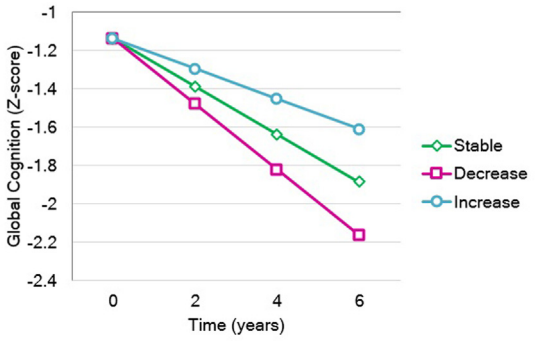

Figure 1. Fitted trajectories displaying global cognition scores over time for women with a mean BMI at baseline (i.e., BMI = 27.05) whose BMI remained stable, decreased, or increased across over time.

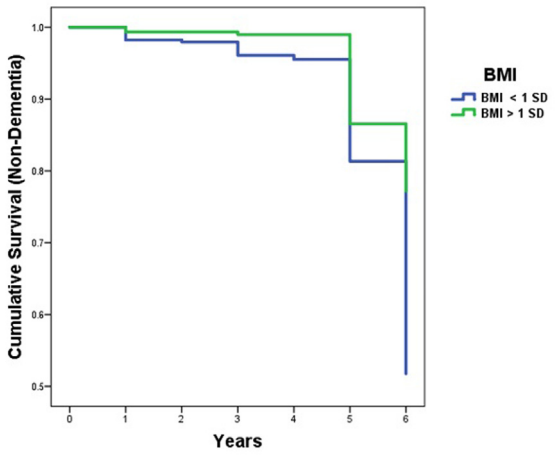

Figure 2. Risk of dementia in men with a baseline BMI 1 SD below and above the mean BMI, obtained from Life Table analysis.

current BMI alone, may be used as a marker of impending cognitive decline in elderly women, whereas current BMI may be used as a marker of prospective dementia in elderly men.

P3-557 ASSOCIATIONS OF PITUITARY-OVARIAN HORMONES AND BRAIN STRUCTURE IN RECENTLY MENOPAUSAL WOMEN USING HORMONE THERAPY

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Background: Treatment with oral conjugated equine estrogen (oCEE) or transdermal 17 β-estradiol (tE2) in recently menopausal women influences the longitudinal increase in white matter hyperintensity volumes on MRI. The relationship of changes in pituitary-ovarian hormone levels during menopausal hormone therapies and the change in white matter hyperintensities (WMH) is unknown. **Methods:** Cognitively healthy women aged 42 - 56 years and within 6-36 months of their last menstrual period enrolled in the Kronos Early Estrogen Prevention Study (KEEPS) were randomized to 4 years of 0.45 mg/d o-CEE daily, 50 µg/d tE2 weekly or placebo pills and patches. Women in the active treatment groups also received oral 200 mg/d micronized progesterone for the first 12 d of each month to protect the uterus. Estradiol (E1), estrone (E2), and follicle stimulating hormone (FSH) were measured by high sensitive liquid chromatography/mass spectroscopy from serum samples collected at baseline prior to randomization and 48 months after randomization. MRIs were also performed at baseline and month 48 (N = 78). The longitudinal change in WMH volume was determined from FLAIR MRIs using a semi-automated image segmentation algorithm. **Results:** No statistically significant associations between FSH, E1 or E2 levels and WMH were found at baseline. During the four years of menopausal hormone therapies, the greater the longitudinal decline in FSH in the tE2 group the lesser the longitudinal increase in WMH volume. In both the tE2 and oCEE groups, the greater the longitudinal increase in E1, the lesser the increase in WMH volume. A similar pattern, which did not reach statistical significance, was observed between increases in E2 and increases in WMH in the tE2 group (Table 1). **Conclusions:** Changes in circulating levels of pituitary-ovarian hormone during menopausal hormone therapies may partially explain the changes in WMH volume in recently menopausal women. Long term follow up in a larger cohort of women measuring all pituitary-ovarian hormones would further clarify these relationships.

Table 1. Pearson's correlations (p-values) between total change in WMH volumes and total changes in hormones levels

	oCEE (n = 23)	tE2 (n = 24)	Placebo (n = 31)
FSH	0.29 (0.18)	0.47 (0.02)	-0.11 (0.56)
E1	-0.44 (0.03)	-0.42 (0.04)	0.19 (0.30)
E2	-0.20 (0.35)	-0.39 (0.06)	0.10 (0.59)

P3-558 EXPOSURES PRIOR TO AGE 16 ARE ASSOCIATED WITH DEMENTIA STATUS IN THE HEALTH AND RETIREMENT STUDY

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Background: Alzheimer's disease (AD) is a prevalent neurodegenerative disease with risk attributed to both genetic and environmental factors. The environmental etiology of AD is not well characterized, and the relevant exposure window of susceptibility is likely prior to symptom onset. Environment in the early life period has not yet been comprehensively tested for association with later life dementia. **Methods:** In the U.S. nationally representative Health and Retirement Study (HRS) (n=16,316; 2010 wave) we examined 23 exposures occurring prior to age 16 via retrospective questionnaire. We tested for associations between exposures and dementia status (dementia, cognitively impaired non-demented, cognitively normal) using proportional odds models. **Results:** Depression prior to age 16 was associated with 2.38 (95% confidence interval (CI): 1.66, 3.41) times higher odds of dementia in later life and 1.91 (95% CI: 1.55, 2.34) times higher odds of cognitive impairment. Headaches or migraines prior to age 16 was associated with 1.53 (95% CI: 1.16, 2.01) times higher odds of dementia in later life and 1.63 (95% CI: 1.41, 1.90) times higher

odds of cognitive impairment. High blood pressure prior to age 16 was associated with 2.76 (95% CI:1.06, 7.19) times higher odds of dementia in later life and 2.68 (95% CI: 1.54, 4.67) times higher odds of cognitive impairment, even after adjusting for current blood pressure. All reported odds ratios are relative to normal cognition. **Conclusions:** Exposures occurring in early life or conditions originating in early life may be important risk factors for later onset of dementia. Though we exclude participants with cognitive impairment at time of questionnaire, longitudinal research may be subject to challenges related to recall of information and differential survival.

P3-559 APATHY IS ASSOCIATED WITH RISK OF INCIDENT DEMENTIA AMONG COMMUNITY-DWELLING OLDER ADULTS

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Background: Neuropsychiatric symptoms (NPS) are common in the clinical phase of dementia. Apathy is the most prevalent NPS in all dementia subtypes and may be an important prodromal sign associated with progression to dementia, yet this has not been rigorously investigated in a population-based sample. **Methods:** We studied 2023 participants from the Health, Aging, and Body Composition (Health ABC) study, a prospective cohort study of community-dwelling white and black older adults. The modified Apathy Evaluation Scale (5 self-reported items with total score 0-15) was administered at year 6, our study baseline. We divided patients into tertiles based on symptoms of low, moderate, or severe apathy. Prevalent dementia was excluded and incident dementia was measured through Year 15, determined by dementia medication use, hospital records, or significant cognitive decline on global cognition ($\geq$ 1.5 SD race-specific decline on the Modified Mini-Mental State Examination). We used ANOVA and Chi Squared tests to examine differences in baseline demographics by apathy severity. We examined the association between baseline apathy group and incident dementia using a logistic regression model with low apathy as a reference. We then adjusted the model for age, gender, race, years of education, and comorbid depression (measured by the Center for Epidemiologic Studies Depression Scale). **Results:** In the cohort, 743 participants (37%) reported moderate symptoms and 509 participants (25%) reported severe symptoms of apathy. There were 381(18%) cases of incident dementia over 9 years of follow-up. At baseline, greater apathy was associated with non-white race ($p<0.001$), fewer years of education ($p<0.001$), tobacco use ($p=0.005$), higher body mass index ($p=0.01$), and depression ($p<0.001$). Moderate apathy (OR 1.4, 95% CI 1.1-1.9) and severe apathy (OR 1.9, 95% CI 1.5-2.6) were associated with an increased risk of incident dementia in unadjusted models. In adjusted models, severe apathy was associated with an increased risk of incident dementia (25% vs. 14%, OR 1.5, 95% CI 1.1-2.1). **Conclusions:** In a diverse cohort of community-dwelling adults, apathy was associated with increased risk of developing dementia. A brief assessment of apathy may have clinical utility in risk stratifying the elderly for progression to dementia.

P3-560 THE ROLES OF ANXIETY AND FAMILY HISTORY OF DEMENTIA IN INFLUENCING SUBJECTIVE COGNITIVE DECLINE IN MIDDLE-AGED ADULTS FROM THE HEALTHY BRAIN PROJECT

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Background: Older adults with a first-degree family history of Alzheimer's disease report greater subjective cognitive decline (SCD). Further, it has been suggested that personal experience with Alzheimer's disease (AD) can influence one's perceived risk of disease and own memory changes. Previous research shows SCD is very closely associated with mood symptoms in older adults. Little is known about these relationships in middle aged adults, a group likely to be caring for parents with dementia. The aim of this study was to investigate the roles of self-reported anxiety and family history of Dementia in predicting SCD severity in healthy middle aged adults. **Methods:** Participants (n=1384) aged 40-70 enrolled in the Healthy Brain Project reported whether they have an immediate family history of dementia. They also completed the Depression Anxiety and Stress Scale (DASS) and the Cognitive Function Instrument (CFI; Amariglio et al., 2015). Regression analyses and a chi square test of independence were conducted. **Results:** There was no relationship between family history of dementia and the total score of SCD self-rated on the CFI. However, a chi square revealed an association between family history and an individual item related to worry about memory and thinking abilities (X^2=5.08, p=.024). A regression analysis, including age and sex as covariates, indicated a significant relationship between anxiety and SCD (β= 0.961, p <.001). No interaction between anxiety and family history on SMC was found. **Conclusions:** Although middle-aged adults with a family history of dementia were not more likely to self-report more severe memory deficits, they still acknowledged greater concern, a core component of the SCD plus criteria (Jessen et al., 2014). As such, these findings support the notion that objective cognitive decline,