The acute effects of cardiorespiratory exercise on telomere-associated genes and microRNA expression in immune cell subsets.

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ABSTRACT

Telomeres are specialized nucleoprotein structures that protect the ends of linear chromosomes from degradation. Habitual physical activity is positively associated with longer leukocyte telomere length; however the molecular mechanisms underpinning the association are unclear. Human telomerase reverse transcriptase (hTERT) is the rate-limiting component of the telomere extending enzyme telomerase. The effective functioning of the adaptive immune system depends heavily upon the replicative potential of T cells, which is largely determined by telomere length and hTERT expression. Sirtuin 6 (SIRT6) also serves important pro-telomeric functions via an interaction with telomeric chromatin and regulatory roles in genome stabilization and DNA repair.

It is unknown if cardiorespiratory exercise acutely regulates mRNA levels of hTERT, SIRT6 or other telomere-associated genes in white blood cells in general and T cell subsets in particular. Additionally, the exercise-induced regulation of microRNAs (short, non-coding RNA molecules that negatively regulate gene expression) with potential telomeric functions is unknown.

Twenty-three healthy males (mean age=23.96 ±1.49 years) undertook 30min of treadmill running at 80% of previously determined VO_{2peak}. Blood samples were taken before exercise, immediately post-exercise and 60min post-exercise. White blood cells and flow cytometry-sorted T cell subsets were assessed via quantitative polymerase chain reaction for differential regulation of telomeric genes and microRNAs.

Expression levels of hTERT and SIRT6 mRNA were up-regulated following exercise in white blood cells and various T cell subsets (CD4+ naïve, CD4+ memory, CD8+ naïve, and CD8+ memory). Additionally, exercise differentially regulated several genes associated with telomere structure. A total of 56 microRNAs were differentially regulated post-exercise, six of which were investigated for potential telomeric functions. MicroRNAs-186, 636, 15a, and 96 showed significant up-regulation 60min post-exercise. MicroRNAs-186 and 636 showed detectable differential regulation in naïve and memory subsets.

Intense cardiorespiratory exercise differentially regulated a host of telomeric genes in white blood cells and T cell subsets. Furthermore, it resulted in differential regulation of 56 microRNAs, some of which have binding potential to telomeric genes. Importantly, we demonstrated cell type-specific expression patterns in telomeric genes and microRNA. These results could have important implications for T cell-dependent immune functions and telomere homeostasis.