

Male sex, BMI, smoking and depression all increase biological age

9 February 2021



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A 'biological age' score predicts that being male, overweight, a smoker and having depression all contribute to biological aging, a study published today in *eLife* reports.

Aging can be measured in different ways. While chronological age is measured by date of birth, scientists have developed a range of measurements to determine our biological age. These include measuring the length of telomeres (little caps on the end of our chromosomes that shorten as we grow older), chemical changes to our DNA (epigenetics), and changes to the proteins and metabolites in our bodies (proteomic and metabolomic measures).

Although studies have linked these individual measurements to physical and mental health, it is not known whether they influence each other—or whether they have a cumulative effect on our overall well being as we age. This new research is the first to combine these individual measurements of biological age and show how they link with mental and physical health.

"To develop a better understanding of the

mechanisms underlying biological aging, we wanted to examine how indicators of biological aging relate to each other, how they link to determinants of physical and mental health, and whether a combined biological clock, made up of all age indicators is a better predictor of health," explains lead author Rick Jansen, Assistant Professor at the Department of Psychiatry, Amsterdam UMC, the Netherlands.

The team used blood samples from nearly 3,000 people taking part in the Netherlands Study of Depression and Anxiety. They applied computer modeling to create individual biological aging indicators based on five commonly used measurements: telomere length, epigenetics, gene levels, metabolites and proteomics. The five indicators were then linked back to different factors such as sex, lifestyle factors and known physical and mental disorders such as depression.

Of the five biological aging indicators, only three were found to significantly interact in individuals, such that an increase in one indicator also paralleled an increase in the other. There were many overlapping and distinct links between particular aging indicators and specific lifestyle factors or diseases. But being male, having a high body mass index (BMI), smoking and having metabolic syndrome were most consistently linked with more advanced biological aging.

The team also confirmed that depression was linked to more advanced aging measured by epigenetics, gene levels and proteomics. This suggests that biological aging is linked to both mental and physical health.

When they combined all five measures into a composite score of biological age, they found more and stronger associations for the composite score than for each individual biological aging indicator. This composite score had greater associations with BMI, sex, smoking, depression severity and



metabolic syndrome, highlighting the interplay between different systems on cumulative biological aging.

"Our work suggests that biological aging indicators largely track distinct, but partially overlapping, aspects of the aging process," concludes senior author Brenda Penninx, Professor of Psychiatric Epidemiology at the Department of Psychiatry, Amsterdam UMC. "Taken together, our findings contribute to the understanding and identification of biological age determinants—important for the development of outcomes for clinical and population-based research."

More information: Rick Jansen et al, An integrative study of five biological clocks in somatic and mental health, *eLife* (2021). DOI: 10.7554/eLife.59479

Provided by eLife

APA citation: Male sex, BMI, smoking and depression all increase biological age (2021, February 9) retrieved 1 May 2021 from https://medicalxpress.com/news/2021-02-male-sex-bmi-depression-biological.html

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