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Pessimistic orientation in relation to telomere length in older men: The VA Normative Aging Study

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Summary
Background: Recent research suggests pessimistic orientation is associated with shorter leukocyte telomere length (LTL). However, this is the first study to look not only at effects of pessimistic orientation on average LTL at multiple time points, but also at effects on the rate of change in LTL over time.
Methods: Participants were older men from the VA Normative Aging Study ($n = 490$). The life orientation test (LOT) was used to measure optimistic and pessimistic orientations at study baseline, and relative LTL by telomere to single copy gene ratio (T:S ratio) was obtained repeatedly over the course of the study (1999—2008). A total of 1010 observations were included in the analysis. Linear mixed effect models with a random subject intercept were used to estimate associations.

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Results: Higher pessimistic orientation scores were associated with shorter average LTL (percent difference by 1-SD increase in pessimistic orientation (95% CI): −3.08 (−5.62, −0.46)), and the finding was maintained after adjusting for the higher likelihood that healthier individuals return for follow-up visits (−3.44 (−5.95, −0.86)). However, pessimistic orientation scores were not associated with rate of change in LTL over time. No associations were found between overall optimism and optimistic orientation subscale scores and LTL.
Conclusion: Higher pessimistic orientation scores were associated with shorter LTL in older men. While there was no evidence that pessimistic orientation was associated with rate of change in LTL over time, higher levels of pessimistic orientation were associated with shorter LTL at baseline and this association persisted over time.

1. Introduction

Telomeres are repetitive structures at the end of eukaryotic chromosomes which protect chromosome ends from deterioration (Wong and Collins, 2001). Numerous studies have documented the gradual shortening of telomere length with increasing age (Slagboom et al., 1994). Additional work has also found shorter telomere length in patients suffering from coronary heart disease compared to controls (Brouilette et al., 2007), in diabetic patients (Sampson et al., 2006) and in individuals with cardiovascular risk factors such as obesity, smoking (Nordfjäll et al., 2008), as well as psychological stress (Epel et al., 2004). Thus, investigators have suggested that telomere shortening is a marker of cellular aging that may be accelerated by chronic stress and may indicate risk of chronic disease development and premature mortality. A growing body of research has identified links between psychological factors (e.g., stress, pessimistic orientation, depression) and incident disease, disease progression, and mortality, but the mechanisms underlying these associations remain to be determined. Building on the rapidly emerging science on telomeres, recent work has begun to consider whether psychological functioning is associated with rate of cellular aging. For example, one cross-sectional study found higher levels of pessimistic orientation were associated with shorter telomere length (O'Donovan et al., 2009).

Pessimism is a cognitive orientation (personality trait) characterized by the general expectation that outcomes will be negative (Chang et al., 1997; Roy et al., 2010). High levels of pessimistic orientation are associated with greater psychological distress; for example, pessimistic orientation is a strong predictor of depressive symptoms even after accounting for other psychological factors (Chang et al., 1997). More recent work has found pessimistic orientation is also associated with physical health outcomes, with studies demonstrating higher levels of pessimistic orientation to be associated with increased risk of heart disease and stroke, and reduced cancer survival (Kubzansky et al., 2001; Nabi et al., 2010; Novotny et al., 2010).

A number of mechanisms might explain the recently observed association between pessimistic orientation and telomere shortening. Pessimistic orientation may induce negative reactions to stressful events thereby increasing the potentially toxic effects of stress-related neuroendocrine activation. Chronic neuroendocrine activation can increase oxidative stress, which induces telomeric DNA damage in the telomere sequence (TTAGGG) (Kawanishi and Oikawa, 2004). Telomeric DNA is synthesized by the enzyme telomerase. Thus, this DNA damage may induce the slowing down of existing telomerase enzymatic activity needed to synthesize telomoric DNA and thus accelerate telomere shortening (von Zglinicki, 2002).

Pessimistic orientation may also affect telomere shortening through behavioral pathways such as increasing the likelihood of smoking or being sedentary. These unhealthy behaviors have been demonstrated to have highly significant effects on biochemical processes (i.e., oxidative stress and inflammation) that can alter telomere dynamics (Nordfjäll et al., 2008). Such damaging effects lead to shorter telomere length and more rapid age-dependent telomere attrition rate.

Only one study to date has examined LTL in relation to pessimistic orientation (O'Donovan et al., 2009); other studies have linked pessimistic orientation to factors associated with telomere length, including increased risk of inflammation (O'Donovan et al., 2009), depression (Isaacowitz and Seligman, 2001), and premature mortality (Brummett et al., 2006). O'Donovan et al. (2009) suggested the association with LTL was stronger in relation to the pessimistic orientation subscale as compared with either the optimistic orientation subscale or the overall optimism score. This finding is consistent with prior work we and others have done showing clearer effects of a pessimistic versus optimistic orientation on measures of inflammation and endothelial function as well as other objective indicators of health (Milam et al., 2004; Ikeda et al., 2011). However, the initial study of pessimistic orientation and telomere length by O'Donovan et al. (2009), employed a cross-sectional design, and was conducted among only 36 healthy post-menopausal women.

To gain greater insight into the relationship between pessimistic orientation and LTL and consider whether and how pessimism may influence rate of LTL change, we examine the association of a pessimistic or optimistic orientation with change in telomere length over time in the VA Normative Aging Study (NAS). The life orientation test (LOT) was used to measure pessimistic or optimistic orientation in the present study. In prior work, it has exhibited significant reliability with a test–retest reliability reported to be 0.79 over a 4-week period and 0.69 over a 3-year period (Scheier and Carver, 1985), supporting the notion that dispositional optimism is relatively stable across time.

We considered a range of covariates which could be associated with the level of pessimistic or optimistic orientation scores in our sample including baseline (time at first visit when