In Nine Human Organ Systems the Genetic Architecture of Biological Age

A team of researchers used a large dataset consisting of participants of European ancestry from the United Kingdom (U.K.) Biobank to explore the genetic underpinnings of the biological age gap or BAG, a comprehensive human aging marker, across nine organ systems.

Study

In the present study, the researchers aimed to investigate the genetic architecture of BAG in nine organ systems using a U.K. Biobank multimodal dataset of over 377,000 participants of European ancestry.

Previously, the same team of researchers had used a genome-wide association study and magnetic resonance imaging to determine the genetic architecture of BAG in the brain. Here, they expanded that work by examining the underlying genetic architecture of BAG across nine organ systems: the cardiovascular, optic, immune, hepatic, metabolic, renal, pulmonary, and musculoskeletal systems.

The researchers hypothesized that the underlying genetic architecture of BAGs would be specific to each organ system but interconnected across the organ systems. To explore this hypothesis, they first performed a genome-wide association study and a genetic correlation and heritability analysis partitioned at the gene level for 154,774 of the U.K.

The multimodal data used for the study also included physiological and physical measurements and phenotypes derived from magnetic resonance imaging data and various other measurements such as blood pressure, pulse rate, blood biomarkers related to the liver, hematology variables, levels of C-reactive protein, lung function measurements, vitamin D levels, and electrolyte regulation and glomerular filtration biomarkers.

The genome-wide association study also included one cognitive variable and six lifestyle factors. The lifestyle factors included coffee, tea, and fresh fruit consumption, sleep duration, body weight, and time spent outdoors, while the cognitive variable included in the analysis was reaction time.

The single nucleotide polymorphism (SNP)-based heritability was estimated, followed by the annotation of the mapped genes and genomic loci associated with BAGs for each organ system. These SNPs were further analyzed for phenome-wide inter-organ connections and organ specificity associations.

For the remaining 222,254 participants, a Mendelian randomization analysis was also conducted to explore potential causality between the BAGs, modifiable lifestyle factors, and chronic diseases such as diabetes and Alzheimer's.

Findings

The results showed that the genetic architecture of the BAGs for the nine organ systems was organ-specific but also exerted inter-organ cross-talk through pleiotropic connections with other organ systems. Furthermore, the genetic and phenotypic correlations between the BAGs of the nine organ systems mirrored each other.

The results from the Mendelian randomization also revealed potential causal associations between the nine BAGs, lifestyle factors such as sleep duration and body weight, and chronic diseases such as diabetes and Alzheimer's disease.

Given that the brain regulates numerous physiological processes and is involved in maintaining homeostasis, the researchers believe that the interconnectedness between the brain and the clinical traits of other organ systems was not surprising. Neither was the finding that various other organ systems exhibited enrichment of metabolic traits.

The musculoskeletal and hepatic BAGs exhibited a bidirectional relationship, which was supported by findings from previous research on the impact of metabolic health and liver function on musculoskeletal health. Moreover, this inter-organ connection could also explain the role of musculoskeletal disorders such as muscle wasting, sarcopenia, and osteoporosis in dysregulating liver metabolism and causing non-alcoholic fatty liver disease.

Conclusion

To summarize, the study analyzed the genetic underpinnings of biological age gaps for nine organ systems and found that each organ system had specific genetic variants associated with the BAGs but were also connected through pleiotropic mechanisms. The findings revealed that examining humans through a multiorgan perspective and considering the impact of lifestyle factors on these inter-organ connections could help better understand complex diseases and design more holistic treatment approaches.

Source:

https://www.news-medical.net/news/20240702/No-organ-is-an-island-Genetic-study-shows-unique-but-interconnected-aging-markers.aspx