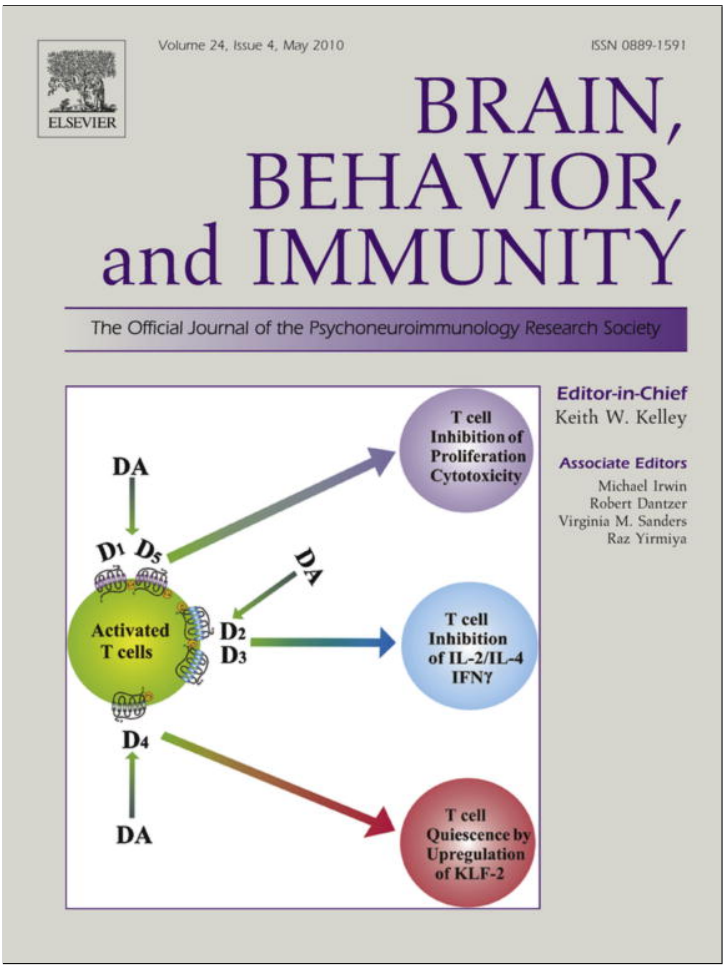

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Brief Commentary

Psychological stress, telomeres, and telomerase

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Telomeres and telomerase, hot topics in the aging literature in recent years, will undoubtedly receive even more attention following the award of the 2009 Nobel Prize in Medicine "for the discovery of how chromosomes are protected by telomeres and the enzyme telomerase" to Elizabeth Blackburn, her former student Carol Greider, and Jack Szostak. The paper by Epel and colleagues in this BBI issue (Epel et al., in press) represents the latest elegant behavioral work on this topic from the investigators who published the first paper linking stress and telomere length (Epel et al., 2004), an observation that has now been confirmed by several laboratories (Damjanovic et al., 2007; Parks et al., 2009).

In this report they replicate their original finding of lower basal telomerase activity associated with chronic stress, and they also show that an acute stressor boosts telomerase reactivity (Epel et al., in press). Furthermore, they provide evidence that the increased telomerase reactivity is independent of changes in numbers or percentages of monocytes, lymphocytes, and specific T-cell types, and they show that two facets of the stress response, the degree of threat and the magnitude of the cortisol response, are both associated with larger increases in telomerase activity.

These studies of stress and cell aging are consequential for several reasons. First, these cell aging measures have clinical significance for health: a growing literature has linked shorter telomeres and lower levels of the enzyme telomerase with adverse health behaviors, aging, age-related diseases, and mortality (Epel et al., in press).

The evidence linking psychological stress and cell aging is also important because it signposts new pathways on the road from stress to mortality—valuable new information about the ways that stress kills. Psychological stress can boost inflammation (Kiecolt-Glaser et al., 2003) as well as oxidative stress (Epel et al., 2004), and both inflammation and oxidative stress accelerate telomere attrition (Aviv, 2004). Inflammation triggers T-cell proliferation and enhances the leukocyte turnover rate, one known cause of telomere shortening, while oxidative stress accelerates telomere attrition by promoting telomere erosion during cellular replication (Aviv, 2004).

Psychological stress impacts telomere length through another route as well. The enhanced replication of memory $CD8^+$ T-cells induced by cytomegalovirus (CMV) and/or Epstein–Barr virus (EBV) antigens can exhaust virus-specific T-cells. These two herpesviruses latently infect their host; their periodic reactivation provides a source of viral antigens that stimulates a cellular immune response to viral proteins. Chronic exposure to high CMV and/or EBV antigen levels can promote progressive telomere shortening in antigen-specific T-cells; sustained stimulation of cell division in virus-specific T-cells has been associated with reductions in telomere length and telomerase activity in the $CD8^+$ T-cells among even normal healthy subjects (Pawelec et al., 2009; van Baarle et al., 2008).

Psychological stress clearly drives replication of several herpesviruses including CMV and EBV by impairing the ability of the cellular immune response to control viral latency (Glaser and Kiecolt-Glaser, 1994). EBV and CMV infections are ubiquitous in adults, e.g., greater than 90% of adults are seropositive for EBV (Glaser and Kiecolt-Glaser, 1994), and thus the risk associated with chronic stress-related reactivation is not trivial. Considerable circumstantial evidence has implicated CMV as a player in immunosenescence as well as mortality (Pawelec et al., 2009). Chronic psychological stress clearly enhances CMV and EBV replication (Glaser and Kiecolt-Glaser, 1994), and through this route could simultaneously promote reductions in telomere length and telomerase activity.

The original observation from Epel et al. linking chronic stress to telomere length and telomerase activity will be a central touchstone for psychoneuroimmunology researchers for the foreseeable future (Epel et al., 2004). Their newest work expands the mechanistic base and tells us useful things about the links between psychological and biological facets of the stress response and telomerase activity.

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