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Cardiovascular risk factors (CVRFs) have been linked to depression, but it is still unclear whether this association becomes stronger or weaker from mid- to later life. Thus, our main aim was to investigate the influence of age on the associations between CRVFs and trajectories of depressed mood. Our sample included 6835 individuals (aged 52–89 years) from the English Longitudinal Study of Ageing (ELSA), who were free of manifest vascular disease at baseline and had bi-yearly measurements of depressed mood over ten years. A composite score incorporated the presence of five CVRFs: hypertension, diabetes, smoking, obesity, and hypercholesterolemia. We used second-order latent growth models to examine the effect of CVRFs, age, and their interaction on levels and changes in depressed mood over time. Our results revealed that baseline CVRFs were associated with higher levels of depressed mood. This association decreased with age and was stronger in midlife compared to later life. CVRFs were not related to changes in depressed mood, indicating that these differences remained stable over time. These findings suggest that CVRFs in midlife, but less so in older age, predict stable differences in depressed mood. They are consistent with reports on the importance of CVRFs in midlife and may support the idea that prevention of vascular burden in this age period may be critical to maintain mental health.

SESSION 10160 (LATE BREAKING POSTER)

BIOLOGY OF AGING

2-DEOXY-D-GLUCOSE-(2-DG) PREVENTS PATHOGEN DRIVEN ACUTE INFLAMMATION AND ASSOCIATED TOXICITY

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Pathogen-associated molecular patterns (PAMPs) associated with viral and bacterial infections trigger multiple inflammatory pathways which may result in oxidative stress driven toxicity, tissue fibrosis organ dysfunction and ageing. Inflammatory events need high energy demands and predominantly depends on the glycolysis. Thus, energy metabolism of the inflammatory events can be targeted to reducing the magnitude of the PAMPs driven inflammation and preventing tissue toxicity. Here we propose that 2-DG, a glycolytic inhibitor, and a potential Energy Restriction Mimetic agent (ERMA) can modulate inflammatory events and can prevent the development of acute as well as chronic pathology. For this study we induced LPS (bacterial PAMP) induced endotoxemia in mice which models infection associated inflammatory acute inflammatory events, tissue damage and organ dysfunction. 2-DG fed mice (0.4% w/v in drinking water) showed reduced LPS driven oxidative stress and capillary damage in lungs. Administration of 2-DG also reduced LPS induced spike in inflammatory cytokines (TNF, IL6 and IL1β) in the BALF and serum. Lungs of 2-DG fed mice showed lesser infiltration of inflammatory cells and reduced inflammatory signaling activation. 2-DG also downregulated the ex-vivo and in-vivo migration of the PMNCs. Furthermore, 2-DG also reduced the activation of the macrophage cells (RAW264.7) which was seen with reduction and the glycolysis and increased mitochondrial functions. Our data suggest that 2-DG administration as ERMA in drinking water can prevent pathogenic exposure driven inflammatory events which may prevent acute as well as chronic inflammatory disorders.

A DNA DAMAGE RESPONSE-INDEPENDENT MECHANISM FOR TELOMERE SHORTENING-ELICITED AGE-RELATED PATHOLOGIES

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Telomere attrition is associated with telomeropathies and age-related pathologies. In telomeropathies, telomere uncapping induces a DNA damage response (DDR) that drives apoptosis or senescence. However, a defined mechanism by which telomere attrition contributes to other age-related pathologies has not been determined. Telomere integrity is maintained by shelterin, a six-protein complex. Rap1 is the only shelterin member that is not essential for telomere capping but engages non-telomeric DNA and regulates gene transcription. We hypothesized that non-telomeric Rap1 accumulation could contribute to age-related pathologies in a DDR-independent manner. To test this, we used CRISPR/Cas9 editing to generate a Rap1 mutant mouse model in which Rap1 at telomeres is prevented, leaving only non-telomeric Rap1. Indirect immunostaining showed no differences in telomere dysfunction-induced DDR foci in Rap1 mutant compared to wild-type primary fibroblasts. Cell fractionation/western blotting of fibroblasts from Rap1 mutants demonstrated decreased Rap1 expression and Rap1 re-localization off telomeres, which mimics the same alteration of Rap1 in human cells with telomere attrition. Rap1 mutant mice exhibited increased body weight and altered metabolic and immune-response transcripts in various tissues, indicating that altered transcription could account for some of the observed phenotypes related to telomere attrition. In conclusion, telomere shortening may facilitate non-telomeric Rap1, which alters gene transcription and drives metabolic and immune dysfunction in a DDR-independent manner.

A NARRATIVE REVIEW ON THE RELATIONSHIP BETWEEN FEMALE REPRODUCTIVE FACTORS AND LONGEVITY

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