cardiovascular disease, hypertension, cerebrovascular disease, and high cholesterol). Results: A total of 5,847 patients have a diagnosis of Alzheimer's disease (AD), and 7,729 have vascular dementia (VaD). The median survival time, calculated based on the Kaplan-Meier estimator, for patients with dementia of any kind, AD, and VaD were 1163, 2448, and 1268 days, respectively. Compared with the control group, the raw and adjusted hazard ratios for dementia were 2.78 (95% CI, 2.71-2.84) and 1.14 (1.13-1.17), respectively. Conclusions: Median survival times were much lower than figures reported by other regions and in screened populations. The high risk of death may be an indicator of late diagnosis and hence call for promoting early diagnosis to ensure timely intervention.

THE RELATIONSHIP OF APOE ε4 TO THE RELATIVE TIMES AND HAZARDS OF DEMENTIA

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Although APOE ε4 is an established risk factor for dementia, it is unclear whether it is associated with elevated risk or earlier symptom onset. Longitudinal study of 10,400 white-race individuals in the ARIC cohort followed from age 60 to incident dementia diagnosis, death, or censoring. All-cause dementia was defined using standardized algorithms incorporating longitudinal cognitive change, proxy report, and hospital or death certificate dementia codes. Death was ascertained via the National Death Index and death certificates. We used a parametric mixture of generalized gamma distributions to simultaneously estimate the distribution of event times and the proportion of individuals who experience each outcome (i.e., dementia and its competing risk, dementia-free death) by APOE ε4 status (≥ 1 allele vs. no alleles). Age-adjustment was through use of age as the time scale. APOE ε4 carrier status was associated with a doubling of the overall frequency of dementia incidence to 25% compared to 13% ($p < 0.001$) in non- ε4 carriers. The distributions of time to dementia was modified by APOE ε4 status ($p=0.007$): median time to dementia onset among APOE ε4 carriers was 81.9 years compared to 83.3 years in non-APOE ε4 carriers ($p = 0.005$). No differences in results were found by sex. APOE ε4 carrier status is associated with both elevated risk and earlier time to dementia onset. These findings clarify the causal role of APOE in dementia etiology, could help better identify at-risk subgroups, and may help facilitate better research recruitment.

SESSION 3080 (SYMPOSIUM)

MECHANISMS OF COGNITIVE AND NEUROLOGICAL AGING

Chair: Catherine Kaczorowski, *The Jackson Laboratory, Bar Harbor, Maine, United States*

This session will focus on recent advances in understanding how biological aging impacts neurological function and risk of developing age-related neurodegenerative diseases.

MECHANISMS OF BRAIN REJUVENATION

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A growing body of work has shown that systemic manipulations, such as heterochronic parabiosis and young blood administration, can partially reverse age-related cellular impairments and loss of cognitive faculties in the aged brain. These studies have revealed an age-dependent bi-directionality in the influence of the systemic environment indicating anti-aging factors in young blood elicit rejuvenation while pro-aging factors in old blood drive aging. It has been proposed that introducing anti-aging factors or mitigating the effect of pro-aging factors may provide effective strategies to rejuvenate aging phenotypes. Despite this potential, much is unknown as to the systemic and molecular mechanisms regulating anti-aging and pro-aging effects of blood-borne factors. I will discuss work from my research group that begins to provide mechanistic insight into the systemic and molecular drivers promoting rejuvenation in the aging brain.

JUMP AROUND, JUMP AROUND: TRANSPOSABLE ELEMENT ACTIVATION IN NEURODEGENERATIVE TAUOPATHY

Bess E. Frost,[1] Wenyan Sun,[1] Hanie Samimi,[2] and Habil Zare[1], *1. University of texas health san antonio, San Antonio, Texas, United States, 2. Texas state university, San Marcos, Texas, United States*

Transposable elements, or "jumping genes," constitute ~45% of the human genome. We have identified transposable element activation as a key mediator of neurodegeneration in tauopathies, a group of disorders that are pathologically defined by deposits of tau protein in the brain. Cellular defenses that limit transposable element mobilization include 1) formation of silencing heterochromatin and 2) generation of piwi-interacting RNAs (piRNAs) that clear transposable element transcripts. Using genetic approaches in Drosophila models of tauopathy, we find evidence for a causal relationship between tau-induced heterochromatin decondensation and piRNA depletion, transposable element mobilization, and neurodegeneration. 3TC, an FDA-approved inhibitor of reverse transcriptase, suppresses transposable element mobilization and neuronal death in tau transgenic Drosophila. We detect a significant increase in transcripts of the human endogenous retrovirus class of transposable elements in postmortem human Alzheimer's disease brains. Our data identify transposable element activation as a conserved, pharmacologically targetable driver of neurodegeneration in tauopathy.

MULTI-OMICS ANALYSIS IDENTIFIES GENE NETWORKS ASSOCIATED WITH COGNITIVE AGING AND ALZHEIMER'S DISEASE

Catherine Kaczorowski,[1] Sarah Heuer,[1] Chris Gaiteri,[2] and Catherine Kaczorowski[1], *1. The Jackson Laboratory, Bar Harbor, Maine, United States, 2. Rush University, Chicago, Illinois, United States*