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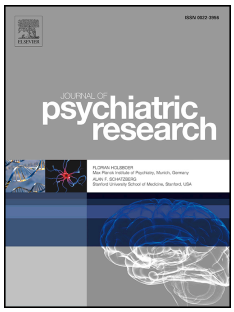

Polygenic risk score of shorter telomere length and risk of depression and anxiety in women

Shun-Chiao Chang, Jennifer Prescott, Immaculata De Vivo, Peter Kraft, Olivia I. Okereke

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ABSTRACT

Prior studies have reported significant cross-sectional associations between depression or anxiety and shorter telomere lengths, but the temporality of associations is uncertain. Little is known regarding whether shorter telomere length is related to risk of developing depression or anxiety. In this study, using the genetic tool of polygenic risk score (PRS), we evaluated the association between genetic predisposition to shorter telomere length and the risks of lifetime clinically significant depression (defined by self-reported clinician/physician diagnosis, antidepressant use, and/or presence of severe depressive symptoms) and of clinically meaningful anxiety symptoms among 17,693 female participants of European ancestry. The weighted PRS of telomere lengths (TLs) combined the dosage of nine alleles that were significantly associated with inter-individual variation in TLs in published genome-wide association studies. Higher score of PRS, corresponding to *shorter* TL in the literature, was significantly associated with shorter relative TLs (p=0.008). However, higher PRS was not associated with the lifetime risk of either depression or anxiety. Furthermore, higher PRS was not associated with long-term patterns of depressive symptom trajectories or specifically with later-life onset of depression or anxiety. In summary, this study did not observe a significant association between genetic predisposition to shorter telomere length and risk of depression and anxiety in a large sample of mid-life and older white women. However, these genetic variants jointly account for a limited proportion of interpersonal variation in leukocyte telomere length. Future studies will need to incorporate more genetic variants to improve the accuracy of predicted power, as such data become available.