Biological age is increased by stress and restored upon recovery

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Background: In contrast to chronological age, biological age is dynamic and influenced by numerous intrinsic and extrinsic factors. However, the extent to which biological age undergoes reversible changes over relatively short time periods throughout life remains unexplored.

Objective: We sought to understand how biological age fluctuates in response to stressful stimuli and to identify situations in which biological age is transiently increased.

Methods: We leveraged advanced DNA methylation (DNAm) clocks to explore the concept of reversible changes in biological age. Using a combination of mouse models, human clinical samples, and analysis of publicly available human methylation data, we applied several DNAm biomarkers to longitudinally assess biological age changes in response to stressful stimuli and following recovery.

Results: We found that reversible biological age changes can be modeled experimentally using heterochronic parabiosis in mice. This procedure induced a biological age increase that resolved following surgical detachment. We further identified several situations including emergency trauma surgery, pregnancy, and COVID-19 disease, in which a transient, reversible increase in biological age is induced.

Conclusion: Our data indicate that biological age undergoes a rapid increase in response to diverse forms of severe stress. This increase is reversed following recovery from stress. These data highlight a new layer of biological age dynamics that should be considered in future studies. Elevated biological age caused by stress may be an actionable target for future geroprotective interventions.