Age is major risk factor for AD; however, relationships between aging and AD are not well understood. Decline in physiological resilience is universal feature of human aging that may also play role in AD. Aging-related pathways (such as IGF-I/P53/mTOR-mediated) that are involved in tissue resilience work in concert to decide outcomes of cell responses to stress/damage, such as survival, apoptosis, autophagy, etc. We hypothesized that interplay among genes in these pathways may influence AD risk as result of epistasis (GxG). We estimated effects of pairwise epistasis between SNPs in 53 genes from respective pathways on AD risk in the LLFS compared with other data (HRS, CHS, LOADFS). We found significant (fdr<0.05) GxG effects on AD risk in older adults across datasets. The SNP rs11765954 in CDK6 gene was involved in top GxG effects on AD in all datasets, when paired with SNPs in BCL2 and PPARGC1A. The CDK6 role in AD could be pleiotropic, depending on its activity in neurons: CDK6 expression is needed for DNA repair and neuronal survival; however, CDK6 overexpression may lead to the cell cycle reentry in postmitotic neurons resulting in apoptosis, which may contribute to neurodegeneration. CDK6 was earlier found to interfere with BCL2 effects on apoptosis, and with PPARGC1A effects on energy metabolism, which might contribute to observed GxG between these genes. We conclude that interactions among genes from biologically connected aging pathways may significantly influence AD risk. Uncovering such GxG effects has a potential to yield new genetic targets for AD prevention/treatment.

INTERGENERATIONAL TRAUMA TRANSMISSION? TEST OF CELLULAR AGING IN MOTHERS EXPOSED TO SEXUAL ABUSE AND THEIR CHILDREN

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Exposure to maltreatment during childhood can lead to increased risk for poor health outcomes in adulthood. Child maltreatment and later poor health may be linked by premature biological aging. We tested whether childhood sexual abuse (CSA) is associated with telomere length (TL) in adult females. We further tested the hypothesis of intergenerational transmission of trauma by measuring TL in both CSA-exposed and non-exposed mothers and their children. TL was measured in a subset of participants and their children from a prospective-longitudinal cohort study of sexually abused females and a demographically matched comparison group. Linear regression models were used to test for associations between CSA-exposure and age-adjusted TL in females (N=108, mean age 36.3 years). Multilevel linear models were used to test the intergenerational effect of maternal-CSA exposure on age-adjusted TL in their children (N=124 children mean age 10.5 years across 61 mothers). CSA-exposure was not associated with TL in females. Replicating previous work in this area, maternal TL and sex were significant predictors of child TL in all models tested. Longer maternal TL predicted longer TL in children, and female children had longer TL than male children. Maternal-CSA exposure did not predict TL in children. This finding is in line with some previous results on CSA and TL measured in adulthood. Previous significant results associating child maltreatment with shorter TL in adulthood may be capturing a population of individuals exposed to either multiple types of maltreatment or maltreatment in childhood with concurrent TL measurements.

METRICS OF PHENOTYPIC AGING FROM THE ENERGETICS PERSPECTIVE

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Identifying the most critical metrics of aging is an ongoing challenge due to a lack of comprehensive measurements and heterogeneity of the aging process. Using the Baltimore Longitudinal Study of Aging, we developed a conceptual framework to identify metrics of aging that capture the hierarchical and temporal relationships between functional aging, phenotypic aging, and biological aging based on four hypothesized domains: energy regulation, body composition, homeostatic mechanisms, and neurodegeneration. Focusing on the energetics domain, we examined trajectories of eight phenotypes using more than 10 years of longitudinal data. The standardized Cronbach's alpha for these variables was 0.80, providing construct validity of our concept. We further implemented item response theory to integrate these phenotypes into a summarized energy score. Linear mixed models were used to assess the cross-sectional and longitudinal associations between the summarized energy score and physical functioning as measured by gait speed and time to walk 400m as quickly as possible (number of participants ~ 811, number of observations ~ 1700). After adjusting for age, sex, weight, and height, a higher summarized energy score was independently associated with faster baseline gait speed (0.13 m/s, p<0.001) and faster 400m time (-35.3 seconds, p<0.001), and longitudinally associated with slower gait speed decline (0.08 m/s/decade, p<0.001) and slower 400m time increase (-37.8 secs/decade, p<0.001). This work demonstrates the utility of our energetics domain-based summarized score. Moving forward, it will be important to clarify relationships between this summarized score and other functional metrics and assess its generalizability to the other cohorts.

NEUTROPHIL-LYMPHOCYTE RATIO AND MORTALITY IN THE LONG LIFE FAMILY STUDY

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Neutrophil to Lymphocyte Ratio (NLR) reflects the balance between the innate (neutrophils) and adaptive (lymphocytes) immunity. Though NLR is a strong predictor of mortality in the general population, the distribution of NLR and its association with mortality has not been evaluated in families with exceptional longevity. Hence, we evaluated this question in the Long Life Family Study, a family based study of exceptional longevity. We used data from offspring of long lived (n=2065) family members and spousal controls (n=673). We used multivariate linear regression models adjusted for age, family relatedness, sex, field center, BMI and comorbidities (diabetes, CVD, cancer) to evaluate differences in NLR between long lived family members and spousal controls. Cox proportional hazard models were used to examine the association between NLR and mortality. 157 (7.6%) offspring in long lived families and 68 (10.1%) spousal controls were deceased during 12 years of follow up. NLR was similar among offspring in long lived families and spousal controls (1.96±1.06 vs.1.98±1.28; p=0.64). There was a significant positive association between NLR and overall mortality [HR: 1.3, 95% CI (1.01, 1.67)), p:0.04]. There was no statistically significant difference in this association among offspring in long lived families and spousal controls (p for interaction =0.16). The association between NLR and overall mortality was no longer significant [HR: 1.24; p:0.36] after adjustment for IL-6 and hsCRP. These results suggest that NLR may be a predictor of mortality in families with exceptional longevity though this association may not be independent of other inflammatory biomarkers.

RACIAL DIFFERENCES IN GLUCOSE HANDLING AND FUNCTION WITH OBESITY REDUCTION: PRELIMINARY FINDINGS

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Blacks have higher rates of obesity and are twice as likely to develop diabetes as non-Hispanic whites. Obesity reduction can improve metabolic health, but physical function and glucose handling may be threatened by concomitant loss of muscle mass. These preliminary findings from a 4-mo. randomized controlled trial assess the racial differences in glucose handling and physical function in obese, older adults with prediabetes (Fasting Plasma Glucose (FPG) ≥95<126 mg/dL or HbA1c 5.7-6.4%) following obesity reduction. At 4 mo. endpoint, participants (n = 31; age = 68.1±5.4 years, BMI =36.0±4.7 kg/m2) had reduced (p<0.05) body weight in both Blacks (5.1%) and Whites (4.1%); HbA1c levels were also reduced (Blacks = -0.3 ±0.3; Whites = -0.1±0.3) with no difference by race. However, FPG was reduced for Blacks compared to Whites (-7.9±9.5 vs. -2.8±6.2 mg/dL; p<0.05). Short Physical Performance Battery (SPPB) score was lower for Blacks than Whites at both baseline (9.8±1.5 vs 10.9±1.2; p<0.05) and 4 mo. (10.17±1.4 vs 11.21±1.3; p<0.05), respectively. A trend towards improvement (p=0.08) in meters walked in 6 minutes was present in both Blacks (13.3±60.8) and Whites (20.0±36.3) with no between-group difference. Interestingly, at baseline, 41% of participants said they modified their behaviors due to a fear of falling despite having a mean SPPB score of 10.3±1.5. Following the intervention, fear of falling was reduced, with 35% of the participants reporting this behavior. Our findings illustrate that modest weight loss improves glucose handling, physical function and perceived fall risk for both Black and White older adults with prediabetes.

SARC-F CAPACITY TO TRACKING SARCOPENIA IN WOMEN FROM MANAUS-AM

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This study aimed to analyze the performance of SARC-F for the identification of sarcopenia in women from Manaus. For the analysis of the performance of the SARC-F, the criteria defined by the EWGSOP (2018) and the SDOC (2019) were considered. The sample consisted of 236 women aged 66.27±5.76 years. In addition to the SARC-F, a dynamometer was used to assess the muscle strength and gait speed was determined on a 2.44 m course. To identify sarcopenia, the following cut-off valueswere used: SARC-F ≥ 4 points; grip strength: EWGSOP <27kg for men and 16kg for women, SDOC <35.5kg for men and <20.0 kg for women; grip over body mass index (BMI, kg/m2) <1.05 for men and 0.79 for women; grip over body weight (BW, kg) <0.45 for men and <0.34 for women; gait speed ≤ 0.8 m/s for both men and women. The results revealed a prevalence of sarcopenia in 54% of the sample. The Kappa statistic intended to analyze the agreement between the SARC-F and the grip strength, the grip strength corrected for BMI or for BM, and the gait speed. The cross-classification analysis showed linear weighted Kappa coefficients near 0 with exception of gait speed (0.264±0.054, agreement in 61.2% of the participants) and grip strength when the cut off is 20 kg (0.248±0.062 - agreement in 63% of the participants). Cross-classification analysis between SARC-F and objective measures of physical capacity (grip strength and gait speed) showed linear weighted Kappa coefficients with slight or fair agreement in women from Manaus.

THE ASSOCIATION OF FREEZER STORAGE TIME WITH VITAMIN K AND VITAMIN D CONCENTRATIONS IN HUMAN BRAIN TISSUE

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Vitamins K and D are present in the human brain and have been implicated in Alzheimer's disease and related dementias