CVs <3%). At baseline and 7-year follow-up visits, physical function was measured using the Short Physical Performance Battery (score 0-12), which consists of gait speed, balance, and chair-rise tests. Grip strength was measured using a handheld dynamometer. The association between log-transformed P3NP and physical function was examined using Generalized Estimating Equations adjusted for familial relatedness, age, sex, height, weight, lifestyle characteristics, chronic disease prevalence and inflammatory cytokines. Participants were aged 73.1 ± 15.2 years, 54% female, had a BMI of 26.6 ± 4.3 kg/m2, and a gait speed of 1.0 ± 0.3 m/s. One standard deviation higher P3NP concentration was related to worse baseline SPPB score (β=-0.9points), gait speed (β=-0.05m/s), chair-rise time (β=8.34seconds), and grip strength (β=-2.0kg; all p<0.001). Higher P3NP concentration was also associated with greater declines in gait speed (β=-1.41, p<.001) and chair-rise performance (β=0.41, p<.001). Plasma P3NP concentration may be a strong, novel biomarker of current and physical function changes with aging. Future research is needed to extend our findings to a larger population, and determine the mechanisms underlying these associations.

STRESSFUL LIFE EVENTS AND INFLAMMATION IN MIDLIFE: COMPARING ASSOCIATIONS WITH SUPAR, CRP, AND IL-6

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Stressful life events are associated with poorer health, but the physiological mechanisms of this association are unclear. One mechanism that might play a role in this association is systemic inflammation. Using participants (n=828) from the Dunedin Longitudinal Study, we studied the association of stressful life events and inflammation from age 32 to 45. Inflammation was assessed using C-reactive protein (CRP), interleukin-6 (IL-6), and suPAR. We examined associations between stressful life events and systemic inflammation, as well as whether adverse childhood experiences (ACEs) moderated these associations. More adult stressful life events were associated with greater suPAR at age 38 ($r = 0.12$, $p < .001$) and age 45 ($r = 0.19$, $p < .001$). CRP and IL-6 did not evidence consistent associations at age 38 and 45. An increase in suPAR from age 38 to 45 was associated with more stressful life events in the interim, $\beta = 0.10$, $p = .001$. SuPAR at age 45 was independently associated with both childhood ACEs, $\beta = 0.20$, $p < .001$, and adult stressful life events, $\beta = 0.18$, $p < .001$. ACEs significantly moderated the association of stressful life events and suPAR at age 45, $\beta = 0.12$, $p = .001$, such that people with more childhood ACEs evidenced a stronger association between stressful life events and inflammation in midlife. These results were robust to controlling for clinical (sex, body mass, smoking) and childhood covariates (childhood IQ, SES, self-control). Systemic inflammation is one mechanism through which stressful life events could impact health.

UNINTERRUPTIBLE POWER SUPPLY IMPROVES PRECISION OF TELOMERE LENGTH MEASUREMENT VIA QPCR

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Epidemiological literature has produced robust associations between telomere length (TL) and health, wherein individuals with shorter TL are at increased risk for chronic disease and death. Even so, technical challenges associated with TL measurement have led some to question their utility as a biomarker of aging. Several pre-analytical factors influence TL assessment via qPCR including tissue source, sample storage, and DNA extraction method. Additional work has investigated how conditions within the PCR run (e.g. mastermix reagents) influences precision and reproducibility of TL measurements. However, the impact of power supply remains unclear. Momentary fluctuations in power supply can affect the functioning of high-performance electronics, including real-time thermocylers. These fluctuations can be mitigated by using an uninterruptible power source (UPS), an electronic apparatus capable of supplying constant, uninterrupted voltage to high-performance electronics. The current study investigated how using a UPS influenced TL assessment via qPCR. Standard deviation and coefficient of variation across replicates were compared for samples assessed with or without the use of a UPS. Samples run with a UPS had significantly lower standard deviation ($p<0.001$) and coefficient of variation ($p=0.002$) than those run without a UPS. Notably, neither the efficiency of exponential amplification ($p=0.674$) nor the standard curve R2 ($p=0.638$) varied as a function of UPS status. Thus, UPS status decreases variability within sample replicates while maintaining the overall quality of the qPCR assay. *The work presented was supported by the Telomere Research Network, an NIH-sponsored working-group recently established to coordinate best practices for measuring telomere length in population-based research.

SESSION 2913 (PAPER)

BIOLOGY OF AGING II

COGNITION, DEPRESSION, AND GENETICS: EXAMINING SEX DIFFERENCES USING POLYGENIC AND GENETIC INFERENCE TECHNIQUES

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Alzheimer's disease and its related dementias (ADRD) are debilitating neurodegenerative diseases. As nearly two-thirds of persons diagnosed with Alzheimer's disease are women, more research is needed to understand sex differences in the biological mechanisms that underlie ADRD. Depression is a risk factor for Alzheimer's disease and higher rates of depression among women, compared to men, suggest that depression-related phenotypes and underlying biological

factors may contribute to sex differences in ADRD. Using the Health and Retirement Study (N = 9908, European ancestry), a US panel-cohort study, the current analysis leverages Mendelian randomization techniques to assess sex-specific inferred causality of depressive symptoms on odds of dementia. All analyses assess most recent cognition and account for sex, education, study cohort, age and year of most recent cognition visit, and genetic ancestry principal components. A one standard deviation increase in depressive polygenic score was associated with 1.11 times higher odds of dementia (95% confidence interval: 1.02-1.21) relative to normal cognition. Each additional endorsed depressive symptom was associated with 1.13 times higher odds of dementia (95% confidence interval: 1.09-1.18) relative to normal cognition. Using the depression genetic instrument, a significant inferred causal relationship was observed between depressive symptoms and dementia (P=0.01, 1.73 odds ratio, 95% confidence interval: 1.12-2.67). When stratified by sex, this relationship was only significant in females (P=0.02, 1.76 odds ratio, 95% confidence interval: 1.08-2.87). These findings demonstrate that depressive symptoms are likely causally related to dementia, and this relationship is most pronounced in females.

DEPRESSION AND PSYCHOLOGICAL WELL-BEING AS DISTINCT CONSTRUCTS: MUTUALLY EXCLUSIVE ASSOCIATIONS WITH BIOMARKER

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Despite increasing emphasis on assessing the mental health of older adults, there has been inconclusive evidence on whether depression and psychological well-being (PWB) are fundamentally distinct constructs or representations of the opposite ends of the mental health spectrum. To instantiate either hypothesis, investigation of the associations between mental health scales and biomarkers have been proposed. First, we assessed depressive symptoms and PWB in community-dwelling older adults (N=59, mean age=67) using the Self-Rating Depression Scale (SDS) and Ryff's Scale of PWB (comprising six sub-scales). We measured a wide range of immune markers employing ELISA and flow cytometry. Subsequently, we used principal component analysis (PCA) to aggregate and derived biomarker factor scores. Lastly, multiple linear regressions were performed to examine the associations between the scales and the derived biomarker factor scores, controlling for covariates. PCA extracted six biomarker factors. Biomarker factor score 1 was significantly associated with PWB (β=-0.029, p=0.035) and the PWB sub-scale, self-acceptance (β=-0.089, p=0.047), while biomarker factor score 4 was significantly associated with the PWB sub-scale, purpose in life (β=-0.087, p=0.025). On the other hand, biomarker factor 6 was significantly associated with SDS (β=-0.070, p=0.008). There were mutually- exclusive associations between the scales with biomarker factor scores, supporting the hypothesis of distinct constructs. Our findings expanded the biomarkers of depression and PWB, deepening understanding of the biological underpinnings of depressive symptoms and PWB. These findings have implications in field work, since researchers could not infer one construct from the other, the examination of both constructs are essential.

LIFESTYLE COMPLEXITY AND DEMENTIA RISK: EXAMINING MODERATION BY APOE GENOTYPE AND MILD COGNITIVE IMPAIRMENT

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Prior studies suggest that the neuroprotective effect of physical exercise is moderated by APOE genotype and MCI status, but it remains unclear whether this extends to lifestyle complexity defined by a broader variety of physical, intellectual, and social activities. Participants were from the Ginkgo Evaluation of Memory (GEM) Study. We used 18 physical, intellectual, or social activities from the Lifestyle Activity Questionnaire. We performed latent class analysis to characterize subgroups with distinct activity response patterns and examined whether they have differential risk of incident dementia over time. A three-class model was chosen based on fit statistics and interpretability. Cox proportional hazards models, adjusted for potential demographic and health confounders, revealed that Class 1 (Highly intellectually/socially active) had a reduced risk of dementia compared to Class 3 (Less socially/less intellectually active; HR=.71, 95% CI: [.56,.88], p=.002). Class 2 (Socially/less intellectually active) did not differ in risk from Class 3 (HR=.90, 95% CI: [.73,1.1], p=.288). There was no evidence for effect modification for APOE e4 allele carriers (p's>.05), but the protective association for Class 1 only held for those without prevalent MCI at baseline (HR=.74, 95% CI: [.56,.98], p=.033). Results showed that subgroups characterized by a greater variety of social and intellectual activities had reduced risk for dementia, but only for those without MCI. This implies that late-life lifestyle complexity may be most neuroprotective for those in the preclinical stages of decline. Results also suggested that lifestyle complexity may act through a cognitive reserve pathway unrelated to amyloid pathology.

MIDLIFE PLASMA Aβ AND LATE-LIFE RISK OF COGNITIVE IMPAIRMENT: THE ATHEROSCLEROSIS RISK IN COMMUNITIES STUDY

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