Shorter white blood cell telomeres linked to higher dementia risk

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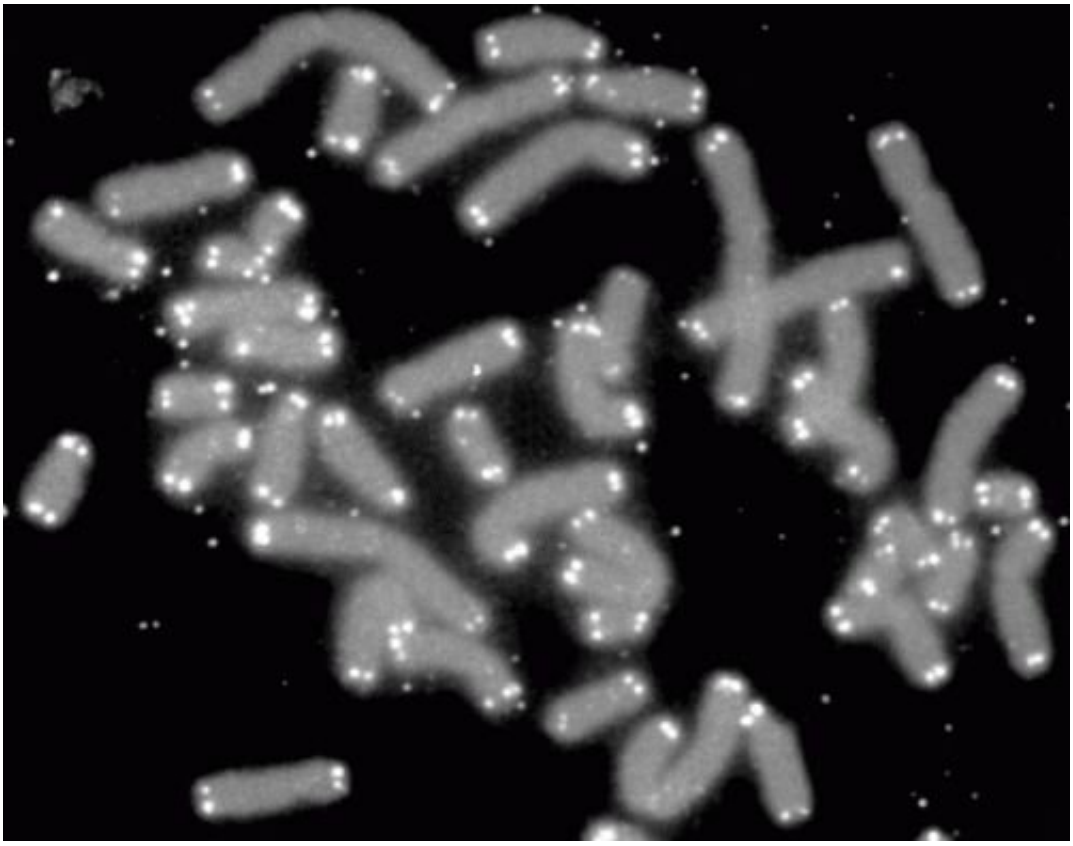

Human chromosomes (grey) capped by telomeres (white). Credit: PD-NASA; PD-USGOV-NASA

Shorter telomeres on the ends of white blood cell chromosomes may signal a heightened dementia risk, suggest the results of a large, long-term study published online in the journal *General Psychiatry*.

They are associated with smaller total and white matter brain volume, which helps the body process information, and may be a predictor of future brain health, say the researchers.

A telomere–the equivalent of a shoelace cap—is intended to prevent the loss of coded DNA by a chromosome fraying or unraveling when it replicates.

Each time a cell divides, chromosomes replicate, and telomeres shorten slightly, so telomeres have emerged as a promising marker for cellular aging and the risk of age-related diseases, note the researchers. But studies looking at telomere length and brain health are few and far between.

To explore this further, they drew on data from the UK Biobank to look at potential associations between the telomere length of leucocytes (white blood cells) and the risk of dementia, including Alzheimer's disease and vascular dementia, and total and regional brain volumes.

The UK Biobank is a large biomedical database containing in-depth genetic and health information for around half a million people in the UK who were enrolled between 2006 and 2010.

Leucocyte telomere length was measured by analyzing blood samples taken at enrollment. These data were available for 439,961 people aged 37 to 73 at the time (average age 56).

During an average monitoring period of nearly 12 years, 1,551 (0.4%) participants were diagnosed with Alzheimer's disease; 767 (0.2%) with vascular dementia; and 5,820 (1.3%) with other type of dementia.

Analysis of the data revealed a significant association between leucocyte telomere length and subsequent risk of dementia.

After accounting for sex and age, participants with the shortest leucocyte telomeres were 14% more likely to be diagnosed with dementia and 28% more likely to be diagnosed with Alzheimer's disease than those with the longest leucocyte telomeres.

The risk of vascular dementia was also increased (18%), although this wasn't statistically significant.

Brain structure was visualized on MRI full body scans for 38,740 participants in 2014. This revealed a linear association between shorter leucocyte telomeres and smaller total brain volume, white matter, as well as brain structures including the hippocampus (involved in learning and memory), the thalamus (sensory processing center), and the nucleus accumbens (the pleasure center).

This is an observational study, and as such, can't establish cause. The researchers also highlight several limitations: telomere length was measured only once so it was impossible to find out whether changes over time might have affected the chances of dementia, added to which telomere length was measured only in leucocytes.

Measurement of telomere length in glial cells (non-neuronal cells in the central nervous system) might have been even more informative, they suggest, but these data weren't available from the UK Biobank.

And dementia diagnoses were obtained only from electronic health records, which may not have been up to date and may not have mentioned milder forms.

Nevertheless, the researchers conclude, "We found that leucocyte telomere length acts as an aging biomarker associated with the risk of dementia. Furthermore, we also observed linear associations of leucocyte telomere length with total and regional brain structure.

"These findings highlight telomere length as a potential biomarker of brain health."

More information: Zhi Cao et al, Leucocyte telomere length, brain volume and risk of dementia: a prospective cohort study, *General Psychiatry* (2023). DOI: 10.1136/gpsych-2023-101120

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