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American Heart Association's (AHA) Life's Simple 7 (LS7), an index of cardiovascular health risks, has been associated with worse brain outcomes but few examined this relationship in midlife. We examined whether LS7 scores at midlife were associated with brain morphometry in early old age. Participants were 471 men who participated in the Vietnam Era Twin Study of Aging. The LS7 index was assessed at mean age 62 (range 55-66) and 68 (range 61-71) and included smoking, physical activity, diet, body mass index, cholesterol, glucose, and blood pressure. Each factor was coded, per AHA criteria, on a 3-point scale (0/poor-2/ideal) and summed to create a composite score (0-14). At mean age 68, participants underwent structural magnetic resonance imaging, which was used to create the previously validated brain measures. Scores included: the ratio of abnormal white matter to white matter, and two Alzheimer's disease brain signatures (cortical thickness/volume signature and a mean diffusivity (MD) signature). Analyses controlled for age, education, income, ethnicity, and APOE genotype. Concurrently at mean age 68, the LS7 was associated with cortical thickness/volume ( $F=4.85$ ,  $p = .028$ ), MD ( $F=10.89$ ,  $p = .001$ ) signatures and abnormal white matter ratio ( $F=14.04$ ,  $p < .001$ ). Prospectively, the LS7 at mean 62 was significantly associated with age 68 cortical thickness/volume ( $F=5.08$ ,  $p = .025$ ) and MD ( $F=5.54$ ,  $p = .019$ ) signatures but not with abnormal white matter ratio. These results suggest that prevention strategies that promote heart healthy behaviors could have implications for healthy brain aging.

#### CONSEQUENCES OF GENOMIC DNA MONO-RIBONUCLEOTIDES FOR CHROMOSOMAL STABILITY

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Mono-ribonucleotides are building blocks for polynucleotide RNA chains (e.g., messenger RNA), but if misincorporated into duplex DNA can cause mutagenesis and chromosomal instability. During DNA synthesis by Pol  $\gamma$ , remnants of unremoved RNA primers contribute to elevated mono-ribonucleotide triphosphates resulting in nucleotide pool imbalance, ultimately favoring mis-incorporated ribonucleotides during replication. Moreover, although polymerases generally replicate DNA with high fidelity, the steric gate occasionally allows a mis-incorporated ribonucleotide. Thus, a mono-ribonucleotide is one of the most abundant lesions in genomic DNA of eukaryotes. If unremoved from double-stranded DNA, the ribonucleotide exerts negative effects on replication, transcription, and genomic maintenance, with lasting effects on cellular homeostasis. Even a single ribonucleotide in telomeric DNA comprises shelterin binding and telomere capping causing vulnerability to spontaneous hydrolysis which potentiates telomere shortening. Consistent with this, a ribonucleotide positioned in double-helical DNA alters its structure by torsionally distorting the sugar-phosphate backbone. Fortunately, cellular response and repair pathways exist to help cells cope with mis-incorporated mono-ribonucleotides. The Ribonucleotide Excision Repair

(RER) or a Topoisomerase 1 (Top1)-mediated pathway remove embedded ribonucleotides. For RER, RNase H2 incises 5' of a mono-ribonucleotide, creating an access point for its removal. If cells are deficient in RNase H2, Top1 initiates removal of the ribonucleotide. However, Top1 is less accurate than RNase H2, which can lead to mutagenesis. Studying the mechanisms in which ribonucleotides are incorporated into DNA or further metabolized should provide insight to their negative consequences for chromosomal integrity, cancer, and auto-immune disease attributed to a genetic deficiency of RNase H2.

#### CONSEQUENTIAL IMPACTS OF TOBACCO USE ON COGNITIVE PERFORMANCE

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Tobacco use represents a pernicious lifestyle factor that may influence processes of aging, including cognitive functioning. As individuals tend to start smoking before adulthood, it may serve as an important factor in cognitive development and maintenance. We explored smoking history-cognition associations in a sample approaching midlife. Study data was derived from the Colorado Adoption/Twin Study of Lifespan behavioral development and cognitive aging (CATSLife 1;  $N = 1195$  [53% F];  $\bar{x}$ age = 33.2 years,  $SD = 5.0$ ). All cognitive measures were t-scored covering working memory, spatial reasoning, processing speed (WAIS-III Digit Span, Block Design, and Digit Symbol, and Colorado Perceptual Speed) and episodic memory domains (Picture Memory, immediate and delayed). Tobacco use measures included ever-smokers, current-smokers, and log-transformed packyears. Mixed-effects regression models were applied, accounting for sex, age, race, ethnicity, and clustering among siblings. Tobacco use was associated with worse episodic memory, spatial and speed performance, but not working memory. When educational attainment was included, patterns remained consistent though attenuated. Results suggested current-smokers scored 0.27 to 0.36 SD lower than non-smokers on speed and spatial reasoning tasks. Episodic memory performance was reduced by approximately 0.07 to 0.1 SD per log packyear. In a sample approaching midlife, the harmful impacts of tobacco use on cognitive performance may be already apparent with cumulative impacts of packyears on episodic memory and current smoking associated with spatial and speed performance. This work helps to elucidate the temporal associations of an important lifestyle factor that may influence cognitive functioning prior to midlife.

#### COVID-19 RELATED MEDIA CONSUMPTION AND MENTAL HEALTH IN OLDER ADULTS

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At the beginning of the COVID-19 pandemic, consuming media was critical to identify precautionary behaviors to reduce the spread of the virus, particularly for older adults.