Pain is Associated with Short Leukocyte Telomere Length in Women with Fibromyalgia

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Background

• Telomeres cap the ends of chromosomes and protect the ends from degradation, recombination and end-to-end fusion (Figure 1). During mitosis, the telomere is not fully replicated thus telomeres shorten with age (1).
• Telomere length can also be influenced by stressors independent of chronological age and is consequently thought to represent an individual’s cumulative exposure to and ability to cope with stress (1-2).
• Telomere length is predictive of the incidence of age-related diseases and mortality (e.g. 3-5).
• Several lines of evidence suggest that telomeres might be shortened in individuals with chronic pain:
  - Psychosocial factors (e.g., depression, anxiety, obesity, trauma) associated with shortened telomeres are all commonly observed in chronic pain populations.
  - Chronic widespread pain has been associated with lifetime comorbidity with age-related diseases and early mortality (6-8).
  - Studies of brain morphology in fibromyalgia have found decreases in gray matter volume consistent with the notion of premature aging (9).
  - A preliminary study in osteoarthritis found an association between telomere shortening and having high levels of both stress and pain (10).

Methods

• Ancillary pilot study to two parent projects of the CPFRC’s, Department of Defense Registry and Web-intervention study by the Avera Research Institute.
• Participants completed questionnaires including:
  - Brief Pain Inventory-Short Form (BPI-SF) (11).
  - State-Trait Personality Inventory (STPI) (14).
  - Perceived Stress Scale (PSS) (13).
  - Center for Epidemiologic Studies Depression (CES-D) scale. A cut-off score for possible depression of ≥ 16 was used (12).
  - Telomere length in women with fibromyalgia and healthy female controls.
  - Participants were divided into two groups: fibromyalgia patients and healthy controls.

Results

• We found that age-adjusted telomere length did not differ between fibromyalgia and controls; however, pain was associated with shorter telomere length in fibromyalgia even after controlling for age (r = -0.27, p = 0.039).
• Fibromyalgia patients with higher levels of pain had shorter telomeres than those with lower levels of pain (age adjusted: p = 0.024). This was not true for depressed versus non-depressed patients (Figure 2).
• When pain and depression were combined, the high pain/high depression group had an age-adjusted telomere length ~ 265 base pairs shorter than the low pain/low depression group (p = 0.043). This difference represents approximately 6% years of chronological aging (Figure 3).
• QST revealed an association between telomere length and pressure pain threshold, as well as sensitivity to pressure pain (e.g., high: r = 0.82, p = 0.002) (Figure 4).
• VBM analyses revealed an association between telomere length and brain gray matter volume in pain processing areas of the brain: left primary somatosensory cortex (r = 0.725), left middle frontal gyrus (r = 0.858), and right precuneus (r = 0.661). Patients with shorter telomeres tended to have less gray matter volume in pain processing regions of the brain (Figure 5).

Conclusions

• Our data suggest that pain in fibromyalgia is associated with shortened telomere length. These effects were largely independent of other factors commonly associated with telomere shortening.
• Short telomere length was directly related to evoked pressure pain threshold and sensitivity, as well as altered brain structure.
• Although these findings are preliminary, they suggest that chronic pain may have unique contributions to cellular aging that require further study.

References

1) Blackburn EH: Telomeres and telomerase: their mechanisms of action & the effects of altering their functions. FASEB J 19:591-600, 2005