The genomic clock: exploring the relationship between telomere length and mental disorders

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In the realm of neurology and cellular aging, a compelling nexus is being drawn between mental disorders and the intricate clockwork of our genetic machinery, specifically telomere length (TL) [1–3]. This bond hints at an unexpected interplay between mental health and aging, promising insights that could reshape our understanding of both arenas.

Telomeres, the protective caps on our chromosomes, are increasingly being recognized as vital indicators of cellular aging [4, 5]. Telomeres are specialized DNA-protein structures located at the ends of eukaryotic chromosomes. Their main function is to maintain chromosome stability and integrity, and their length typically ranges between 5-15KB. Due to the loss of a section of the telomere sequence after each cell division, telomeres shorten. While largely genetically determined, TL is also influenced by age, lifestyle factors such as smoking, diet, environmental conditions, and stress, inflammation, and oxidative stress [6–8]. When telomeres become exceedingly short, cells stop proliferating, triggering signals of cellular aging and DNA damage, activating the DNA damage response pathway, leading eventually to cellular apoptosis, thereby affecting cell lifespan [9].

Yet, what’s particularly fascinating is the mounting evidence suggesting a linkage between shortened TL and common mental disorders like depression (DE), major depressive disorder (MDD), schizophrenia (SCZ), and manic episode (ME). Studies have shown that patients with mental disorders are more susceptible to aging-related diseases such as cardiovascular diseases, dementia, and strokes [10–12]. With increasing age, the prevalence of these diseases surges dramatically. Accelerated cellular aging might play a pivotal role in the connection between mental diseases and physical health [13]. A cursory glance at global health data reveals the gravity of these ailments. For instance, over 3 billion people suffer from DE, according to the World Health Organization [14]. If these disorders do indeed influence TL and consequently, the pace of cellular aging, the ramifications are substantial.

Underlying these disorders are complex mechanisms, many of which—such as inflammation, oxidative stress, and the hypothalamic-pituitary-adrenal axis dysregulation in DE—are themselves implicated in accelerated telomere attrition [15, 16]. The resultant scenario paints a vivid picture: mental disorders might not only wreak havoc on the mind but could simultaneously set the stage for accelerated aging and related health complications.

However, the path to deciphering this puzzle isn’t without obstacles. As with many groundbreaking areas of research, the results have been mixed. While numerous studies document shortened TL in patients with mental disorders, others contrastingly report elongated TL or no association at all. Such inconsistencies underscore the multifaceted nature of the subject, with confounders ranging from demographic variables to methodological differences.

Herein lies the promise of mendelian randomization (MR) [17–19]. By leveraging the innate randomness of genetic variations, MR offers a method that potentially sidesteps the pitfalls of confounding variables and reverse causation. Using single nucleotide polymorphisms as instrumental variables, MR might provide clearer insights into whether the observed links between mental disorders and TL are indeed causal.

In conclusion, the emerging body of evidence sketching a relationship between mental disorders and telomere length is an exciting frontier in medical research. While challenges abound, methodologies like MR are propelling the scientific community closer to unraveling the intricacies of this association. The eventual revelations could reshape therapeutic strategies, emphasizing holistic approaches that address both mental well-being and cellular aging. As we continue down this investigative path, the intertwined narratives of mind and cell promise to offer profound insights into the essence of human health and longevity.

References

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Competing interests
The authors declare no conflicts of interest.

Abbreviations
TL, telomere length; DE, depression; MDD, major depressive disorder; SCZ, schizophrenia; ME, manic episode; MR, mendelian randomization.

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