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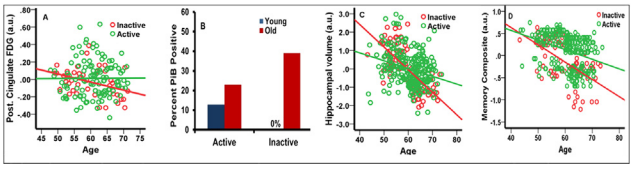
ALZHEIMER'S IMAGING CONSORTIUM (IC)
IC-01
LIFESTYLE AND RISK FACTORS

IC-01-01 PHYSICAL ACTIVITY MODIFIES ALZHEIMER'S BIOMARKERS IN PRECLINICAL AD: EVIDENCE FROM THE WISCONSIN REGISTRY FOR ALZHEIMER'S PREVENTION

Ozioma Okonkwo[1], Jennifer Oh[2], Stephanie Schultz[2], Jordan Larson[2], Dorothy Farrar Edwards[3], Dane Cook[4], Rebecca Koscik[5], Maritza Dowling[6], Catherine Gallagher[2], Cynthia Carlsson[7], Barbara B. Bendlin[8], Asenath LaRue[5], Howard Rowley[2], Brad Christian[4], Sanjay Asthana[9], Bruce Hermann[10], Sterling Johnson[11], Mark A. Sager[12], *[1]UW-Madison, Madison, Wisconsin, United States; [2]Wisconsin Alzheimer's Disease Research Center, Madison, Wisconsin, United States; [3]University of Wisconsin Madison, Madison, Wisconsin, United States; [4]UW Madison, Madison, Wisconsin, United States; [5]University of Wisconsin-Madison, Madison, Wisconsin, United States; [6]University of Wisconsin-Madison, Middleton, Wisconsin, United States; [7]University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin, United States; [8]University of Wisconsin-Madison, Madison, Wisconsin, United States; [9]UW Section of Geriatrics/Gerontology, Madison, Wisconsin, United States; [10]UW, Madison, Wisconsin, United States; [11]VA GRECC, Madison, Wisconsin, United States; [12]University of Wisconsin School of Medicine, Madison, Wisconsin, United States. Contact e-mail: ozioma@medicine.wisc.edu*

Background: Without effective therapies, the number of persons living with Alzheimer's disease (AD) is projected to increase exponentially owing to the rapid growth in the elderly segment of the United States' population. To thwart this public health epidemic that AD is poised to become, there is a critical need to uncover preventative approaches capable of curbing the progression of the underlying disease process and thereby delaying the onset of overt symptoms. This study examined whether engagement in physical activity might favorably alter the age-dependent evolution of AD-related brain and cognitive changes in a cohort of at-risk, late-middle-aged adults. **Methods:** Three hundred and seventeen enrollees in the Wisconsin Registry for Alzheimer's Prevention (age= 60.29±6.29 years, 68% women, 40% APOE4 carriers, and 74% with family history of AD) underwent T1 MRI; and a subset also underwent PiB-PET (n=186) and FDG-PET (n=152) imaging. Their responses on a self-report measure of current physical activity were used to compute MET-hours/week scores. These scores were then used to classify the participants as either Physically Active or Physically Inactive based on American Heart Association guidelines. The participants also completed a comprehensive neuropsychological battery that assessed 6 domains: Immediate Memory, Verbal Learning & Memory, Working Memory, Speed & Flexibility, Visuospatial Ability, and Verbal Ability. Regression analyses were used to test whether the known effect of age on AD biomarkers and cognition was modified by physical activity, after controlling for relevant covariates. **Results:** There were significant age–physical activity interactions for hippocampal volume (p=.025), amyloid burden (p=.015), and glucose metabolism (p=.015) such that, with advancing age, Physically Active individuals had reduced hippocampal degeneration, slower accumulation of amyloid, and attenuated glucose hypometabolism compared with the Physically Inactive. Similar age–physical activity interactions were also observed on cognitive domains of Immediate Memory, Visuospatial Ability, and Verbal Ability. **Conclusions:** In a middle-aged, at-risk cohort, engagement in physical activity is associated with an attenuation of the deleterious influence of age on key AD biomarkers. Randomized controlled trials in such risk-enriched cohorts, with longitudinal follow up, would help clarify the extent to which midlife participation in structured physical exercise protects against the development of AD and related disorders in later life.



Age-associated glucose hypometabolism (a), amyloid deposition (b), hippocampal shrinkage (c), and memory decline (d) are attenuated in physically-active subjects but pronounced in inactive subjects. P values for interaction are .025, .015, .015, .042 respectively.

IC-01-02 AMYLOID ACCUMULATION IN EARLY AND MIDDLE ADULTHOOD: THE IMPACT OF LIFE EXPERIENCE

Michelle E. Farrell[1], Gerard Nisal Bischof[1], Kristen M. Kennedy[1], Karen M. Rodrigue[1], Michael Devous[2], Denise C. Park[1], *[1]University of Texas at Dallas, Dallas, Texas, United States; [2]Avid Radiopharmaceuticals, Philadelphia, Pennsylvania, United States. Contact e-mail: michelle.farrell1@utdallas.edu*

Background: Increasing evidence indicates that lifestyle factors such as high levels of education and lifetime cognitive activity predict lower levels of amyloid deposition in healthy older adults, suggesting these experiences may confer protection against accumulation. Little is known, however about amyloid in young and middle age. We assessed whether there were reliable increases in amyloid deposition in 266 healthy adults from 30 to 89, and primarily focused on identifying variables that predicted amyloid accumulation in those aged 30 to 59. **Methods:** Data were analyzed from a sample of 266 healthy adults, aged 30-89 from the Dallas Lifespan Brain Study who received PET with florbetapir. Eight bilateral ROIs were normalized to cerebellar hemispheres to estimate the mean cortical standardized uptake value ratio (SUVR). Twenty eight subjects with elevated amyloid were isolated using an iterative outlier method. Using GLM, age, education, lifetime cognition, and APOE 4 carrier status were used to predict mean cortical SUVR in separate samples of non-elevated middle aged adults 30-59 (n=81), non-elevated older adults aged 60-89 (n=157) and all older adults including those with elevated amyloid (n = 176). **Results:** We found that age, APOE 4 status and lifestyle variables had the strongest effects on non-elevated amyloid in middle age. Most notably, higher age (p<.001) and low lifetime cognition in 4 carriers (p=.001) predicted higher SUVR in the middle-aged group. In older adults without elevated SUVR, only trend significant effects of lifetime cognition (p=.06) and a lifetime cognition x Education interaction (p=.056) were detected. If elevated SUVR subjects were included, age, APOE, education and lifetime cognition all interactively predicted SUVR, most notably with increasing amyloid across age for older adults with low but not high lifetime cognition (p<.001). **Conclusions:** Meaningful amounts of amyloid begin to accrue in middle-aged adults and accumulation is modified by both genetics and experiences, despite no evidence for accumulation at "preclinical" amyloid levels. These results suggest that amyloid systematically increases in vulnerable individuals beginning in young adulthood and that early experiences could modify accumulation and play a key role in delaying dementia onset.