The Association of PTSD and Deployment with Telomere Erosion

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Human telomeres are regions of tandem TTAGGG repeats at chromosomal ends that protect chromosomes from degradation, fusion and recombination. Over time, because of each cell division, the telomere ends become shorter. Thus, DNA telomere length (TL) has been considered a cellular marker for age-related diseases and mortality. One recent line of research suggests that TL has an important association with indicators of differential aging due to stress. Therefore TL may serve as a biomarker of lifetime stress and provide leverage for studying the association with stress and health even among the generally healthy and young.

Shorter telomeres have also been linked to military deployment and, in two studies, to posttraumatic stress disorder (PTSD). As such there is great interest in examining to what extent TL may provide new insight into the negative health related outcomes of both PTSD and deployment. We utilize a subsample of the Pre- and Post- Deployment Study (PPDS) of the Army Study to Asses Risk and Resilience in Servicemembers (Army STARRS). This subsample examines 176 soldiers who at pre-deployment had no PTSD, but post-deployment were diagnosed with PTSD. Those cases were age and deployment stress matched to controls that never had PTSD.

This study extends the literature in several important ways. First, we compare telomere lengths of soldiers who recently developed PTSD compared to similar soldiers and controlling for past experiences. Past examinations of PTSD and TL compared lifetime PTSD cases to matched controls in cross sectional evaluations. Examining, prospectively, recent development of PTSD provides a measure of how tightly TL and PTSD are connected and provides stronger evidence of a causal connection.

Second, we examine changes in TL (or telomere erosion, TE) from pre-deployment to post-deployment among a subset of high deployment stress cases and controls. This will be the first TE study of soldiers. More broadly this study will provide new insight into short duration changes in TL because other longitudinal studies of TE have examined changes over 5, 10, and 20 years. Knowing to the pace telomeres erode will help provide important information for future research on stress and TL.

Third, deployment provides an intense exogenous stressor in adulthood—whereas other TE studies have typically examined early childhood stressors and their influence on later TE. There is some evidence to suggest that TL changes less quickly in adulthood than in childhood. As well stress appears to influence TL of children more the TL of adults. Further, most of these stressors while often powerful may be endogenous to the individual. Although not perfectly exogenous, differential stress exposure given the same general duties may be considered more exogenous. This again provides a more powerful examination of the stress and TL connection.

Fourth, a major limitation to nearly all past TL studies is that they utilize tissues (typically whole blood, leucocyte, or saliva) that contain several different cell types. Because different cell types have different replication rates (and therefore different TL), one confounder of TL work is differential cell distribution for individuals. We address this issue by controlling for cell distributions for our leucocyte sample estimated from DNA methylation on 100 CpG cites which are known to differentiate the different cell types. Not only are we the first to use this method to study TL, but we also examine if changes in cell distributions account for the TE.

Similarly, fourth, most TL studies do not account for the important genetic differences due to ancestry. Since TL is estimated to be approximately 80% heritable accounting for ancestry is vital—but rarely if ever done. Although our sample has been sampled to contain European American

individuals, we also control for five within European American principal components estimated using genome-wide data.

Finally, fifth, TL measurement, like epigenetic measures, may suffer from batch and DNA quality effects but unlike epigenetic work, research on TL has not accounted for these possible confounders. We test the influence of both analysis batch and DNA concentration (a measure of sample quality) to determine the extent these variables influence TL and TE and the relationship of these two outcomes with PTSD and deployment.

In sum using a novel sample of soldiers who recently developed PTSD measured pre and post deployment we will provide new insights into the connection between TL and stress. Further we provide several new methodological innovations, which may help examine some of the discrepancy in the TL literature.

Although results are available from this study I am gaining Army approval to present the results. I expect approval in the next several weeks.