78th AAN ANNUAL MEETING ABSTRACT

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Abstract Title: Improvements in Biological Age Acceleration Lead to Better Neuroimaging, Clinical, and Cognitive Markers of Brain Health

Press Release Title: Improving your biological age gap is associated with better brain health

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Objective: We tested whether biological age acceleration (BAA) and improvements in BAA were associated with subsequent MRI markers of small vessel disease, cognition, and stroke.

Background: BAA, the discrepancy between chronological and biological age, captures multisystem aging and is associated with adverse neurological outcomes. Whether improving BAA leads to future brain health benefits remains unknown**.**

Design/Methods: KDmAge, a biological age measure built from 18 routine blood biomarkers, was derived at baseline (T0) for 258,169 UK Biobank participants (mean age: 56, mean KDmAge: 54, 53% female) and at the repeat visit (T1) (n=6,085, age: 62, KDmAge: 58, 50% female). BAA was obtained by residualizing KDmAge on chronological age. Exposures were baseline BAA and annualized change (ΔBAA/yr, T0->T1). Outcomes were: MRI markers at T2; cognitive performance at T2; and incident stroke (all-type, ischemic) over a median 10-year follow-up. Multivariable linear models were used for MRI and cognition, and Cox for clinical events.

Results: Higher BAA at T0 was associated with poorer MRI profiles at T2, worse cognitive metrics, and higher risk of incident stroke (HR/SD: 1.41, 95%CI: [1.38-1.45]). Improving BAA was associated with more favorable MRI profiles at T2: lower white matter hyperintensity volume (Beta/SD: -0.13 (SE:0.03), $p<0.001$), better white-matter diffusion metrics, and smaller ventricular volume (Beta/SD: -0.08 (SE:0.02), $p=0.002$); reduced risk of any stroke (HR/SD: 0.77 [0.61-0.97]), and ischemic stroke (HR/SD: 0.73 [0.56-0.96]). Associations with cognitive metrics at T2 were observed but not significant after adjustment for cardiovascular risk factors, likely reflecting limited power.

Conclusions: BAA and improvement in BAA are associated with lower subsequent risk of stroke and improvements in MRI markers of small vessel disease years later, independent of socioeconomic and vascular risk factors. Taken together, these findings support targeting biological aging as a modifiable pathway to preserve brain health and motivate trials testing whether lowering BAA reduces later-life brain injury and disease.

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