Amy Borenstein - selected references

1 Borenstein, A. R., Wu, Y., Bowen, J. D., McCormick, W. C., Uomoto, J., McCurry, S. M. et al. (2014). Incidence rates of dementia, Alzheimer disease, and vascular dementia in the Japanese American population in Seattle, WA: the Kame Project. *Alzheimer Disease and Associated Disorders, 28,* 23-29.
Notes: There are few studies on the incidence of dementia in representative minority populations in the United States; however, no population-based study has been conducted on Japanese American women. We identified 3045 individuals aged 65+ with at least 1 parent of Japanese descent living in King County, WA in the period 1992 to 1994, of whom 1836 were dementia-free and were examined every 2 years (1994 to 2001) to identify incident cases of all dementias, Alzheimer disease (AD), vascular dementia (VaD), and other dementias. Cox regression was used to examine associations with age, sex, years of education, and apolipoprotein (APOE)-epsilon4. Among 173 incident cases of dementia, the overall rate was 14.4/1000/y, with rates being slightly higher among women (15.9/1000) than men (12.5/1000). Rates roughly doubled every 5 years for dementia and AD; the age trend for VaD and other dementias was less consistent. Sex was not significantly related to incidence of dementia or its subtypes in adjusted models. There was a trend for an inverse association with increasing years of education. APOE-epsilon4 was a strong risk factor for all dementias [hazard ratio (HR)=2.89; 95% confidence interval (CI), 1.88-4.46], AD (HR=3.27; 95% CI, 2.03-5.28), and VaD (HR=3.33; 95% CI, 1.34-8.27). This study is the first to report population-based incidence rates for both Japanese American men and women

2 Borenstein, A. R., Copenhaver, C. I., & Mortimer, J. A. (2006). Early-life risk factors for Alzheimer disease. *Alzheimer Disease and Associated Disorders, 20,* 63-72.
Notes: Research findings obtained over the past 20 years suggest that Alzheimer disease (AD) may have its origins in early life. In this review, we consider the evidence for early-life risk factors for this illness. We propose that risk factors that predict neuropathology are largely distinct from those related to the clinical expression of Alzheimer disease. Early-life risk factors for pathology include genes, chromosomal abnormalities, head injury, insulin resistance, and inflammation. With regard to risk factors for clinical expression of Alzheimer disease, six general groups of childhood exposures are reviewed: (1) perinatal conditions, (2) early-life brain development, (3) early-life body growth, (4) early-life socioeconomic conditions, (5) environmental enrichment, and (6) cognitive reserve. The literature reviewed suggests that risk of Alzheimer disease is probably not determined in any single time period but results from the complex interplay between genetic and environmental exposures throughout the life course. Enhancement or preservation of brain or cognitive reserve could delay the onset of Alzheimer disease and in some cases prevent the disease from occurring altogether

3 Borenstein-Graves, A., Mortimer, J. A., Bowen, J. D., McCormick, W. C., McCurry, S. M., Schellenberg, G. D. et al. (2001). Head circumference and incident Alzheimer's disease: modification by apolipoprotein E. *Neurology, 57,* 1453-1460.
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BACKGROUND: The clinical expression of AD likely occurs when the accumulation of degeneration in specific brain regions leads to the descent below a critical threshold of "brain reserve" beyond which normal cognitive function cannot be maintained. The association between head circumference (HC), a measure of brain reserve, and the incidence of probable AD was examined in a large nondemented cohort that has been followed since 1992 and its modification by APOE epsilon 4 genotype. METHODS: Fifty-nine incident cases of probable AD were identified from 1,869 initially nondemented individuals seen at the baseline examination (1992 to 1994) and followed for a mean of 3.8 years. Variables measured at baseline included age, education, gender, HC, height, weight, and score on the National Adult Reading Test-Revised. APOE was genotyped at the time of the first biennial examination (1994 to 1996) and was available for 1,111 individuals in the cohort. Cox proportional hazard regression was performed to estimate hazard ratios (HR) for probable AD for HC and other covariates.

RESULTS: Incident cases were significantly older, less educated, shorter, and lighter, had lower estimated verbal IQ scores, and were more likely to have at least one APOE epsilon 4 allele than unaffected individuals. The HR associated with the lowest tertile of HC (<21.4 inches) adjusted for education, gender, and APOE epsilon 4 was 2.3 (95% CI 0.7 to 6.9, p = 0.16). The HR for one or two APOE epsilon 4 alleles was significant (HR = 4.8, 95% CI 1.8 to 12.9, p = 0.002). The combination of low HC and APOE epsilon 4 strongly predicted earlier onset of AD with HR = 14.1 (95% CI 3.0 to 65, p = 0.0007). CONCLUSIONS: Smaller HC, in the presence of the APOE epsilon 4 allele, hastens the age at onset of AD. These results support the brain reserve hypothesis and its importance in precipitating the clinical expression of AD among genetically predisposed individuals