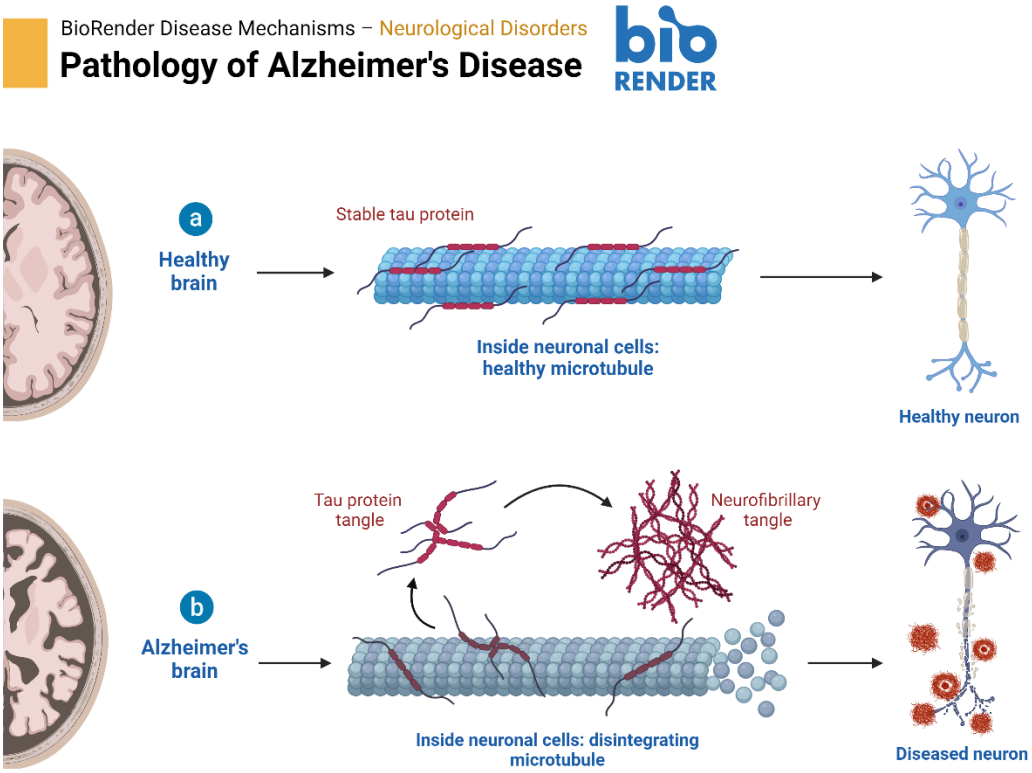
The Mayo Clinic brain bank has been a crucial resource for advancing our knowledge of neurodegenerative disorders. For over 25 years, this invaluable resource has helped uncover important genetic and neuropathologic insights that have changed how we understand these conditions. The bank contains over 10,600 preserved and cataloged brains donated by people nationwide. We are humbled and grateful for their altruistic donation in helping us make transformative discoveries.

Why does brain donation make a difference?

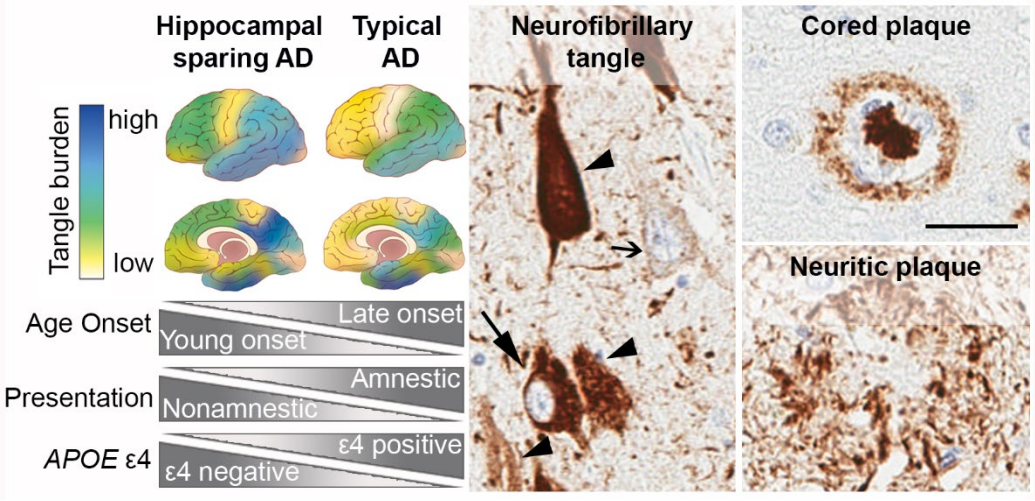
Brain tissue analysis after death remains a gold standard for reaching a definitive diagnosis in dementia and other neurodegenerative disorders. This not only helps families find closure but also supports physicians to understand the disease better. Dementia, an umbrella term that encompasses different disorders with similar symptoms affecting how patients operate in their daily living, presents unique challenges for each patient and their families. Each brain donation, a selfless act of generosity, becomes part of an invaluable repository to support discovery and ultimately meet the needs of patients and families. Neuronal cells, responsible for our daily activities of living, such as walking, thinking, dressing, personal hygiene, and eating, are deeply affected during a neurodegenerative disease. Understanding this process is crucial in our quest to prevent and stop the disease. The neuronal cells and the brain are deeply investigated using several methods, such as molecular and biochemical pathways, microscopic observations, imaging, and genetic analysis, and each of these analyses provides a piece in the neurodegeneration puzzle.

Why do neuronal cells die?

The abnormal accumulation of certain proteins in the brain is involved in neuronal cell death. For instance, in Alzheimer's disease, amyloid-beta and tau protein deposits 'trap' the neuronal cells and affect their cross-talk activity to provide daily function. Moreover, they start a neuroinflammatory response in the brain, and all these events are linked to clinical symptoms, brain atrophy, and cell death. Abnormal protein accumulation is also observed in Parkinson's disease, frontotemporal dementia, and dementia with Lewy bodies. Apart from protein changes, disease disrupts other pathways as well. It has been shown that lipid metabolism, neuronal functions, such as cell-to-cell communication and metabolism, and vascular changes are equally profoundly affected. Overall, multiple adverse factors interact to change cell-to-cell communication and cell metabolism which ends in cell death and loss of brain function. The research aims to understand the dysregulated pathways and their relationship with dementia and neurodegeneration.



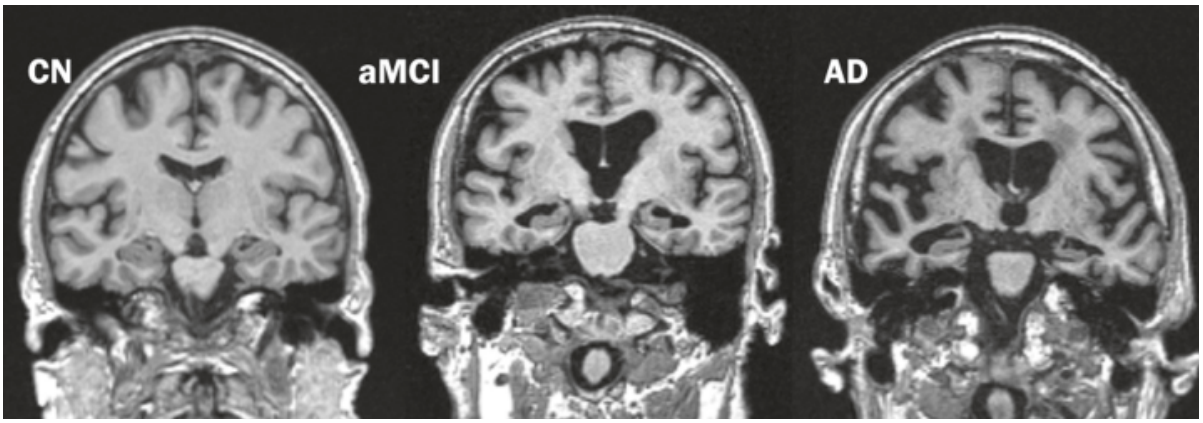
How do scientists discover these proteins and cell metabolism changes?
During the disease, radiologic imaging such as MRI and PET scans associated with symptoms and laboratory screening gives physicians clues to a diagnosis. Studying the autopsied brain tissue of patients with neurodegeneration changes in cells of specific brain regions allows the definitive differential diagnosis. The fixed and frozen tissue samples are processed, and these molecular changes are analyzed. The fixed tissue undergoes a detailed microscopic evaluation using specialized dyes and stains to reveal the brain changes. Once these changes are identified, the final diagnosis is reached. Investigations using the frozen tissue opens the door for genetic and biochemical tests to identify the altered proteins and other changes in biofluids like cerebrospinal fluid and blood-based biological markers (biomarkers). Other types of biomarker discoveries may include evaluation of the inner metabolism of cells, revealing candidates for scientific validation. Neuropathologic validation of new biomarkers remains critical to form solid knowledge to enable effective clinical trials.



Graaf-Radford et al., 2021[1]

What is the impact of this knowledge on the lives of patients?
Carefully studying abnormal protein accumulation and distribution patterns has allowed the development of diagnostic methods, improved disease progression prediction, and better patient treatment outcomes. For instance, PET scans using biomarkers for amyloid-beta and tau can show physicians the distribution of these proteins in the living brain, allowing earlier diagnosis[2], and the differentiation among dementia-related diseases[3]. Detection of these proteins, previously discovered in autopsied brain tissue, can also be found in cerebrospinal fluid and blood, improving accessibility and cost for wider use of biomarkers to track disease progression. This way, they can be relied upon for early diagnosis, prevention, and definitive diagnosis before death, leading to better treatment. Another benefit that impacts patients' and families' lives is that this knowledge leads to new drug discovery to prevent or stop disease progression effectively.

Magnetic resonance imaging (MRI) can also show brain atrophy when the brain shrinks due to neurodegeneration (loss of neuronal cells). In the image below, you can appreciate normal changes in older individuals (CN), compare them to mild changes when cognitive impairment is present (aMCI), and compare them to a severe case of brain atrophy in an Alzheimer's disease case (AD).



Vemuri & Jack, 2010[4]

These discoveries, among numerous others, are remarkable achievements that have facilitated the development of genetic tests for earlier diagnosis, preventive strategies, counseling, and personalized care, all made possible through brain donations. The challenges in deciphering the intricacies of disease mechanisms have not stopped progress, which has been remarkable. We endeavor to unravel these mysteries through unwavering dedication and collaborative efforts, identifying biomarkers for early diagnosis and disease progression monitoring and molecular targets crucial for drug discovery. In doing so, our overarching goal is to alleviate the burden of disease and enhance the quality of life for both current patients and future generations.

Link to ALZ Association brochure https://www.alz.org/alzheimers-dementia/facts-figures

[1] Graff-Radford J, Yong KXX, Apostolova LG, Bouwman FH, Carrillo M, Dickerson BC, Rabinovici GD, Schott JM, Jones DT, Murray ME: New insights into atypical Alzheimer's disease in the era of biomarkers. Lancet Neurology 2021, 20:222-34.
[2] Cho H, Mundada NS, Apostolova LG, Carrillo MC, Shankar R, Amuiri AN, Zeltzer E, Windon CC, Soleimani-Meigooni DN, Tanner JA, Heath CL, Lesman-Segev OH, Aisen P, Eloyan A, Lee HS, Hammers DB, Kirby K, Dage JL, Fagan A, Foroud T, Grinberg LT, Jack CR, Kramer J, Kukull WA, Murray ME, Nudelman K, Toga A, Vemuri P, Atri A, Day GS, Duara R, Graff-Radford NR, Honig LS, Jones DT, Masdeu J, Mendez M, Musiek E, Onyike CU, Riddle M, Rogalski EJ, Salloway S, Sha S, Turner RS, Wingo TS, Wolk DA, Koeppe R, Iaccarino L, Dickerson BC, La Joie R, Rabinovici GD, Consortium L: Amyloid and tau-PET in early-onset AD: Baseline data from the Longitudinal Early-onset Alzheimer's Disease Study (LEADS). Alzheimers Dement 2023, 19 Suppl 9:S98-S114.
[3] Lowe VJ, Lundt ES, Albertson SM, Przybelski SA, Senjem ML, Parisi JE, Kantarci K, Boeve B, Jones DT, Knopman D, Jack CR, Jr., Dickson DW, Petersen RC, Murray ME: Neuroimaging correlates with neuropathologic schemes in neurodegenerative disease. Alzheimers Dement 2019, 15:927-39.
[4] Vemuri P, Jack CR, Jr.: Role of structural MRI in Alzheimer's disease. Alzheimers Res Ther 2010, 2:23.