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Non-dynamic association of Depressive and Anxiety Disorders with Leukocyte Telomere Length?

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We applaud the attempt of Verhoeven and colleagues (1) to examine the relationship over time between depression/anxiety and leukocyte telomere length (LTL) shortening. We propose, however, that the absence of a relationship in their data may be due to measurement error. For the following reasons, measurement precision in their study was low relative to the effect that was assessed, i.e. depression/anxiety-related variation in the LTL shortening slope which was on average 13.3 base pairs (bp)/year:

i. The authors reported that over 6 years, 26% of participants showed LTL lengthening, which should not be expected for low measurement error. We showed that LTL lengthening is primarily an artifact of measurement error, especially for short follow-ups such as six years (2).

ii. Verhoeven et al. measured LTL using qPCR, reporting inter-assay coefficients of variation (CVs) of 4.6% at baseline and 3.0% at follow-up of presumably the T/S ratio (the telomere product T/the single gene product S). Presuming an overall CV of 3.8 % (mean of 4.6% and 3.0%), and a mean LTL of about 5,400 bp (see their Figure 1), the standard deviation (SD) of replicate measurements would amount to about 205 bp. That is more than 2.5 fold higher than the average LTL shortening (13.3 bp/year × 6 years = 79.8 bp) in their study.

iii. Verhoeven et al. reported r=0.48 for the association between baseline and follow-up LTL, which is considerably lower than correlations of 0.91–0.96 between baseline and follow-up LTLs over ~ 12 years reported elsewhere (3).

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iv. The authors reported r=−0.72 between baseline LTL and LTL change. However, correlations between baseline LTL and LTL change largely reflect regression to the mean (4), a phenomenon exacerbated by measurement error.

We therefore suggest reexamination of the LTL-depression/anxiety nexus in studies with more precise LTL measurements and longer follow-up periods (2, 5). Given the reported cross-sectional LTL-depression/anxiety association, studying LTL in birth cohorts would be advantageous, since a principal determinant of LTL throughout life is LTL at birth (6).

REFERENCES

1. Verhoeven JE, van Oppen P, Révész D, et al. Depressive and anxiety disorders showing robust, but non-dynamic, 6-year longitudinal association with short leukocyte telomere length. Am J Psychiatry. 2016; 173(6):617–624. [PubMed: 26940806]
2. Steenstrup T, Hjelmborg JV, Kark JD, et al. The telomere lengthening conundrum--artifact or biology? Nucleic Acids Res. 2013; 41(13):e131. [PubMed: 23671336]
3. Benetos A, Kark JD, Susser E, et al. Tracking and fixed ranking of leukocyte telomere length across the adult life course. Aging Cell. 2013; 12(4):615–621. [PubMed: 23601089]
4. Verhulst S, Aviv A, Benetos A, et al. Do leukocyte telomere length dynamics depend on baseline telomere length? An analysis that corrects for 'regression to the mean'. Eur J Epidemiol. 2013; 28(11):859–866. [PubMed: 23990212]
5. Verhurlst S, Susser E, Factor-Litvak PR, et al. Reliability and validity of telomere length measurement. Int J Epidemiol. In press.
6. Factor-Litvak P, Susser E, Kezios K, et al. Leukocyte Telomere Length in Newborns: Implications for the Role of Telomeres in Human Disease. Pediatrics. 2016; 137(4) pii: e20153927.